Clinical trial results:
Phase 1/2 Study of PF-06463922 (an ALK/ROS1 Tyrosine Kinase Inhibitor) in Patients With Advanced Non-Small Cell Lung Cancer Harboring Specific Molecular Alterations

Summary

EudraCT number	2013-002620-17
Trial protocol	ES DE GB IT BE
Global end of trial date	24 May 2023

Results information

Result version number	v2 (current)
This version publication date	08 June 2024
First version publication date	24 March 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	B7461001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01970865
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	31 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of Phase 1 of the study was to assess safety and tolerability of PF-06463922 as a single agent at increasing dose levels in participants with advanced anaplastic lymphoma kinase (ALK) positive or advanced ROS1-positive non-small cell lung cancer (NSCLC) in order to estimate the Maximum Tolerated Dose (MTD) and select the Recommended Phase 2 Dose (RP2D). Primary objective of Phase 2 of the study was to evaluate overall (intra- and extra-cranial) and intra-cranial anti-tumor activity of single-agent PF-06463922 at RP2D in participants with advanced ALK-positive NSCLC and advanced ROS1-positive NSCLC.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of participants.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 January 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 26
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Hong Kong: 2
Country: Number of subjects enrolled	Italy: 36
Country: Number of subjects enrolled	Japan: 42
Country: Number of subjects enrolled	Korea, Republic of: 9
Country: Number of subjects enrolled	Singapore: 29
Country: Number of subjects enrolled	Spain: 31
Country: Number of subjects enrolled	Switzerland: 7
Country: Number of subjects enrolled	Taiwan: 11
Country: Number of subjects enrolled	United States: 132
Worldwide total number of subjects	364
EEA total number of subjects	99

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)	295
From 65 to 84 years	68
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 364 participants were enrolled in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	10 mg QD (Phase 1)

Arm description:

PF-06463922 10 mg was orally given once daily (QD) on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 10 mg was administered QD with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	25 mg QD (Phase 1)

Arm description:

PF-06463922 25 mg was orally given QD in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal. Midazolam 2 mg was orally given QD on Day -7 and Cycle 1 Day 15.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 25 mg was administered QD with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Investigational medicinal product name	Midazolam
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Syrup
Routes of administration	Oral use

Dosage and administration details:

Midazolam 2 mg was administered alone on Day -7 and concurrently with PF-06463922 on Cycle 1 Day 15.

Arm title	50 mg QD (Phase 1)

Arm description:

PF-06463922 50 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 50 mg was administered QD with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	75 mg QD (Phase 1)

Arm description:

PF-06463922 75 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 75 mg was administered QD with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	100 mg QD (Phase 1)

Arm description:

PF-06463922 100 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 100 mg was administered BID with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	150 mg QD (Phase 1)

Arm description:

PF-06463922 150 mg was orally given QD in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal. Midazolam 2 mg was orally given QD on Day -7 and Cycle 1 Day 15.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 150 mg was administered QD with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Investigational medicinal product name	Midazolam
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Syrup
Routes of administration	Oral use

Dosage and administration details:

Midazolam 2 mg was administered alone on Day -7 and concurrently with PF-06463922 on Cycle 1 Day 15.

Arm title	200 mg QD (Phase 1)

Arm description:

PF-06463922 200 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 200 mg was administered QD with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	35 mg BID (Phase 1)

Arm description:

PF-06463922 35 mg was orally given twice daily (BID) on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 35 mg was administered BID with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	75 mg BID (Phase 1)

Arm description:

PF-06463922 75 mg was orally given BID on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 75 mg was administered BID with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	100 mg BID (Phase 1)

Arm description:

PF-06463922 100 mg was orally given BID on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 100 mg was administered BID with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	EXP-1 (Phase 2)

Arm description:

Treatment-naïve participants with advanced ALK-positive NSCLC with or without asymptomatic central nervous system (CNS) metastases were given PF-06463922 100 mg orally QD on Day -7 (only participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 100 mg was administered QD with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	EXP-2 (Phase 2)

Arm description:

Participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after only crizotinib therapy were given PF-06463922 100 mg orally QD on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 100 mg was administered QD with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	EXP-3 (Phase 2)

Arm description:

Participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after crizotinib therapy and 1 or 2 prior regimens of chemotherapy given before or after crizotinib therapy, or participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after 1 ALK inhibitor therapy other than crizotinib with or without any number of prior chemotherapy regimens in any disease setting were given PF-06463922 100 mg orally QD on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental

Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 100 mg was administered QD with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	EXP-4 (Phase 2)

Arm description:

Participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after 2 prior lines of ALK inhibitor therapies were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 100 mg was administered QD with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	EXP-5 (Phase 2)

Arm description:

Participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after 3 prior lines of ALK inhibitor therapies were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for participant scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 100 mg was administered QD with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	EXP-6 (Phase 2)

Arm description:

Participants with advanced ROS1-positive NSCLC who were treatment naïve or had any number of prior cancer therapies with or without asymptomatic CNS metastases were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 100 mg was administered QD with at least 240 mL of water on an empty stomach. No

food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	Japan Lead-In Cohort (LIC)

Arm description:

Few Japanese participants were given PF-06463922 100 mg orally once daily (QD) in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal to evaluate safety of PF-06463922 in Japanese participants, in order to support inclusion of Japanese participants in Phase 2.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06463922 100 mg was administered QD with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Arm title	DDI Substudy

Arm description:

Participants with advanced ALK positive or ROS1-positive NSCLC who were treatment naïve or had any number of prior cancer therapies with or without asymptomatic CNS metastases were administered a single dose of a probe substrate alone on Day -2. Participants were given PF-06463922 100 mg orally QD starting on Cycle1 Day 1 and along with probe substrate on Day 15 Cycle 1.

Arm type	Experimental
Investigational medicinal product name	PF-06463922
Investigational medicinal product code	
Other name	Lorlatinib
Pharmaceutical forms	Tablet
Routes of administration	Intratumoral use, Oral use

Dosage and administration details:

PF-06463922 100 mg was administered QD with at least 240 mL of water on an empty stomach. No food or liquids other than water were consumed for 2 hours before and 2 hours following each dose.

Number of subjects in period 1	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)
Started	3	3	3
Completed	0	0	0
Not completed	3	3	3
Death	3	2	3
Study terminated by sponsor	-	-	-
Unspecified	-	1	-
Subject refused further follow-up	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	75 mg QD (Phase 1)	100 mg QD (Phase 1)	150 mg QD (Phase 1)

Started	12	17	3
Completed	2	3	0
Not completed	10	14	3
Death	6	9	3
Study terminated by sponsor	-	-	-
Unspecified	1	1	-
Subject refused further follow-up	2	3	-
Lost to follow-up	1	1	-

Number of subjects in period 1	200 mg QD (Phase 1)	35 mg BID (Phase 1)	75 mg BID (Phase 1)
Started	3	3	3
Completed	0	0	1
Not completed	3	3	2
Death	2	3	2
Study terminated by sponsor	-	-	-
Unspecified	1	-	-
Subject refused further follow-up	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	100 mg BID (Phase 1)	EXP-1 (Phase 2)	EXP-2 (Phase 2)
Started	4	30	27
Completed	2	18	7
Not completed	2	12	20
Death	2	8	13
Study terminated by sponsor	-	-	-
Unspecified	-	2	3
Subject refused further follow-up	-	1	4
Lost to follow-up	-	1	-

Number of subjects in period 1	EXP-3 (Phase 2)	EXP-4 (Phase 2)	EXP-5 (Phase 2)
Started	60	65	46
Completed	18	8	3
Not completed	42	57	43
Death	25	46	37
Study terminated by sponsor	-	1	-
Unspecified	8	2	2
Subject refused further follow-up	7	8	3
Lost to follow-up	2	-	1

Number of subjects in period 1	EXP-6 (Phase 2)	Japan Lead-In Cohort (LIC)	DDI Substudy
Started	47	3	32
Completed	7	2	6
Not completed	40	1	26

Death	22	1	17
Study terminated by sponsor	-	-	-
Unspecified	3	-	2
Subject refused further follow-up	11	-	6
Lost to follow-up	4	-	1

Reporting groups	
Reporting group title	10 mg QD (Phase 1)
Reporting group description:	
PF-06463922 10 mg was orally given once daily (QD) on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	25 mg QD (Phase 1)
Reporting group description:	
PF-06463922 25 mg was orally given QD in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal. Midazolam 2 mg was orally given QD on Day -7 and Cycle 1 Day 15.	
Reporting group title	50 mg QD (Phase 1)
Reporting group description:	
PF-06463922 50 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	75 mg QD (Phase 1)
Reporting group description:	
PF-06463922 75 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	100 mg QD (Phase 1)
Reporting group description:	
PF-06463922 100 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	150 mg QD (Phase 1)
Reporting group description:	
PF-06463922 150 mg was orally given QD in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal. Midazolam 2 mg was orally given QD on Day -7 and Cycle 1 Day 15.	
Reporting group title	200 mg QD (Phase 1)
Reporting group description:	
PF-06463922 200 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	35 mg BID (Phase 1)
Reporting group description:	
PF-06463922 35 mg was orally given twice daily (BID) on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	75 mg BID (Phase 1)
Reporting group description:	
PF-06463922 75 mg was orally given BID on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	100 mg BID (Phase 1)
Reporting group description:	
PF-06463922 100 mg was orally given BID on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	EXP-1 (Phase 2)
Reporting group description:	
Treatment-naïve participants with advanced ALK-positive NSCLC with or without asymptomatic central nervous system (CNS) metastases were given PF-06463922 100 mg orally QD on Day -7 (only	

participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	EXP-2 (Phase 2)

Reporting group description:

Participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after only crizotinib therapy were given PF-06463922 100 mg orally QD on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	EXP-3 (Phase 2)

Reporting group description:

Participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after crizotinib therapy and 1 or 2 prior regimens of chemotherapy given before or after crizotinib therapy, or participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after 1 ALK inhibitor therapy other than crizotinib with or without any number of prior chemotherapy regimens in any disease setting were given PF-06463922 100 mg orally QD on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	EXP-4 (Phase 2)

Reporting group description:

Participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after 2 prior lines of ALK inhibitor therapies were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	EXP-5 (Phase 2)

Reporting group description:

Participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after 3 prior lines of ALK inhibitor therapies were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for participant scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	EXP-6 (Phase 2)

Reporting group description:

Participants with advanced ROS1-positive NSCLC who were treatment naïve or had any number of prior cancer therapies with or without asymptomatic CNS metastases were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	Japan Lead-In Cohort (LIC)

Reporting group description:

Few Japanese participants were given PF-06463922 100 mg orally once daily (QD) in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal to evaluate safety of PF-06463922 in Japanese participants, in order to support inclusion of Japanese participants in Phase 2.

Reporting group title	DDI Substudy

Reporting group description:

Participants with advanced ALK positive or ROS1-positive NSCLC who were treatment naïve or had any number of prior cancer therapies with or without asymptomatic CNS metastases were administered a single dose of a probe substrate alone on Day -2. Participants were given PF-06463922 100 mg orally QD starting on Cycle1 Day 1 and along with probe substrate on Day 15 Cycle 1.

Reporting group values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)
Number of subjects	3	3	3
Age Categorical Units: Participants			
<18 years	0	0	0

18-44 years	0	1	0
45-64 years	1	1	3
>=65 years	2	1	0
Sex: Female, Male Units: Participants			
Female	2	0	1
Male	1	3	2
Race/Ethnicity, Customized Units: Subjects			
WHITE	2	2	3
BLACK	1	0	0
ASIAN	0	1	0
OTHER	0	0	0
UNSPECIFIED	0	0	0

Reporting group values	75 mg QD (Phase 1)	100 mg QD (Phase 1)	150 mg QD (Phase 1)
Number of subjects	12	17	3
Age Categorical Units: Participants			
<18 years	0	0	0
18-44 years	5	7	1
45-64 years	6	9	1
>=65 years	1	1	1
Sex: Female, Male Units: Participants			
Female	7	11	2
Male	5	6	1
Race/Ethnicity, Customized Units: Subjects			
WHITE	7	13	2
BLACK	0	0	1
ASIAN	3	2	0
OTHER	0	1	0
UNSPECIFIED	2	1	0

Reporting group values	200 mg QD (Phase 1)	35 mg BID (Phase 1)	75 mg BID (Phase 1)
Number of subjects	3	3	3
Age Categorical Units: Participants			
<18 years	0	0	0
18-44 years	1	0	0
45-64 years	2	2	2
>=65 years	0	1	1
Sex: Female, Male Units: Participants			
Female	2	2	3
Male	1	1	0
Race/Ethnicity, Customized Units: Subjects			
WHITE	2	1	2

BLACK	0	1	0
ASIAN	1	0	0
OTHER	0	0	0
UNSPECIFIED	0	1	1

Reporting group values	100 mg BID (Phase 1)	EXP-1 (Phase 2)	EXP-2 (Phase 2)
Number of subjects	4	30	27
Age Categorical Units: Participants			
<18 years	0	0	0
18-44 years	2	4	5
45-64 years	1	18	13
>=65 years	1	8	9
Sex: Female, Male Units: Participants			
Female	2	13	17
Male	2	17	10
Race/Ethnicity, Customized Units: Subjects			
WHITE	3	10	13
BLACK	0	1	0
ASIAN	0	17	10
OTHER	0	1	2
UNSPECIFIED	1	1	2

Reporting group values	EXP-3 (Phase 2)	EXP-4 (Phase 2)	EXP-5 (Phase 2)
Number of subjects	60	65	46
Age Categorical Units: Participants			
<18 years	0	0	0
18-44 years	14	19	13
45-64 years	34	37	26
>=65 years	12	9	7
Sex: Female, Male Units: Participants			
Female	38	37	25
Male	22	28	21
Race/Ethnicity, Customized Units: Subjects			
WHITE	25	32	27
BLACK	1	0	0
ASIAN	23	23	14
OTHER	1	3	2
UNSPECIFIED	10	7	3

Reporting group values	EXP-6 (Phase 2)	Japan Lead-In Cohort (LIC)	DDI Substudy
Number of subjects	47	3	32
Age Categorical Units: Participants			
<18 years	0	0	0

18-44 years	12	2	5
45-64 years	27	1	20
>=65 years	8	0	7
Sex: Female, Male Units: Participants			
Female	27	2	15
Male	20	1	17
Race/Ethnicity, Customized Units: Subjects			
WHITE	25	0	21
BLACK	1	0	0
ASIAN	16	3	11
OTHER	3	0	0
UNSPECIFIED	2	0	0

Reporting group values	Total		
Number of subjects	364		
Age Categorical Units: Participants			
<18 years	0		
18-44 years	91		
45-64 years	204		
>=65 years	69		
Sex: Female, Male Units: Participants			
Female	206		
Male	158		
Race/Ethnicity, Customized Units: Subjects			
WHITE	190		
BLACK	6		
ASIAN	124		
OTHER	13		
UNSPECIFIED	31		

End points reporting groups

Reporting group title	10 mg QD (Phase 1)
Reporting group description:	
PF-06463922 10 mg was orally given once daily (QD) on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	25 mg QD (Phase 1)
Reporting group description:	
PF-06463922 25 mg was orally given QD in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal. Midazolam 2 mg was orally given QD on Day -7 and Cycle 1 Day 15.	
Reporting group title	50 mg QD (Phase 1)
Reporting group description:	
PF-06463922 50 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	75 mg QD (Phase 1)
Reporting group description:	
PF-06463922 75 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	100 mg QD (Phase 1)
Reporting group description:	
PF-06463922 100 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	150 mg QD (Phase 1)
Reporting group description:	
PF-06463922 150 mg was orally given QD in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal. Midazolam 2 mg was orally given QD on Day -7 and Cycle 1 Day 15.	
Reporting group title	200 mg QD (Phase 1)
Reporting group description:	
PF-06463922 200 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	35 mg BID (Phase 1)
Reporting group description:	
PF-06463922 35 mg was orally given twice daily (BID) on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	75 mg BID (Phase 1)
Reporting group description:	
PF-06463922 75 mg was orally given BID on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	100 mg BID (Phase 1)
Reporting group description:	
PF-06463922 100 mg was orally given BID on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.	
Reporting group title	EXP-1 (Phase 2)
Reporting group description:	
Treatment-naïve participants with advanced ALK-positive NSCLC with or without asymptomatic central nervous system (CNS) metastases were given PF-06463922 100 mg orally QD on Day -7 (only	

participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	EXP-2 (Phase 2)

Reporting group description:

Participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after only crizotinib therapy were given PF-06463922 100 mg orally QD on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	EXP-3 (Phase 2)

Reporting group description:

Participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after crizotinib therapy and 1 or 2 prior regimens of chemotherapy given before or after crizotinib therapy, or participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after 1 ALK inhibitor therapy other than crizotinib with or without any number of prior chemotherapy regimens in any disease setting were given PF-06463922 100 mg orally QD on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	EXP-4 (Phase 2)

Reporting group description:

Participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after 2 prior lines of ALK inhibitor therapies were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	EXP-5 (Phase 2)

Reporting group description:

Participants with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after 3 prior lines of ALK inhibitor therapies were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for participant scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	EXP-6 (Phase 2)

Reporting group description:

Participants with advanced ROS1-positive NSCLC who were treatment naïve or had any number of prior cancer therapies with or without asymptomatic CNS metastases were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	Japan Lead-In Cohort (LIC)

Reporting group description:

Few Japanese participants were given PF-06463922 100 mg orally once daily (QD) in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal to evaluate safety of PF-06463922 in Japanese participants, in order to support inclusion of Japanese participants in Phase 2.

Reporting group title	DDI Substudy

Reporting group description:

Participants with advanced ALK positive or ROS1-positive NSCLC who were treatment naïve or had any number of prior cancer therapies with or without asymptomatic CNS metastases were administered a single dose of a probe substrate alone on Day -2. Participants were given PF-06463922 100 mg orally QD starting on Cycle1 Day 1 and along with probe substrate on Day 15 Cycle 1.

Subject analysis set title	ALK Positive Population (Phase 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This reporting arm includes all Phase 1 participants who had documented ALK rearrangement.

Subject analysis set title	ROS1 Positive Population (Phase 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This reporting arm includes all Phase 1 participants who had documented ROS1 rearrangement.

Subject analysis set title	ALK Positive Population (Phase 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This reporting arm includes all Phase 1 participants who had documented ALK rearrangement.

Subject analysis set title	ROS1 Positive Population (Phase 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This reporting arm includes all Phase 1 participants who had documented ROS1 rearrangement.

Subject analysis set title	Phase 1 ITT Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This reporting group includes all Phase 1 participants in the ITT analysis set.

Subject analysis set title	ALK Positive Population (Phase 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This reporting arm includes all Phase 1 participants who had documented ALK rearrangement.

Subject analysis set title	Phase 1 PRO Evaluable Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This reporting group includes all Phase 1 participants who received at least 1 dose of PF-06463922 and completed a baseline and at least 1 post-baseline PRO assessment.

Subject analysis set title	Phase 2 ITT Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This reporting group includes all Phase 2 participants in the ITT analysis set.

Subject analysis set title	Phase 2 and Japan LIC PK Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK parameters of PF-06463922 were determined for a small subset of Phase 2 participants and Japan LIC. These participants received PF-06463922 100 mg orally QD and were combined into 1 reporting group for PK analysis. Japan LIC was not included in single-dose PK analysis, ie, they did not contribute to Day -7 data.

Subject analysis set title	Phase 2 and Japan LIC PK Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK parameters of PF-06463922 were determined for a small subset of Phase 2 participants and Japan LIC. These participants received PF-06463922 100 mg orally QD and were combined into 1 reporting group for PK analysis. Japan LIC was not included in single-dose PK analysis, ie, they did not contribute to Day -7 data.

Subject analysis set title	Phase 2 and Japan LIC PK Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK parameters of PF-06463922 were determined for a small subset of Phase 2 participants and Japan LIC. These participants received PF-06463922 100 mg orally QD and were combined into 1 reporting group for PK analysis. Japan LIC was not included in single-dose PK analysis, ie, they did not contribute to Day -7 data.

Subject analysis set title	Phase 2 and Japan LIC PK Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK parameters of PF-06463922 were determined for a small subset of Phase 2 participants and Japan LIC. These participants received PF-06463922 100 mg orally QD and were combined into 1 reporting group for PK analysis. Japan LIC was not included in single-dose PK analysis, ie, they did not contribute to Day -7 data.

Subject analysis set title	Phase 2
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with advanced ROS1-positive NSCLC who were treatment naïve or had any number of prior cancer therapies with or without asymptomatic CNS metastases were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Primary: Number of Participants with Cycle 1 Dose-Limiting Toxicities (DLTs) in Phase 1

End point title	Number of Participants with Cycle 1 Dose-Limiting Toxicities (DLTs) in Phase 1[1][2]

End point description:

DLT: any of following AEs:hematologic: grade (G)4 neutropenia for >7 days; febrile neutropenia; grade >=3 neutropenic infection; grade >=3 thrombocytopenia with bleeding; G4 thrombocytopenia; non-hematologic: grade >=3 pancreatitis; grade >=3 toxicities (excluding grade >=3 laboratory abnormalities not requiring dose modifications) persisting after optimal treatment with standard medical therapy; symptomatic grade >=3 QTc prolongation, or asymptomatic grade >=3 prolongation confirmed by repeat testing, persisted after correction of reversible causes; >=20% decrease from baseline in left ventricular ejection fraction (LVEF); other: failure to deliver at least 16 out of 21 prescribed daily total doses due to toxicite; failure to restart dosing after 21 days (1 cycle) delay due to toxicity. MTD evaluable population: all enrolled participants who received at least 75% of planned PF-06463922 dose in Cycle 1 and who received <75% of planned PF-06463922 doses in Cycle 1 due to DLT.

End point type	Primary

End point timeframe:

Cycle 1 (21 days)

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: No statistical analysis was planned

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	11
Units: Participants				
With DLT	0	0	0	0
No DLT	3	2	3	6
Data missing	0	1	0	5

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	3	3	2
Units: Participants				
With DLT	0	0	1	0
No DLT	8	2	1	2
Data missing	8	1	1	0

End point values	75 mg BID	100 mg BID		

	(Phase 1)	(Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Participants				
With DLT	0	0		
No DLT	3	2		
Data missing	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Overall and Intracranial Objective Response (Phase 2)

End point title	Percentage of Participants with Overall and Intracranial Objective Response (Phase 2)[3][4]

End point description:

Objective response (OR): confirmed CR or PR according to Response Evaluation Criteria in Solid Tumor (RECIST) version 1.1. Intracranial OR: confirmed CR or PR considering only lesions within brain. CR: disappearance of all non-lymph node target lesions (where all target lesions are recorded with a length of 0 milliliter (mm) on Target Lesions eCRF). Any pathological lymph nodes (recorded as target lesion) must have reduction in short axis to <10 mm. PR:30% or more decrease in sum of lesion dimensions (SLD) of target lesions, taking as reference the baseline SLD. Results presented here were based on independent central review.ITT analysis set: all enrolled participants with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922; participants with central nervous system (CNS) metastases in ITT analysis set were used for intracranial response assessment. "Number Analyzed": participants evaluable for specified rows.

End point type	Primary

End point timeframe:

3 years

Notes:

[3] - 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: No statistical analysis was planned

[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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	27	60	65
Units: Percentage of participants				
number (confidence interval 95%)				
OR, n=30,27,59,65,46, 47,32	90.0 (73.5 to 97.9)	74.1 (53.7 to 88.9)	50.8 (37.5 to 64.1)	41.5 (29.4 to 54.4)
Intracranial OR,n=8,17,32,45,38, 25	75.0 (34.9 to 96.8)	58.8 (32.9 to 81.6)	62.5 (43.7 to 78.9)	55.6 (40.0 to 70.4)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	47		
Units: Percentage of participants				
number (confidence interval 95%)				
OR, n=30,27,59,65,46, 47,32	34.8 (21.4 to 50.2)	36.2 (22.7 to 51.5)		
Intracranial OR,n=8,17,32,45,38, 25	39.5 (24.0 to 56.6)	56.0 (34.9 to 75.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Overall and Intracranial Objective Response (Phase 1)

End point title	Percentage of Participants With Overall and Intracranial Objective Response (Phase 1)

End point description:

Objective response (OR) refers to confirmed CR or PR according to RECIST version 1.1. Intracranial OR refers to confirmed CR or PR considering only lesions within brain. CR was defined as the disappearance of all non-lymph node target lesions (where all target lesions are recorded with a length of 0 mm on Target Lesions eCRF). Any pathological lymph nodes (recorded as target lesion) must have reduction in short axis to <10 mm. PR was defined as a 30 % or more decrease in SLD of target lesions, taking as reference the baseline SLD. Results presented here were based on independent central review.The ITT analysis set was used for overall response assessment and included all enrolled participants with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922; participants with CNS metastases in the ITT analysis set was used for intracranial response assessment. Here, "Number Analyzed" signifies participants analyzed for this outcome measure.

End point type	Secondary

End point timeframe:

From start of study treatment until CR or PR (maximum of 96.58 months of treatment exposure)

End point values	ALK Positive Population (Phase 1)	ROS1 Positive Population (Phase 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	41	12		
Units: Percentage of participants				
number (confidence interval 95%)				
OR, n= 41, 12	39.0 (24.2 to 55.5)	50.0 (21.1 to 78.9)		
Intracranial OR, n=34, 8	41.2 (24.6 to 59.3)	50.0 (15.7 to 84.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Tumor Response (TTR) and Intracranial TTR (Phase 1)

End point title	Time to Tumor Response (TTR) and Intracranial TTR (Phase 1)

End point description:

TTR: time from first dose of study treatment to first documentation of objective tumor response (CR or PR). For participants whose objective response proceeded from PR to CR, onset of PR was taken as onset of response. CR:disappearance of all non-lymph node target lesions (where all target lesions are recorded with a length of 0 mm on Target Lesions eCRF). Any pathological lymph nodes (recorded as target lesion) must have reduction in short axis to <10 mm. PR: 30 % or more decrease in SLD of target lesions, taking as reference the baseline SLD. TTR was calculated for subgroup of participants with confirmed objective tumor response. Intracranial TTR was only calculated for participants with confirmed intracranial OR. Results presented here were based on independent central review.TTR analysis set:all ITT participants who had confirmed objective response; intracranial TTR analysis set:all ITT participants who had CNS metastases and achieved confirmed intracranial objective response

End point type	Secondary

End point timeframe:

From start of study treatment to the first documentation of objective tumor response (CR or PR) (maximum of 96.58 months of treatment exposure)

End point values	ALK Positive Population (Phase 1)	ROS1 Positive Population (Phase 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	6		
Units: Months				
median (full range (min-max))				
TTR, n=16, 6	1.4 (1.2 to 15.2)	1.4 (1.2 to 2.8)		
Intracranial TTR, n=14, 4	1.4 (1.2 to 20.1)	1.4 (1.1 to 2.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Duration of Response (DOR) and Intracranial DOR (Phase 1)

End point title	Number of Participants With Duration of Response (DOR) and Intracranial DOR (Phase 1)

End point description:

DOR: time from first documentation of objective tumor response (CR/PR) to first documentation of disease progression (PD) or death due to any cause. Intracranial DOR:calculated for participants with confirmed intracranial (IC) OR. CR:disappearance of all non-lymph node target lesions (where all target lesions are recorded with length of 0mm on Target Lesion eCRF). Pathological lymph node (recorded as target lesion) must have reduction in short axis to <10mm. PR:30% or more decrease in SLD of target lesion, taking as reference baseline SLD. PD:20% or more increase in SLD of target lesion relative to baseline/smallest SLD (nadir) recorded since first dose,demonstrate absolute increase of atleast 5mm(>=5mm) relative to baseline/smallest SLD recorded since first dose.DOR analysis set: ITT participant who had confirmed OR; IC DOR set: ITT participant who had CNS metastases, achieved confirmed IC OR.99999:Number of participant with confirmed OR was too small to provide summary

End point type	Secondary

End point timeframe:

From start of study treatment to first documentation of disease progression (PD) or to death due to any cause, whichever occurred first (maximum of 96.58 months of treatment exposure)

End point values	ALK Positive Population (Phase 1)	ROS1 Positive Population (Phase 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	6		
Units: Participants				
number (not applicable)				
DOR, <3 Months, n=16,6	1	0		
DOR,3 Months < 6 Months, n=16,6	6	0		
DOR, 6 Months -< 9 Months, n=16,6	0	1		
DOR, 9 Months -< 12 Months, n=16,6	0	1		
DOR,12 Months -< 15 Months, n=16,6	1	0		
DOR, 15 Months -< 18 Months, n=16,6	0	0		
DOR, 18 Months -< 21 Months, n=16, 6	0	0		
DOR, 21 Months -< 24 Months, n=16, 6	1	0		
DOR,>= 24 Months, n=16, 6	1	2		
Intracranial DOR, <3 Months, n=14, 4	1	0		
Intracranial DOR, 3 Months < 6 Months, n=14, 4	0	0		
Intracranial DOR, 6 Months -< 9 Months, n=14, 4	1	0		
Intracranial DOR, 9 Months -< 12 Months, n=14, 4	0	0		
Intracranial DOR, 12 Months -< 15 Months, n=14, 4	1	0		
Intracranial DOR, 15 Months -< 18 Months, n=14, 4	0	0		
Intracranial DOR, 18 Months -< 21 Months, n=14, 4	0	0		
Intracranial DOR, 21 Months -< 24 Months, n=14, 4	0	0		
Intracranial DOR, >= 24 Months, n=14, 4	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Disease Control and Intracranial Disease Control at 12 and 24 Weeks (Phase 1)

End point title	Percentage of Participants Achieving Disease Control and Intracranial Disease Control at 12 and 24 Weeks (Phase 1)

End point description:

Tumor response was evaluated as per to RECIST v1.1, disease control: confirmed CR, confirmed PR, or stable disease (SD). Intracranial assessment was only performed for participants CNS metastases. CR:disappearance of all non-lymph node target lesions (where all target lesions are recorded with length of 0mm on Target Lesions eCRF). Any pathological lymph nodes (recorded as target lesion) must have reduction in short axis to <10 mm. PR: 30% or more decrease in SLD of target lesion, taking as reference baseline SLD. Progressive disease: 20% or more increase in SLD of target lesions relative to baseline or smallest SLD (nadir) recorded since first dose. SLD must demonstrate absolute increase of atleast 5mm (>=5mm) relative to baseline or smallest SLD (nadir). ITT analysis set: all enrolled

participants with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922; participants with CNS metastases in ITT analysis set was used for intracranial response assessment.

End point type	Secondary

End point timeframe:

12 and 24 weeks

End point values	ALK Positive Population (Phase 1)	ROS1 Positive Population (Phase 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	41	12		
Units: Percentage of participants				
number (confidence interval 95%)				
DCR at Week 12, n=41,12	53.7 (37.4 to 69.3)	58.3 (27.7 to 84.8)		
DCR at Week 24, n=41,12	39.0 (24.2 to 55.5)	50.0 (21.1 to 78.9)		
Intracranial DCR at Week 12, n=34, 8	50.0 (32.4 to 67.6)	37.5 (8.5 to 75.5)		
Intracranial DCR at Week 24, n=34, 8	41.2 (24.6 to 59.3)	37.5 (8.5 to 75.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Probability of First Event Being a Central Nervous System (CNS) Progression, Non CNS Progression, or Death (Phase 1)

End point title	Probability of First Event Being a Central Nervous System (CNS) Progression, Non CNS Progression, or Death (Phase 1)

End point description:

Probability of first event being a CNS progression, a non-CNS progression, or death was evaluated with a competing risk approach by estimating cumulative incidence functions (range: 0-1) relative to the analysis set. The time to first event being a Competing Event (either "CNS progression" or "non CNS progression" or "Death") was defined as time from first dose until the date of that specific event. Participants not known to have any of the Competing Events were censored on the date they were last assessed for disease status for PFS. Participants who presented one type of event were counted as a competing cause of failure for the analysis of other type of events. For each type of event, the cumulative incidence function corresponding to the nearest time point preceding 1 year is presented. Results are based on independent central review. intent-to-treat (ITT) analysis set: all enrolled participants with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922.

End point type	Secondary

End point timeframe:

From start of study treatment until first event of CNS progression (maximum of 96.58 months of treatment exposure)

End point values	Phase 1 ITT Population			
Subject group type	Subject analysis set			
Number of subjects analysed	53			
Units: Probability of events				
number (not applicable)				
CNS progression	0.260			
Non CNS progression	0.352			
Death	0.060			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) (Phase 1)

End point title	Progression-Free Survival (PFS) (Phase 1)

End point description:

PFS was defined as the time from the first dose of study treatment to the first documentation of objective disease progression or to death on study due to any cause, whichever came first. Progressive disease was defined by a 20% or more increase in the SLD of target lesions relative to baseline or the smallest SLD (nadir) recorded since first dose. In addition to the relative increase of 20%, SLD must also demonstrate an absolute increase of at least 5 mm (>= 5 mm) relative to baseline or the smallest SLD (nadir) recorded since the first dose. Results presented here were based on independent central review. PFS analysis set included all participants with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922.

End point type	Secondary

End point timeframe:

From start of study treatment to first documentation of disease progression (PD) or to death due to any cause, whichever occurred first (maximum of 96.58 months of treatment exposure)

End point values	ALK Positive Population (Phase 1)	ROS1 Positive Population (Phase 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	41	12		
Units: Months				
median (confidence interval 95%)	5.4 (2.7 to 11.8)	10.1 (1.6 to 33.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) (Phase 1)

End point title	Overall Survival (OS) (Phase 1)

End point description:

OS was defined as the time from first dose to the date of death due to any cause. For participants still alive at the time of analysis, the OS time was censored on the last date the participants were known to

be alive. Estimates of OS and its 95% confidence interval were determined using Kaplan-Meier method. ITT analysis set: all enrolled participants with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922."Number Analyzed": participants analyzed for this outcome measure. 99999 represents “A large proportion of participants in the analysis set had their OS data censored, and number of participants dead by the cutoff date of this report was small, so it's impossible to derive such summary statistics.”

End point type	Secondary

End point timeframe:

3 years

End point values	ALK Positive Population (Phase 1)	ROS1 Positive Population (Phase 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	41	12		
Units: Months				
median (confidence interval 95%)	22.3 (11.4 to 99999)	99999 (4.7 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of PF-06463922 Following Single Oral Doses (Phase 1)

End point title	Maximum Observed Plasma Concentration (Cmax) of PF-06463922 Following Single Oral Doses (Phase 1)[5]

End point description:

Maximum observed plasma concentration (Cmax) of PF-06463922 was observed directly from data. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. 99999 represents “Summary statistics were not calculated when fewer than 3 participants had reportable values. Individual values are 390 and 423 ng/mL, respectively.”

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 1 for 25 mg QD and 150 mg QD groups; pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24, 48, 72, 96 and 120 hours post-dose on Day -7 for all other groups.

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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	2	12
Units: Nanograms per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)	50.80 (± 17)	149.2 (± 71)	99999 (± 99999)	489.1 (± 45)

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	3	3	3
Units: Nanograms per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)	595.5 (± 37)	760.0 (± 58)	1201 (± 19)	202.2 (± 57)

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: Nanograms per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)	594.9 (± 27)	507.2 (± 51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of PF-06463922 Following Multiple Oral Doses (Phase 1)

End point title	Maximum Observed Plasma Concentration (Cmax) of PF-06463922 Following Multiple Oral Doses (Phase 1)[6]

End point description:

Maximum Observed Plasma Concentration (Cmax) of PF-06463922 was observed directly from data. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. 99999 represents "Summary statistics were not calculated when fewer than 3 participants had reportable values. Individual values are 760 and 1430 ng/mL, respectively." and "when fewer than 3 participants had reportable values. The individual value is 370 ng/mL"

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24 hours post-dose on Cycle 1 Day 15 (24-hour samples not collected for BID groups).

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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	12
Units: ng/mL				
geometric mean (geometric coefficient of variation)	67.29 (± 18)	138.1 (± 35)	359.7 (± 27)	429.6 (± 48)

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	3	3	3
Units: ng/mL				
geometric mean (geometric coefficient of variation)	550.2 (± 32)	541.0 (± 42)	99999 (± 99999)	99999 (± 99999)

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	550.0 (± 23)	600.5 (± 27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time for Cmax (Tmax) of PF-06463922 Following Single Oral Doses (Phase 1)

End point title	Time for Cmax (Tmax) of PF-06463922 Following Single Oral Doses (Phase 1)[7]

End point description:

Tmax of PF-06463922 was observed directly from data as time of first occurrence. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 1 for 25 mg QD and 150 mg QD groups; pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24, 48, 72, 96 and 120 hours post-dose on Day -7 for all other groups.

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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	2	12
Units: Hours				
median (full range (min-max))	1.98 (1.00 to 2.97)	2.00 (0.50 to 2.05)	1.25 (0.50 to 2.00)	1.09 (0.50 to 4.03)

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	3	3	3
Units: Hours				
median (full range (min-max))	1.96 (0.517 to 4.33)	1.05 (1.00 to 3.00)	2.00 (1.18 to 3.00)	1.20 (0.50 to 1.97)

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: Hours				
median (full range (min-max))	1.23 (1.00 to 2.00)	2.00 (1.10 to 3.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time for Cmax (Tmax) of PF-06463922 Following Multiple Oral Doses (Phase 1)

End point title	Time for Cmax (Tmax) of PF-06463922 Following Multiple Oral Doses (Phase 1)[8]

End point description:

Tmax of PF-06463922 was observed directly from data as time of first occurrence. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24 hours post-dose on Cycle 1 Day 15 (24-hour samples not collected for BID groups).

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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	12
Units: Hours				
median (full range (min-max))	1.00 (1.00 to 1.08)	1.00 (1.00 to 2.00)	2.00 (1.92 to 2.75)	1.03 (0.50 to 2.00)

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	3	3	3
Units: Hours				
median (full range (min-max))	1.13 (1.00 to 4.00)	1.30 (1.00 to 24.0)	1.61 (1.22 to 2.00)	0.50 (0.50 to 0.50)

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Hours				
median (full range (min-max))	0.55 (0.50 to 2.05)	2.00 (1.00 to 2.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the Plasma Concentration-Time profile from Time Zero to Time Tau (AUCtau) of PF-06463922 Following Single Oral Doses (Phase 1)

End point title	Area under the Plasma Concentration-Time profile from Time Zero to Time Tau (AUCtau) of PF-06463922 Following Single Oral Doses (Phase 1)[9]

End point description:

Tau refers to the dosing interval, and it equals to 12 or 24 hours for BID or QD dosing, respectively. AUCtau was determined using linear/log trapezoidal method. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. 99999 represents "Summary statistics were not calculated when fewer than 3 participants had reportable values. Individual values are 3310 and 3880 ng*hr/mL, respectively."

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 1 for 25 mg QD and 150 mg QD groups; pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, and 24 hours post-dose on Day -7 for all other groups.

Notes:

[9] - 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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	2	12
Units: Nanogram*hour/milliliter (ng*hr/mL)				
geometric mean (geometric coefficient of variation)	488.2 (± 21)	1387 (± 35)	99999 (± 99999)	3990 (± 55)

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	3	3	3
Units: Nanogram*hour/milliliter (ng*hr/mL)				
geometric mean (geometric coefficient of variation)	5110 (± 28)	7474 (± 73)	11410 (± 43)	982.4 (± 9)

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: Nanogram*hour/milliliter (ng*hr/mL)				
geometric mean (geometric coefficient of variation)	2996 (± 20)	2925 (± 47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the Plasma Concentration-Time profile from Time Zero to Time Tau (AUCtau) of PF-06463922 Following Multiple Oral Doses (Phase 1)

End point title	Area under the Plasma Concentration-Time profile from Time Zero to Time Tau (AUCtau) of PF-06463922 Following Multiple Oral Doses (Phase 1)[10]

End point description:

Tau refers to the dosing interval, and it equals to 12 or 24 hours for BID or QD dosing, respectively. AUCtau was determined using linear/log trapezoidal method. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. 99999 represents "Summary statistics were not calculated when fewer than 3 participants had reportable values. Individual values are 4480 and 12900 ng*hr/mL, respectively and when fewer than 3 participants had reportable values. The individual value is 2140 ng*hr/mL."

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24 hours post-dose on Cycle 1 Day 15 (24-hour samples not collected for BID groups)

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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	12
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	752.1 (± 26)	1701 (± 29)	3367 (± 39)	4107 (± 53)

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	3	2	1
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	5121 (± 30)	6157 (± 9)	99999 (± 99999)	99999 (± 99999)

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	3574 (± 35)	4058 (± 33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the Plasma Concentration-Time Profile from Time Zero Extrapolated to Infinite Time (AUCinf) of PF-06463922 Following Single Oral Doses (Phase 1)

End point title	Area under the Plasma Concentration-Time Profile from Time Zero Extrapolated to Infinite Time (AUCinf) of PF-06463922 Following Single Oral Doses (Phase 1)[11]

End point description:

AUCinf was calculated as AUClast+(Clast*/kel),where AUClast was area under plasma concentration-time profile from time 0 to time of last quantifiable concentration,Clast* was predicted plasma concentration at last quantifiable time point estimated from log-linear regression analysis, kel was rate constant for terminal phase.PK parameter analysis set for PF-06463922:all enrolled participants who received at least 1 dose of PF-06463922,had sufficient information to estimate at least one of PK parameter.Overall Number of Participants Analyzed: participants evaluable for this outcome measure.99999:Summary statistics were not calculated when fewer than 3 participants had reportable value.Individual value:698 ng*hr/mL;when fewer than 3 participant had reportable value.Individual values are 7210 and 7240 ng*hr/mL; when fewer than 3 participant had reportable value.Individual

2630 and 3690 ng*hr/mL. when fewer than 3 participant had reportable value.Individual value:6860 ng*hr/mL.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 1 for 25 mg QD and 150 mg QD groups; pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24, 48, 72, 96 and 120 hours post-dose on Day -7 for all other groups.

Notes:

[11] - 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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)	100 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	2	11	15
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	99999 (± 99999)	7663 (± 79)	8236 (± 25)

End point values	200 mg QD (Phase 1)	35 mg BID (Phase 1)	75 mg BID (Phase 1)	100 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	1	4
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	18340 (± 61)	99999 (± 99999)	99999 (± 99999)	6318 (± 56)

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Oral Clearance (CL/F) of PF-06463922 Following Single Oral Doses (Phase 1)

End point title	Apparent Oral Clearance (CL/F) of PF-06463922 Following Single Oral Doses (Phase 1)[12]

End point description:

Clearance of drug is measure of rate at which drug is metabolized or eliminated by normal biological processes. CL/F was calculated as dose/AUCinf, where AUCinf was area under plasma concentration-time profile from time 0 extrapolated to infinite time. PK parameter analysis set for PF-06463922: all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of PK parameters of interest for PF-06463922.Overall Number of Participants Analyzed: participants evaluable for this outcome measure. Summary statistics were not calculated when fewer than 3 participants had reportable values. individual value is 14.3 L/hr; when fewer than 3 participants had reportable values. Individual values are 6.91 and 6.94 L/hr, respectively; when fewer than 3 participants had reportable values. Individual values are 9.48 and 13.3 L/hr, respectively; when fewer than 3 participants had reportable values. The individual value is 10.9 L/hr.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 1 for 25 mg QD and 150 mg QD groups; pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24, 48, 72, 96 and 120 hours post-dose on Day -7 for all other groups.

Notes:

[12] - 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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)	100 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	2	11	15
Units: Liter/hour (L/hr)				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	99999 (± 99999)	9.788 (± 79)	12.14 (± 25)

End point values	200 mg QD (Phase 1)	35 mg BID (Phase 1)	75 mg BID (Phase 1)	100 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	1	4
Units: Liter/hour (L/hr)				
geometric mean (geometric coefficient of variation)	10.90 (± 61)	99999 (± 99999)	99999 (± 99999)	15.83 (± 56)

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Oral Clearance (CL/F) of PF-06463922 Following Multiple Oral Doses (Phase 1)

End point title	Apparent Oral Clearance (CL/F) of PF-06463922 Following Multiple Oral Doses (Phase 1)[13]

End point description:

Clearance of a drug is a measure of the rate at which a drug is metabolized or eliminated by normal biological processes. CL/F was calculated as dose/AUCinf, where AUCinf was the area under the plasma concentration-time profile from time 0 extrapolated to infinite time. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. 99999: Summary statistics were not calculated when fewer than 3 participants had reportable values. Individual values are 15.5 and 44.6 L/hr, respectively and when fewer than 3 participants had reportable values. The individual value is 16.3 L/hr.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24 hours post-dose on Cycle 1 Day 15 (24-hour samples not collected for BID groups)

Notes:

[13] - 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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	12
Units: L/hr				
geometric mean (geometric coefficient of variation)	13.27 (± 26)	14.72 (± 29)	14.84 (± 39)	17.66 (± 48)

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	3	2	1
Units: L/hr				
geometric mean (geometric coefficient of variation)	19.52 (± 30)	24.37 (± 9)	99999 (± 99999)	99999 (± 99999)

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: L/hr				
geometric mean (geometric coefficient of variation)	20.99 (± 35)	22.37 (± 47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution (Vz/F) of PF-06463922 Following Single Oral Doses (Phase 1)

End point title	Apparent Volume of Distribution (Vz/F) of PF-06463922 Following Single Oral Doses (Phase 1)[14]

End point description:

Vz/F was defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired plasma concentration of a drug, and calculated as dose/(AUCinf*kel), where AUCinf was the area under the plasma concentration-time profile from time 0 extrapolated to infinite time, kel was the rate constant for terminal phase. Summary statistics were not calculated when fewer than 3 participants had reportable values. The individual value is 373 L; when fewer than 3 participants had reportable values. Individual values are 166 and 307 L, respectively; when fewer than 3 participants had reportable values. Individual values are 362 and 472 L, respectively. Summary statistics were not calculated when fewer than 3 participants had reportable values. The individual value is 410 L.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 1 for 25 mg QD and 150 mg QD groups; pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24, 48, 72, 96 and 120 hours post-dose on Day -7 for all other groups.

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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)	100 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	2	11	15
Units: Liters (L)				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	99999 (± 99999)	367.9 (± 54)	356.3 (± 39)

End point values	200 mg QD (Phase 1)	35 mg BID (Phase 1)	75 mg BID (Phase 1)	100 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	1	4
Units: Liters (L)				
geometric mean (geometric coefficient of variation)	307.8 (± 41)	99999 (± 99999)	99999 (± 99999)	378.3 (± 54)

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Accumulation Ratio (Rac) of PF-06463922 Following Multiple Oral Doses (Phase 1)

End point title	Observed Accumulation Ratio (Rac) of PF-06463922 Following Multiple Oral Doses (Phase 1)[15]

End point description:

Rac was calculated as Day 15 AUCtau/Day -7 AUCtau or Day 1 AUCtau, where AUCtau was the area under the plasma concentration-time profile from time 0 to time tau (12 and 24 hours for BID and QD dosing regimen, respectively). PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. Here, "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure.Standard deviation was not calculated when fewer than 3 participants had reportable values and when fewer than 3 participants had reportable values. The individual value is 2.09.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24 hours post-dose on Cycle 1 Day 15 (24-hour samples not collected for BID groups)

Notes:

[15] - 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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	2	12
Units: Ratio				
arithmetic mean (standard deviation)	1.543 (± 0.075056)	1.237 (± 0.20817)	1.105 (± 99999)	1.121 (± 0.44575)

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	3	2	1
Units: Ratio				
arithmetic mean (standard deviation)	1.071 (± 0.31138)	1.000 (± 0.79137)	0.6500 (± 99999)	99999 (± 99999)

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Ratio				
arithmetic mean (standard deviation)	1.231 (± 0.35228)	1.523 (± 0.29569)		

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Half-Life of PF-06463922 Following Single Oral Doses (Phase 1)

End point title	Terminal Half-Life of PF-06463922 Following Single Oral Doses (Phase 1)[16]

End point description:

Terminal plasma half-life: time measured for plasma concentration to decrease by one half, and calculated as loge(2)/kel, where kel was rate constant for terminal phase. PK parameter analysis set for PF-06463922: all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of PK parameters of interest for PF-06463922. "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure. 99999: Summary statistics were not calculated when fewer than 3 participants had reportable values. Individual value is 18.0 hr; when fewer than 3 participants had reportable values. Individual values are 16.6 and 30.8 hr, respectively; Standard deviation was not calculated when fewer than 3 participants had reportable values. Individual values are 24.6 and 26.5 hr, respectively; Summary statistics were not calculated when fewer than 3 participants had reportable values. individual value is 26.0 hr.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 1 for 25 mg QD and 150 mg QD groups; pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24, 48, 72, 96 and 120 hours post-dose on Day -7 for all other groups.

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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)	100 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	2	11	15
Units: Hours (hr)				
arithmetic mean (standard deviation)	99999 (± 99999)	23.70 (± 99999)	27.22 (± 8.2961)	20.89 (± 5.0308)

End point values	200 mg QD (Phase 1)	35 mg BID (Phase 1)	75 mg BID (Phase 1)	100 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	1	4
Units: Hours (hr)				
arithmetic mean (standard deviation)	19.80 (± 3.3045)	25.55 (± 99999)	99999 (± 99999)	17.18 (± 5.1874)

Statistical analyses

No statistical analyses for this end point

Secondary: Steady State Accumulation Ratio (Rss) of PF-06463922 Following Multiple Oral Doses (Phase 1)

End point title	Steady State Accumulation Ratio (Rss) of PF-06463922 Following Multiple Oral Doses (Phase 1)[17]

End point description:

Rss was calculated as Day 15 AUCtau/Day -7 AUCinf, where AUCtau was area under plasma concentration-time profile from time 0 to time tau (12 and 24 hours for BID and QD dosing regimen, respectively).PK parameter analysis set for PF-06463922: all enrolled participants who received at least 1 dose of PF-06463922, had sufficient information to estimate at least one of PK parameters of interest. Overall Number of Participants Analyzed: participants evaluable for this outcome measure. 99999: summary statistics were not calculated when fewer than 3 participants had reportable values,individual value:0.993; SD was not calculated when fewer than 3 participants had reportable values. Individual values:0.401 and 0.719,when fewer than 3 participants had reportable values. Individual values:0.384 and 0.403, summary statistics were not calculated when fewer than 3 participants had reportable values. individual value:0.815; fewer than 3 participants had reportable values. individual value:0.542.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24 hours post-dose on Cycle 1 Day 15 (24-hour samples not collected for BID groups)

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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)	100 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	2	11	14
Units: Ratio				
arithmetic mean (standard deviation)	99999 (± 99999)	0.5600 (± 99999)	0.6131 (± 0.29021)	0.6603 (± 0.18604)

End point values	200 mg QD (Phase 1)	35 mg BID (Phase 1)	75 mg BID (Phase 1)	100 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	1	3
Units: Ratio				
arithmetic mean (standard deviation)	0.3935 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.7687 (± 0.13552)

Statistical analyses

No statistical analyses for this end point

Secondary: Renal Clearance (CLr) of PF-06463922 (Phase 1)

End point title	Renal Clearance (CLr) of PF-06463922 (Phase 1)[18]

End point description:

Renal clearance was calculated as Aetau/AUCtau, where Aetau was cumulative amount of drug recovered unchanged in urine up to dosing interval tau (24 hours for QD dosing regimen), and AUCtau was area under plasma concentration-time profile from time 0 to time tau (24 hours for QD dosing regimen). PK parameter analysis set for PF-06463922: all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of PK parameters of interest for PF-06463922. "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

0-4 hours, 4-12 hours and 12-24 hours post-dose on Cycle 1 Day 15

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: This endpoint is reporting statistics for the arms specified

End point values	100 mg QD (Phase 1)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ml/hour				
geometric mean (geometric coefficient of variation)	61.31 (± 58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of PF-06463922 Recovered Unchanged in Urine up to Dosing Interval (AEtau%) (Phase 1)

End point title	Percent of PF-06463922 Recovered Unchanged in Urine up to Dosing Interval (AEtau%) (Phase 1)[19]

End point description:

Dosing interval was 24 hours for QD dosing regimen. Aetau% was calculated as 100*Ae24/dose, where Ae24 was the cumulative amount of drug recovered unchanged in urine up to 24 hours post-dose. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. As planned, this parameter was only analyzed for 100 mg QD group. Here, "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

0-4 hours, 4-12 hours and 12-24 hours post-dose on Cycle 1 Day 15

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: This endpoint is reporting statistics for the arms specified

End point values	100 mg QD (Phase 1)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of recovered PF-06463922				
arithmetic mean (standard deviation)	0.4017 (± 0.11074)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Midazolam (Phase 1)

End point title	Maximum Observed Plasma Concentration (Cmax) of Midazolam (Phase 1)[20]

End point description:

Cmax of midazolam was observed directly from data. Only participants in 25 mg and 150 mg QD groups were given midazolam. Day -7 data reflected the PK assessment before administration of PF-06463922, and Cycle 1 Day 15 data reflected the PK assessment after multiple doses of PF-06463922 were administered. PK parameter analysis set for PF-06463922: all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Day -7 and pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 15

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: This endpoint is reporting statistics for the arms specified

End point values	25 mg QD (Phase 1)	150 mg QD (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day -7	16.06 (± 42)	11.56 (± 48)		
Cycle 1 Day 15	9.697 (± 40)	5.734 (± 43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time for Cmax (Tmax) of Midazolam (Phase 1)

End point title	Time for Cmax (Tmax) of Midazolam (Phase 1)[21]

End point description:

Tmax of midazolam was observed directly from data as time of first occurrence. Only participants in 25 mg and 150 mg QD groups were given midazolam. Day -7 data reflect the PK assessment before administration of PF-06463922, and Cycle 1 Day 15 data reflect the PK assessment after multiple doses of PF-06463922 were administered. PK parameter analysis set for midazolam: all participants who received at least 1 dose of midazolam and for which at least 1 midazolam PK parameter of interest was available.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Day -7 and pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 15

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: This endpoint is reporting statistics for the arms specified

End point values	25 mg QD (Phase 1)	150 mg QD (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Hours				
median (full range (min-max))				
Day -7	0.50 (0.50 to 1.00)	0.50 (0.50 to 0.50)		
Cycle 1 Day 15	0.50 (0.50 to 1.00)	0.50 (0.50 to 0.533)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the Plasma Concentration-Time profile from Time Zero to the Time of the Last Quantifiable Concentration (AUClast) of Midazolam (Phase 1)

End point title	Area under the Plasma Concentration-Time profile from Time

	Zero to the Time of the Last Quantifiable Concentration (AUClast) of Midazolam (Phase 1)[22]

End point description:

Area under plasma concentration-time profile from time 0 to time of last quantifiable concentration (AUClast) of midazolam was determined using linear/log trapezoidal method. Only participants in 25 mg and 150 mg QD groups were given midazolam. Day -7 data reflect PK assessment before administration of PF-06463922, and Cycle 1 Day 15 data reflect PK assessment after multiple doses of PF-06463922 were administered. PK parameter analysis set for midazolam: all participants who received at least 1 dose of midazolam and for which at least 1 midazolam PK parameter of interest was available

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Day -7 and pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 15

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: This endpoint is reporting statistics for the arms specified

End point values	25 mg QD (Phase 1)	150 mg QD (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
Day -7	51.30 (± 47)	36.49 (± 20)		
Cycle 1 Day 15	20.43 (± 18)	14.44 (± 25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the Plasma Concentration-Time Profile from Time Zero Extrapolated to Infinite Time (AUCinf) of Midazolam (Phase 1)

End point title	Area under the Plasma Concentration-Time Profile from Time Zero Extrapolated to Infinite Time (AUCinf) of Midazolam (Phase 1)[23]

End point description:

AUCinf was calculated as AUClast + (Clast*/kel), where AUClast was area under plasma concentration-time profile from time 0 to time of last quantifiable concentration, Clast* was predicted plasma concentration at last quantifiable time point estimated from the log-linear regression analysis, and kel was rate constant for terminal phase. Only participants in 25 mg and 150 mg QD groups were given midazolam. Day -7 data reflect PK assessment before administration of PF-06463922, and Cycle 1 Day 15 data reflect PK assessment after multiple doses of PF-06463922 were administered. PK parameter analysis set for midazolam: all participants who received at least 1 dose of midazolam and for which at least 1 midazolam PK parameter of interest was available. 99999: Summary statistics were not calculated when fewer than 3 participants had reportable values. Individual values are 42.2 and 46.8 ng*hr/mL, respectively.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Day -7 and pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 15

Notes:

[23] - 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: This endpoint is reporting statistics for the arms specified

End point values	25 mg QD (Phase 1)	150 mg QD (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
Day -7, n=3, 2	54.53 (± 43)	99999 (± 99999)		
Cycle 1 Day 15, n=3 ,3	21.32 (± 18)	16.09 (± 29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Oral Clearance (CL/F) of Midazolam (Phase 1)

End point title	Apparent Oral Clearance (CL/F) of Midazolam (Phase 1)[24]

End point description:

Clearance of drug is measure of rate at which drug is metabolized or eliminated by normal biological processes. CL/F was calculated as dose/AUCinf, where AUCinf was area under plasma concentration-time profile from time 0 extrapolated to infinite time. Only participants in 25 and 150 mg QD groups were given midazolam. Day -7 data reflect PK assessment before administration of PF-06463922, and Cycle 1 Day 15 data reflect PK assessment after multiple doses of PF-06463922 were administered.PK parameter analysis set: all participants who received at least 1 dose of midazolam and for which at least 1 midazolam PK parameter of interest was available.Number Analyzed:participants evaluable for specified rows.99999: Summary statistics were not calculated when fewer than 3 participants had reportable values. Individual values are 42.7 and 47.4 L/hr.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Day -7 and pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 15

Notes:

[24] - 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: This endpoint is reporting statistics for the arms specified

End point values	25 mg QD (Phase 1)	150 mg QD (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: L/hr				
geometric mean (geometric coefficient of variation)				
Day -7, n=3, 2	36.68 (± 43)	99999 (± 99999)		
Cycle 1 Day 15, n=3, 3	93.86 (± 18)	124.2 (± 29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution (Vz/F) of Midazolam (Phase 1)

End point title	Apparent Volume of Distribution (Vz/F) of Midazolam (Phase

End point description:

Vz/F was defined as theoretical volume in which total amount of drug would need to be uniformly distributed to produce desired plasma concentration of drug, and calculated as dose/(AUCinf*kel), where AUCinf was area under plasma concentration-time profile from time 0 extrapolated to infinite time, kel was rate constant for terminal phase. Only participants in 25 mg and 150 mg QD groups were given midazolam. Day -7 data reflect PK assessment before administration of PF-06463922, and Cycle 1 Day 15 data reflect PK assessment after multiple doses of PF-06463922 were administered. PK parameter analysis set for midazolam: all participants who received at least 1 dose of midazolam and for which at least 1 midazolam PK parameter of interest was available. Here, 'Number Analyzed' signifies participants evaluable for specified rows. 99999:Summary statistics were not calculated when fewer than 3 participants had reportable values. Individual values are 161 and 486 L, respectively

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Day -7 and pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 15

Notes:

[25] - 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: This endpoint is reporting statistics for the arms specified

End point values	25 mg QD (Phase 1)	150 mg QD (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Liters				
geometric mean (geometric coefficient of variation)				
Day -7, n=3, 2	229.0 (± 7)	99999 (± 99999)		
Cycle 1 Day 15, n=3, 3	404.4 (± 51)	702.2 (± 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Half-Life of Midazolam (Phase 1)

End point title	Terminal Half-Life of Midazolam (Phase 1)[26]

End point description:

Terminal plasma half-life was defined as time measured for plasma concentration to decrease by one half, and calculated as loge(2)/kel, where kel was rate constant for terminal phase. Only participants in

25 mg and 150 mg QD groups were given midazolam. Day -7 data reflect PK assessment before administration of PF-06463922, and Cycle 1 Day 15 data reflect PK assessment after multiple doses of PF-06463922 were administered. PK parameter analysis set for midazolam: all participants who received at least 1 dose of midazolam and for which at least 1 midazolam PK parameter of interest was available. Here, 'Number Analyzed' signifies participants evaluable for specified rows.99999 represents "Standard deviation was not calculated when fewer than 3 participants had reportable values. Individual values are 2.35 and 7.89 hr, respectively"

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Day -7 and pre-dose, 0.5, 1, 2, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 15

Notes:

[26] - 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: This endpoint is reporting statistics for the arms specified

End point values	25 mg QD (Phase 1)	150 mg QD (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Hour				
arithmetic mean (standard deviation)				
Day -7, n=3, 2	4.620 (± 1.9328)	5.120 (± 99999)		
Cycle 1 Day 15, n=3, 3	3.343 (± 2.0358)	5.257 (± 5.0639)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with ALK Mutation Based on Plasma CNA Analysis (Phase 1)

End point title	Number of Participants with ALK Mutation Based on Plasma CNA Analysis (Phase 1)

End point description:

Plasma circulating nucleic acid (CNA) samples were analyzed for ALK kinase domain mutations by digital polymerase chain reaction (PCR) BEAMing technology. Number of participants with one or more ALK mutations is presented.

End point type	Secondary

End point timeframe:

Screening (up to 28 days)

End point values	ALK Positive Population (Phase 1)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: Participants	14			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with ALK Mutation Based on Tumor Tissue Analysis (Phase 1)

End point title	Number of Participants with ALK Mutation Based on Tumor Tissue Analysis (Phase 1)

End point description:

Tumor tissues from archived tissue specimens and/or a de novo biopsy were analyzed for ALK kinase domain mutations. Number of participants with one or more ALK mutations is presented.

End point type	Secondary

End point timeframe:

Screening (up to 28 days)

End point values	ALK Positive Population (Phase 1)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: Participants	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Improved, Worsened or Remained Stable in EORTC QLQ-C30 (Phase 1)

End point title	Number of Participants Who Improved, Worsened or Remained Stable in EORTC QLQ-C30 (Phase 1)

End point description:

European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ)-C30 (version 3.0) consists of 30 questions assessing 5 functional domains (physical, role, emotional, cognitive and social), global quality of life (QoL), disease/treatment related symptoms (fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation and diarrhea), and the perceived financial impact of disease. Each scale was transformed to a range of 0 to 100 using standard EORTC algorithm. For global QoL and functional scales, higher score indicate better performance, and improvement was defined as an increase of at least 10 points, worsening was defined as a decrease of at least 10 points. For symptom scales, higher score indicates worse symptoms, and improvement was defined as a decrease of at least 10 points, worsening was defined as an increase of at least 10 points. All scales which had not improved nor worsened were considered stable.

End point type	Secondary

End point timeframe:

From start of study treatment until end of treatment (maximum of 96.58 months of treatment

End point values	Phase 1 PRO Evaluable Population			
Subject group type	Subject analysis set			
Number of subjects analysed	43			
Units: participants				
Improved in global QoL	19			
Stable in global QoL	13			
Worsened in global QoL	11			
Improved in physical functioning	5			
Stable in physical functioning	29			
Worsened in physical functioning	9			
Improved in role functioning	14			
Stable in role functioning	15			
Worsened in role functioning	14			
Improved in emotional functioning	15			
Stable in emotional functioning	21			
Worsened in emotional functioning	7			
Improved in cognitive functioning	8			
Stable in cognitive functioning	21			
Worsened in cognitive functioning	14			
Improved in social functioning	13			
Stable in social functioning	17			
Worsened in social functioning	13			
Improved in fatigue	17			
Stable in fatigue	19			
Worsened in fatigue	7			
Improved in nausea and vomiting	10			
Stable in nausea and vomiting	32			
worsened in nausea and vomiting	1			
Improved in pain	17			
Stable in pain	16			
Worsened in pain	10			
Improved in dyspnea	13			
Stable in dyspnea	19			
Worsened in dyspnea	11			
Improved in insomnia	19			
Stable in insomnia	17			
Worsened in insomnia	7			
Improved in appetite loss	14			
Stable in appetite loss	27			
Worsened in appetite loss	2			
Improved in constipation	10			
Stable in constipation	28			
Worsened in constipation	5			
Improved in diarrhea	9			
Stable in diarrhea	28			

Worsened in diarrhea	6			
Improved in financial difficulties	7			
Stable in financial difficulties	20			
Worsened in financial difficulties	16			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Improved, Worsened or Remained Stable in EORTC QLQ-LC13 (Phase 1)

End point title	Number of Participants Who Improved, Worsened or Remained Stable in EORTC QLQ-LC13 (Phase 1)

End point description:

EORTC QLQ-LC13 is the lung cancer module of EORTC QLQ-C30 and includes questions specific to the disease associated symptoms (dyspnea, cough, hemoptysis, and site specific pain), treatment-related symptoms (sore mouth, dysphagia, neuropathy and alopecia), and analgesic use of lung cancer patients. The scale was transformed to a range of 0 to 100 using standard EORTC algorithm. Higher score indicates worse symptoms, and improvement was defined as a decrease of at least 10 points, worsening was defined as an increase of at least 10 points. All scales which had not improved nor worsened were considered stable.

End point type	Secondary

End point timeframe:

From start of study treatment until end of treatment (maximum of 96.58 months of treatment exposure)

End point values	Phase 1 PRO Evaluable Population			
Subject group type	Subject analysis set			
Number of subjects analysed	43			
Units: Participants				
Improved in dyspnea	9			
Stable in dyspnea	23			
Worsened in dyspnea	11			
Improved in coughing	23			
Stable in coughing	12			
Worsened in coughing	8			
Improved in hemoptysis	1			
Stable in hemoptysis	42			
Worsened in hemoptysis	0			
Improved in sore mouth	0			
Stable in sore mouth	40			
Worsened in sore mouth	3			
Improved in dysphagia	4			
Stable in dysphagia	37			
Worsened in dysphagia	2			
Improved in peripheral neuropathy	6			
Stable in peripheral neuropathy	21			

Worsened in peripheral neuropathy	16			
Improved in alopecia	4			
Stable in alopecia	29			
Worsened in alopecia	9			
Improved in chest pain	16			
Stable in chest pain	22			
Worsened in chest pain	5			
Improved in arm or shoulder pain	10			
Stable in arm or shoulder pain	27			
Worsened in arm or shoulder pain	6			
Improved in pain in other parts	20			
Stable in pain in other parts	12			
Worsened in pain in other parts	11			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Mini Mental State Examination (MMSE) Score (Phase 1)

End point title	Change from Baseline in Mini Mental State Examination (MMSE) Score (Phase 1)[27]

End point description:

In Phase 1, MMSE was collected to assess mental status. MMSE is 30 item questionnaire that tests 5 areas of cognitive function: orientation, registration, attention and calculation, recall and language. Maximum score is 30 and minimum score is 0. Highest score indicates no cognitive impairment, lowest score indicates severe cognitive impairment. MMSE was removed under Amendment 6 of study protocol, and not required for Phase 2, as tool was not considered meaningful for assessment of cognitive function. MMSE assessment evaluable analysis set: all participants in safety analysis set (all participants who received at least 1 dose of PF-06463922) who completed baseline and at least 1 post-baseline assessment. Overall Number of Participants Analyzed: participants evaluable for this outcome measure. Number Analyzed: participants evaluable for specified rows. 99999:SD could not be calculated as only 1 participant was analyzed.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycle 1-52, and end of treatment (up to 3 years)

Notes:

[27] - 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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	3	9
Units: Units on a scale				
arithmetic mean (standard deviation)				
Cycle 1 Day 1, n=2,0,2,7,9,0,0,0,1,1	1.0 (± 1.41)	99999 (± 99999)	-0.5 (± 0.71)	-0.9 (± 2.27)
Cycle 2 Day 1, n=1,3,1,9,16,3,2,2,2,3	2.0 (± 99999)	-0.3 (± 0.58)	2.0 (± 99999)	0.3 (± 1.41)
Cycle 3 Day 1,2,3,2,8,15,2,2,0,1,3	2.0 (± 0.00)	0.3 (± 0.58)	-0.5 (± 0.71)	-0.6 (± 1.85)
Cycle 4 Day 1, n=1,2,2,8,14,3,2,0,1,3	5.0 (± 99999)	0.5 (± 0.71)	1.5 (± 2.12)	-1.1 (± 1.81)

Cycle 5 Day 1, n=2,2,2,7,11,3,2,0,1,3	0.5 (± 3.54)	0.5 (± 0.71)	1.5 (± 2.12)	0.3 (± 1.25)
Cycle 6 Day 1, =1,2,2,7,12,3,2,0,1,3	2.5 (± 2.12)	0.5 (± 0.71)	1.0 (± 1.41)	-0.4 (± 2.70)
Cycle 7 Day 1, n=0,2,1,7,11,2,1,0,0,3	2.0 (± 99999)	0.5 (± 0.71)	1.5 (± 2.12)	-0.1 (± 1.21)
Cycle 8 Day 1, n=1,2,1,5,10,2,1,0,1,3	-4.0 (± 99999)	0.5 (± 0.71)	1.5 (± 2.12)	-0.1 (± 2.34)
Cycle 9 Day 1, n=0,2,1,7,11,2,1,0,0,3	99999 (± 99999)	0.0 (± 0.00)	0.0 (± 99999)	-1.0 (± 2.31)
Cycle 10 Day 1, n=1,2,1,5,10,2,1,0,1,3	-5.0 (± 99999)	0.5 (± 0.71)	0.0 (± 99999)	0.0 (± 0.00)
Cycle 11 Day 1, n=0,2,1,7,12,2,2,0,1,3	99999 (± 99999)	-0.5 (± 0.71)	0.0 (± 99999)	0.3 (± 1.70)
Cycle 12 Day 1, n=0,2,0,5,12,2,2,0,1,2	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	-0.6 (± 2.19)
Cycle 13 Day 1, n=0,2,0,5,10,2,2,0,1,2	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	0.8 (± 1.79)
Cycle 14 Day 1, n=0,2,0,6,11,2,2,0,1,3	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	-0.3 (± 3.20)
Cycle 15 Day 1, n=0,2,0,6,9,0,2,0,1,3	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	-1.7 (± 5.43)
Cycle 16 Day 1, n=0,2,0,5,9,1,2,0,1,2	99999 (± 99999)	0.0 (± 1.41)	99999 (± 99999)	-0.2 (± 2.49)
Cycle 17 Day 1, n=0,2,0,5,9,1,2,0,1,3	99999 (± 99999)	-2.0 (± 2.83)	99999 (± 99999)	0.6 (± 1.95)
Cycle 18 Day 1, n=0,2,0,5,9,1,2,0,0,2	99999 (± 99999)	-0.5 (± 0.71)	99999 (± 99999)	0.8 (± 1.79)
Cycle 19 Day 1, n=0,2,0,5,9,1,2,0,1,2	99999 (± 99999)	-0.5 (± 0.71)	99999 (± 99999)	0.8 (± 1.79)
Cycle 20 Day 1, n=0,2,0,5,9,1,2,0,1,2	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.0 (± 1.41)
Cycle 21 Day 1, n=0,2,0,5,9,1,2,0,1,2	99999 (± 99999)	-0.5 (± 0.71)	99999 (± 99999)	0.0 (± 1.41)
Cycle 22 Day 1, n=0,2,0,5,9,1,2,0,1,3	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.4 (± 1.52)
Cycle 23 Day 1, n=0,2,0,5,8,1,2,0,1,2	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	0.0 (± 1.41)
Cycle 24 Day 1, n=0,2,0,5,8,1,2,0,1,2	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	-0.4 (± 0.89)
Cycle 25 Day 1, n=0,2,0,5,7,1,2,0,1,2	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.8 (± 1.79)
Cycle 26 Day 1, n=0,2,0,5,8,1,2,0,1,3	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	0.8 (± 1.79)
Cycle 27 Day 1, n=0,2,0,5,7,1,2,0,1,2	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	0.8 (± 1.79)
Cycle 28 Day 1, n=0,2,0,4,7,1,2,0,1,3	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	1.0 (± 2.00)
Cycle 29 Day 1, n=0,2,0,4,8,1,2,0,1,3	99999 (± 99999)	-1.5 (± 2.12)	99999 (± 99999)	0.5 (± 1.73)
Cycle 30 Day 1, n=0,2,0,4,5,1,2,0,1,3	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.8 (± 1.50)
Cycle 31 Day 1, n=0,2,0,3,6,1,2,0,0,3	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	1.0 (± 2.65)
Cycle 32 Day 1, n=0,2,0,3,5,0,2,0,1, 2	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	1.3 (± 2.31)
Cycle 33 Day 1, n=0,2,0,3,4,0,2,0,1, 2	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	1.3 (± 2.31)
Cycle 34 Day 1, n=0,2,0,2,4,0,2,0,1, 2	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.0 (± 0.00)
Cycle 35 Day 1, n=0,2,0,1,4,0,2,0,1, 1	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	0.0 (± 99999)
Cycle 36 Day 1, n=0,2,0,1,3,0,2,0,1, 1	99999 (± 99999)	-0.5 (± 0.71)	99999 (± 99999)	0.0 (± 99999)
Cycle 37 Day 1, n=0,2,0,1,2,0,2,0,0,0	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	-1.0 (± 99999)

Cycle 38 Day 1, n=0,2,0,1,2,0,2,0,1,0	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.0 (± 99999)
Cycle 39 Day 1, n=0,1,0,1,2,0,2,0,0,0	99999 (± 99999)	0.0 (± 99999)	99999 (± 99999)	0.0 (± 99999)
Cycle 40 Day 1, n=0,1,0,1,1,0,2,0,0,0	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	-1.0 (± 99999)
Cycle 41 Day 1, n=0,2,0,1,1,0,2,0,0,0	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	0.0 (± 99999)
Cycle 42 Day 1, n=0,2,0,1,1,0,2,0,0,0	99999 (± 99999)	-0.5 (± 0.71)	99999 (± 99999)	0.0 (± 99999)
Cycle 43 Day 1, n=0,2,0,1,0,0,2,0,0,0	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.0 (± 99999)
Cycle 44 Day 1, n=0,2,0,1,0,0,2,0,0,0	99999 (± 99999)	1.0 (± 99999)	99999 (± 99999)	-1.0 (± 99999)
Cycle 45 Day 1, n=0,1,0,1,0,0,1,0,0,0	99999 (± 99999)	1.0 (± 99999)	99999 (± 99999)	0.0 (± 99999)
Cycle 46 Day 1, n=0,1,0,1,0,0,0,0,0,0	99999 (± 99999)	0.0 (± 99999)	99999 (± 99999)	-1.0 (± 99999)
Cycle 47 Day 1, n=0,1,0,1,0,0,0,0,0,0	99999 (± 99999)	0.0 (± 99999)	99999 (± 99999)	0.0 (± 99999)
Cycle 48 Day 1, n=0,1,0,1,0,0,0,0,0,0	99999 (± 99999)	-3.0 (± 99999)	99999 (± 99999)	0.0 (± 99999)
Cycle 49 Day 1, n=0,2,0,0,0,0,0,0,0,0	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	99999 (± 99999)
Cycle 50 Day 1, n=0,1,0,0,0,0,0,0,0,0	99999 (± 99999)	-3.0 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 51 Day 1, n=0,1,0,0,0,0,0,0,0,0	99999 (± 99999)	-0.5 (± 0.71)	99999 (± 99999)	99999 (± 99999)
Cycle 52 Day 1, n=0,1,0,0,0,0,0,0,0,0	99999 (± 99999)	1.0 (± 99999)	99999 (± 99999)	99999 (± 99999)
End of treatment, n=1,0,3,1,4,0,0,1,1	-8.0 (± 99999)	99999 (± 99999)	0.7 (± 1.15)	-2.0 (± 99999)

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	3	2	2
Units: Units on a scale				
arithmetic mean (standard deviation)				
Cycle 1 Day 1, n=2,0,2,7,9,0,0,0,1,1	0.8 (± 1.39)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 2 Day 1, n=1,3,1,9,16,3,2,2,2,3	0.0 (± 1.79)	4.7 (± 8.08)	4.0 (± 4.24)	0.0 (± 0.00)
Cycle 3 Day 1,2,3,2,8,15,2,2,0,1,3	0.2 (± 1.52)	5.0 (± 8.49)	3.0 (± 2.83)	99999 (± 99999)
Cycle 4 Day 1, n=1,2,2,8,14,3,2,0,1,3	0.0 (± 1.47)	2.0 (± 6.24)	-0.5 (± 3.54)	99999 (± 99999)
Cycle 5 Day 1, n=2,2,2,7,11,3,2,0,1,3	-0.2 (± 1.72)	4.7 (± 8.14)	0.5 (± 6.36)	99999 (± 99999)
Cycle 6 Day 1, =1,2,2,7,12,3,2,0,1,3	0.3 (± 0.90)	4.3 (± 5.86)	2.0 (± 4.24)	99999 (± 99999)
Cycle 7 Day 1, n=0,2,1,7,11,2,1,0,0,3	0.4 (± 0.90)	4.7 (± 8.33)	3.0 (± 4.24)	99999 (± 99999)
Cycle 8 Day 1, n=1,2,1,5,10,2,1,0,1,3	0.2 (± 1.34)	3.0 (± 7.81)	4.0 (± 4.24)	99999 (± 99999)
Cycle 9 Day 1, n=0,2,1,7,11,2,1,0,0,3	0.3 (± 2.10)	6.0 (± 8.49)	6.0 (± 99999)	99999 (± 99999)
Cycle 10 Day 1, n=1,2,1,5,10,2,1,0,1,3	-0.1 (± 0.88)	6.5 (± 9.19)	6.0 (± 99999)	99999 (± 99999)

Cycle 11 Day 1, n=0,2,1,7,12,2,2,0,1,3	-0.2 (± 1.53)	7.0 (± 8.49)	3.5 (± 3.54)	99999 (± 99999)
Cycle 12 Day 1, n=0,2,0,5,12,2,2,0,1,2	-0.2 (± 2.33)	6.5 (± 9.19)	3.5 (± 3.54)	99999 (± 99999)
Cycle 13 Day 1, n=0,2,0,5,10,2,2,0,1,2	0.5 (± 2.22)	5.5 (± 7.78)	3.0 (± 4.24)	99999 (± 99999)
Cycle 14 Day 1, n=0,2,0,6,11,2,2,0,1,3	0.3 (± 0.79)	6.0 (± 8.49)	2.5 (± 3.54)	99999 (± 99999)
Cycle 15 Day 1, n=0,2,0,6,9,0,2,0,1,3	0.1 (± 1.36)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 16 Day 1, n=0,2,0,5,9,1,2,0,1,2	-0.2 (± 1.99)	1.0 (± 99999)	1.5 (± 6.36)	99999 (± 99999)
Cycle 17 Day 1, n=0,2,0,5,9,1,2,0,1,3	0.1 (± 1.17)	-3.0 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 18 Day 1, n=0,2,0,5,9,1,2,0,0,2	0.0 (± 1.73)	-2.0 (± 99999)	3.0 (± 4.24)	99999 (± 99999)
Cycle 19 Day 1, n=0,2,0,5,9,1,2,0,1,2	-0.6 (± 2.65)	0.0 (± 99999)	3.5 (± 4.95)	99999 (± 99999)
Cycle 20 Day 1, n=0,2,0,5,9,1,2,0,1,2	0.7 (± 2.12)	0.0 (± 99999)	3.5 (± 3.54)	99999 (± 99999)
Cycle 21 Day 1, n=0,2,0,5,9,1,2,0,1,2	0.1 (± 2.09)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 22 Day 1, n=0,2,0,5,9,1,2,0,1,3	0.1 (± 1.45)	0.0 (± 99999)	3.5 (± 3.54)	99999 (± 99999)
Cycle 23 Day 1, n=0,2,0,5,8,1,2,0,1,2	0.1 (± 1.81)	-1.0 (± 99999)	1.5 (± 3.54)	99999 (± 99999)
Cycle 24 Day 1, n=0,2,0,5,8,1,2,0,1,2	0.6 (± 0.74)	1.0 (± 99999)	1.5 (± 4.95)	99999 (± 99999)
Cycle 25 Day 1, n=0,2,0,5,7,1,2,0,1,2	-0.9 (± 2.27)	-2.0 (± 99999)	2.5 (± 4.95)	99999 (± 99999)
Cycle 26 Day 1, n=0,2,0,5,8,1,2,0,1,3	-0.4 (± 2.77)	-1.0 (± 99999)	2.0 (± 4.24)	99999 (± 99999)
Cycle 27 Day 1, n=0,2,0,5,7,1,2,0,1,2	-0.1 (± 2.67)	-1.0 (± 99999)	3.5 (± 3.54)	99999 (± 99999)
Cycle 28 Day 1, n=0,2,0,4,7,1,2,0,1,3	0.7 (± 0.76)	-2.0 (± 99999)	3.0 (± 2.83)	99999 (± 99999)
Cycle 29 Day 1, n=0,2,0,4,8,1,2,0,1,3	0.1 (± 1.81)	0.0 (± 99999)	3.5 (± 3.54)	99999 (± 99999)
Cycle 30 Day 1, n=0,2,0,4,5,1,2,0,1,3	0.4 (± 0.55)	0.0 (± 99999)	3.0 (± 2.83)	99999 (± 99999)
Cycle 31 Day 1, n=0,2,0,3,6,1,2,0,0,3	0.7 (± 0.82)	0.0 (± 99999)	3.0 (± 4.24)	99999 (± 99999)
Cycle 32 Day 1, n=0,2,0,3,5,0,2,0,1, 2	0.4 (± 0.55)	99999 (± 99999)	3.5 (± 3.54)	99999 (± 99999)
Cycle 33 Day 1, n=0,2,0,3,4,0,2,0,1, 2	0.5 (± 0.58)	99999 (± 99999)	3.5 (± 3.54)	99999 (± 99999)
Cycle 34 Day 1, n=0,2,0,2,4,0,2,0,1, 2	0.3 (± 0.50)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 35 Day 1, n=0,2,0,1,4,0,2,0,1, 1	0.3 (± 0.50)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 36 Day 1, n=0,2,0,1,3,0,2,0,1, 1	0.0 (± 0.00)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 37 Day 1, n=0,2,0,1,2,0,2,0,0,0	0.0 (± 0.00)	99999 (± 99999)	3.5 (± 4.95)	99999 (± 99999)
Cycle 38 Day 1, n=0,2,0,1,2,0,2,0,1,0	0.0 (± 0.00)	99999 (± 99999)	3.0 (± 2.83)	99999 (± 99999)
Cycle 39 Day 1, n=0,1,0,1,2,0,2,0,0,0	-0.5 (± 0.71)	99999 (± 99999)	3.5 (± 4.95)	99999 (± 99999)
Cycle 40 Day 1, n=0,1,0,1,1,0,2,0,0,0	0.0 (± 99999)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 41 Day 1, n=0,2,0,1,1,0,2,0,0,0	0.0 (± 99999)	99999 (± 99999)	1.5 (± 6.36)	99999 (± 99999)

Cycle 42 Day 1, n=0,2,0,1,1,0,2,0,0,0	0.0 (± 99999)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 43 Day 1, n=0,2,0,1,0,0,2,0,0,0	99999 (± 99999)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 44 Day 1, n=0,2,0,1,0,0,2,0,0,0	99999 (± 99999)	99999 (± 99999)	3.0 (± 4.24)	99999 (± 99999)
Cycle 45 Day 1, n=0,1,0,1,0,0,1,0,0,0	99999 (± 99999)	99999 (± 99999)	1.0 (± 99999)	99999 (± 99999)
Cycle 46 Day 1, n=0,1,0,1,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 47 Day 1, n=0,1,0,1,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 48 Day 1, n=0,1,0,1,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 49 Day 1, n=0,2,0,0,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 50 Day 1, n=0,1,0,0,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 51 Day 1, n=0,1,0,0,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 52 Day 1, n=0,1,0,0,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
End of treatment, n=1,0,3,1,4,0,0,1,1	-2.3 (± 5.19)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Cycle 1 Day 1, n=2,0,2,7,9,0,0,0,1,1	0.0 (± 99999)	0.0 (± 99999)		
Cycle 2 Day 1, n=1,3,1,9,16,3,2,2,2,3	0.0 (± 0.00)	-0.3 (± 1.15)		
Cycle 3 Day 1,2,3,2,8,15,2,2,0,1,3	0.0 (± 99999)	-1.0 (± 1.00)		
Cycle 4 Day 1, n=1,2,2,8,14,3,2,0,1,3	0.0 (± 99999)	-0.7 (± 1.15)		
Cycle 5 Day 1, n=2,2,2,7,11,3,2,0,1,3	0.0 (± 99999)	-0.5 (± 0.71)		
Cycle 6 Day 1, =1,2,2,7,12,3,2,0,1,3	0.0 (± 99999)	-1.3 (± 2.31)		
Cycle 7 Day 1, n=0,2,1,7,11,2,1,0,0,3	0.0 (± 99999)	-0.7 (± 1.15)		
Cycle 8 Day 1, n=1,2,1,5,10,2,1,0,1,3	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 9 Day 1, n=0,2,1,7,11,2,1,0,0,3	99999 (± 99999)	-0.3 (± 0.58)		
Cycle 10 Day 1, n=1,2,1,5,10,2,1,0,1,3	0.0 (± 99999)	-1.7 (± 1.53)		
Cycle 11 Day 1, n=0,2,1,7,12,2,2,0,1,3	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 12 Day 1, n=0,2,0,5,12,2,2,0,1,2	0.0 (± 99999)	-0.7 (± 0.58)		
Cycle 13 Day 1, n=0,2,0,5,10,2,2,0,1,2	0.0 (± 99999)	-0.5 (± 0.71)		
Cycle 14 Day 1, n=0,2,0,6,11,2,2,0,1,3	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 15 Day 1, n=0,2,0,6,9,0,2,0,1,3	0.0 (± 99999)	-0.3 (± 0.58)		
Cycle 16 Day 1, n=0,2,0,5,9,1,2,0,1,2	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 17 Day 1, n=0,2,0,5,9,1,2,0,1,3	0.0 (± 99999)	-1.3 (± 1.53)		
Cycle 18 Day 1, n=0,2,0,5,9,1,2,0,0,2	99999 (± 99999)	0.0 (± 0.00)		
Cycle 19 Day 1, n=0,2,0,5,9,1,2,0,1,2	0.0 (± 99999)	-0.5 (± 0.71)		
Cycle 20 Day 1, n=0,2,0,5,9,1,2,0,1,2	0.0 (± 99999)	-0.5 (± 0.71)		
Cycle 21 Day 1, n=0,2,0,5,9,1,2,0,1,2	0.0 (± 99999)	-0.5 (± 0.71)		

Cycle 22 Day 1, n=0,2,0,5,9,1,2,0,1,3	-1.0 (± 99999)	-0.3 (± 0.58)		
Cycle 23 Day 1, n=0,2,0,5,8,1,2,0,1,2	0.0 (± 99999)	-2.3 (± 4.04)		
Cycle 24 Day 1, n=0,2,0,5,8,1,2,0,1,2	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 25 Day 1, n=0,2,0,5,7,1,2,0,1,2	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 26 Day 1, n=0,2,0,5,8,1,2,0,1,3	0.0 (± 99999)	-0.3 (± 0.58)		
Cycle 27 Day 1, n=0,2,0,5,7,1,2,0,1,2	0.0 (± 99999)	-1.0 (± 1.41)		
Cycle 28 Day 1, n=0,2,0,4,7,1,2,0,1,3	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 29 Day 1, n=0,2,0,4,8,1,2,0,1,3	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 30 Day 1, n=0,2,0,4,5,1,2,0,1,3	0.0 (± 99999)	-1.0 (± 1.00)		
Cycle 31 Day 1, n=0,2,0,3,6,1,2,0,0,3	99999 (± 99999)	0.0 (± 0.00)		
Cycle 32 Day 1, n=0,2,0,3,5,0,2,0,1, 2	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 33 Day 1, n=0,2,0,3,4,0,2,0,1, 2	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 34 Day 1, n=0,2,0,2,4,0,2,0,1, 2	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 35 Day 1, n=0,2,0,1,4,0,2,0,1, 1	0.0 (± 99999)	0.0 (± 99999)		
Cycle 36 Day 1, n=0,2,0,1,3,0,2,0,1, 1	0.0 (± 99999)	0.0 (± 99999)		
Cycle 37 Day 1, n=0,2,0,1,2,0,2,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 38 Day 1, n=0,2,0,1,2,0,2,0,1,0	0.0 (± 99999)	99999 (± 99999)		
Cycle 39 Day 1, n=0,1,0,1,2,0,2,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 40 Day 1, n=0,1,0,1,1,0,2,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 41 Day 1, n=0,2,0,1,1,0,2,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 42 Day 1, n=0,2,0,1,1,0,2,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 43 Day 1, n=0,2,0,1,0,0,2,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 44 Day 1, n=0,2,0,1,0,0,2,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 45 Day 1, n=0,1,0,1,0,0,1,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 46 Day 1, n=0,1,0,1,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 47 Day 1, n=0,1,0,1,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 48 Day 1, n=0,1,0,1,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 49 Day 1, n=0,2,0,0,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 50 Day 1, n=0,1,0,0,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 51 Day 1, n=0,1,0,0,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)		
Cycle 52 Day 1, n=0,1,0,0,0,0,0,0,0,0	99999 (± 99999)	99999 (± 99999)		
End of treatment, n=1,0,3,1,4,0,0,1,1	-15.0 (± 99999)	0.0 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Tumor Response (TTR) and Intracranial TTR (Phase 2 and DDI sub-study)

End point title	Time to Tumor Response (TTR) and Intracranial TTR (Phase 2 and DDI sub-study)[28]

End point description:

TTR: time from first dose of study treatment to first documentation of objective tumor response (CR or PR). For participants whose objective response proceeded from PR to CR, onset of PR was taken as onset of response. TTR was calculated for subgroup of participants with confirmed objective tumor response. Intracranial TTR was calculated for participants with confirmed intracranial objective response. CR: disappearance of all non-lymph node target lesions (where all target lesions are recorded with length of 0 mm on Target Lesions eCRF). Any pathological lymph nodes (recorded as target lesion) must have reduction in short axis to <10 mm. PR: 30% or more decrease in SLD of target lesions, taking as reference baseline SLD. TTR analysis set: ITT participants who had confirmed objective response; intracranial TTR analysis set:all ITT participants who had CNS metastases,achieved confirmed intracranial objective response."Number Analyzed": participants evaluable for specified rows.

End point type	Secondary

End point timeframe:

From first dose of study treatment until CR or PR (maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[28] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	21	34	26
Units: Months				
median (full range (min-max))				
TTR, n=27,21,34,26,17,18,13	1.4 (1.2 to 5.4)	1.4 (1.2 to 18.0)	1.4 (1.1 to 16.6)	2.6 (1.2 to 16.4)
Intracranial TTR, n=6,10,22,24,16,14,4	2.1 (1.2 to 2.8)	1.4 (1.2 to 1.5)	1.4 (1.1 to 5.7)	1.7 (1.2 to 17.5)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)	DDI Substudy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	13	
Units: Months				
median (full range (min-max))				
TTR, n=27,21,34,26,17,18,13	1.4 (1.2 to 9.3)	1.4 (1.3 to 29.7)	1.4 (1.2 to 11.0)	
Intracranial TTR, n=6,10,22,24,16,14,4	1.4 (1.2 to 10.6)	1.4 (1.2 to 28.9)	2.0 (1.1 to 4.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) and Intracranial DOR (Phase 2 and DDI

Substudy)

End point title	Duration of Response (DOR) and Intracranial DOR (Phase 2 and DDI Substudy)[29]

End point description:

DOR: time from first documentation of objective tumor response (CR/PR) to first documentation of PD or to death due to any cause, whichever occurred first. DOR: calculated for subgroup of participants with confirmed objective tumor response. Intracranial(IC) DOR: calculated for participants with confirmed IC OR. CR:disappearance of all non-lymph node target lesions (where all target lesions are recorded with length of 0mm on Target Lesion eCRF). Any pathological lymph node (recorded as target lesion) must have reduction in short axis to <10mm. PR:30% or more decrease in SLD of target lesion, taking as reference baseline SLD. PD:20% or more increase in SLD of target lesion relative to baseline or smallest SLD (nadir) recorded since first dose, demonstrate absolute increase of at least 5mm (>=5mm) relative to baseline or smallest SLD.99999: Upper limit could not be calculated due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From first dose of study treatment to first documentation of PD or to death due to any cause, whichever occurred first (maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[29] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	21	34	26
Units: Months				
median (confidence interval 95%)				
DOR, n=27,21,34,26,17,18,13	17.16 (12.45 to 35.09)	16.56 (4.20 to 99999)	11.10 (5.55 to 99999)	15.08 (5.55 to 26.28)
Intra-cranial DOR, n=6,10,22,24,16,14,4	99999 (8.28 to 99999)	99999 (20.99 to 99999)	37.12 (8.38 to 99999)	14.52 (11.07 to 99999)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)	DDI Substudy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	13	
Units: Months				
median (confidence interval 95%)				
DOR, n=27,21,34,26,17,18,13	7.03 (4.17 to 11.01)	19.61 (11.10 to 99999)	5.19 (4.17 to 99999)	
Intra-cranial DOR, n=6,10,22,24,16,14,4	10.32 (6.90 to 14.98)	17.62 (4.99 to 99999)	99999 (2.76 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Disease Control and Intracranial

Disease Control at Week 12 and 24 (Phase 2 and DDI Substudy)

End point title	Percentage of Participants Achieving Disease Control and Intracranial Disease Control at Week 12 and 24 (Phase 2 and DDI Substudy)[30]

End point description:

Tumor response was evaluated according to RECIST version 1.1, and disease control:confirmed CR, PR, or stable disease (SD). CR: disappearance of all non-lymph node target lesions (where all target lesions are recorded with length of 0 mm on Target Lesions eCRF). Any pathological lymph nodes (recorded as target lesion) must have reduction in short axis to <10 mm. PR: 30 % or more decrease in SLD of target lesions, taking as reference the baseline SLD. SD= when neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD is observed, taking as reference smallest sum diameters while on study. Intracranial assessment was only performed for participants CNS metastases. ITT analysis set:all enrolled participants with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922; participants with CNS metastases in ITT analysis set was used for intracranial response assessment. 'Number Analyzed': participants evaluable for specified rows.

End point type	Secondary

End point timeframe:

Weeks 12 and 24

Notes:

[30] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	27	60	65
Units: Percentage of participants				
number (confidence interval 95%)				
DCR at Week 12, n=30,27,60,65,47,47,32	93.3 (77.9 to 99.2)	85.2 (66.3 to 95.8)	68.3 (55.0 to 79.7)	64.6 (51.8 to 76.1)
DCR at Week 24, n=30,27,60,65,47,47,32	83.3 (65.3 to 94.4)	63.0 (42.4 to 80.6)	51.7 (38.4 to 64.8)	49.2 (36.6 to 61.9)
Intra-cranial DCR at Week 12,n=8,17,33,45,37,25,16	87.5 (47.3 to 99.7)	94.1 (71.3 to 99.9)	75.8 (57.7 to 88.9)	75.6 (60.5 to 87.1)
Intra-cranial DCR at Week 24,n=8,17,33,45,37,25,16	75.0 (34.9 to 96.8)	70.6 (44.0 to 89.7)	60.6 (42.1 to 77.1)	62.2 (46.5 to 76.2)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)	DDI Substudy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	47	32	
Units: Percentage of participants				
number (confidence interval 95%)				
DCR at Week 12, n=30,27,60,65,47,47,32	50.0 (34.9 to 65.1)	66.0 (50.7 to 79.1)	56.3 (37.7 to 73.6)	
DCR at Week 24, n=30,27,60,65,47,47,32	32.6 (19.5 to 48.0)	48.9 (34.1 to 63.9)	34.4 (18.6 to 53.2)	
Intra-cranial DCR at Week 12,n=8,17,33,45,37,25,16	67.6 (50.2 to 82.0)	72.0 (50.6 to 87.9)	56.3 (29.9 to 80.2)	
Intra-cranial DCR at Week 24,n=8,17,33,45,37,25,16	48.6 (31.9 to 65.6)	52.0 (31.3 to 72.2)	43.8 (19.8 to 70.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression on the Last Prior Therapy (Phase 2)

End point title	Time to Progression on the Last Prior Therapy (Phase 2)[31]

End point description:

TTP on last prior therapy was defined as time from first dose date of last prior treatment regimen to date of progression. Progressive disease: 20% or more increase in SLD of target lesions relative to baseline or smallest SLD (nadir) recorded since first dose. SLD must also demonstrate an absolute increase of at least 5 mm (>= 5 mm) relative to baseline or smallest SLD (nadir) recorded since first dose.ITT analysis set: all enrolled participants with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922. As planned in SAP, this outcome measure was not analyzed for EXP-1 and EXP-6 groups. Number Analyzed: participants evaluable for specified rows. 99999: Upper limit could not be calculated due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From first dose of study treatment until progression (maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[31] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)	EXP-5 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	60	65	46
Units: Months				
median (confidence interval 95%)				
Prior systemic therapy before PF-06463922	11.5 (7.2 to 19.6)	12.8 (10.9 to 16.9)	10.2 (7.6 to 15.9)	3.7 (2.1 to 6.4)
Prior ALK+/ROS1+ TKI treatment	11.5 (7.2 to 19.6)	13.8 (11.2 to 18.1)	12.1 (7.9 to 16.4)	3.7 (2.1 to 6.6)
Prior systemic therapy other than ALK+/ROS1+ TKI	19.6 (16.1 to 99999)	8.5 (5.0 to 12.6)	5.0 (3.1 to 10.0)	5.6 (3.5 to 11.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Tumor Progression (TTP) and Intracranial TTP (Phase 2 and DDI Substudy)

End point title	Time to Tumor Progression (TTP) and Intracranial TTP (Phase 2 and DDI Substudy)[32]

End point description:

TTP: time from first dose of study treatment to first documentation of objective PD. Intracranial TTP: time from first dose of study treatment to date of first documentation of objective progression of intracranial disease, based on either new brain metastases or progression of existing brain metastases.PD: 20% or more increase in SLD of target lesions relative to baseline or smallest SLD (nadir) recorded since first dose. SLD must also demonstrate absolute increase of at least 5 mm (>= 5 mm) relative to baseline or the smallest SLD (nadir) recorded since first dose. ITT analysis set: all enrolled participants with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922; ITT participants with CNS metastases were analyzed for intracranial TTP.99999: Upper limit could not be calculated due to insufficient number of participants with events. Median and Upper limit could not be calculated due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From first dose of study treatment until progression (maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[32] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	27	60	65
Units: Months				
median (confidence interval 95%)				
TTP	17.7 (12.5 to 40.5)	20.6 (5.5 to 99999)	8.2 (5.5 to 12.5)	8.4 (5.6 to 13.7)
Intracranial TTP	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (15.0 to 99999)	22.1 (15.7 to 99999)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)	DDI Substudy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	47	32	
Units: Months				
median (confidence interval 95%)				
TTP	5.6 (4.0 to 8.3)	12.5 (8.2 to 26.2)	5.7 (4.1 to 8.3)	
Intracranial TTP	16.4 (12.7 to 99999)	99999 (34.5 to 99999)	99999 (6.9 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Probability of First Event Being a Central Nervous System (CNS) Progression, Non CNS Progression, or Death (Phase 2)

End point title	Probability of First Event Being a Central Nervous System (CNS) Progression, Non CNS Progression, or Death (Phase 2)

End point description:

Probability of first event being CNS progression, non-CNS progression, or death was evaluated with competing risk approach by estimating cumulative incidence functions (range: 0-1) relative to analysis set. Time to first event being Competing Event (either CNS progression or non CNS progression or Death)=time from first dose until date of that specific event. Participants not known to have any of Competing Events were censored on date they were last assessed for disease status for PFS. Participants who presented one type of event were counted as competing cause of failure for analysis of other type of events. PD:20% or more increase in SLD of target lesion relative to baseline or smallest SLD (nadir) recorded since first dose. SLD must demonstrate absolute increase of atleast 5mm(>=5 mm) relative to baseline or smallest SLD (nadir) recorded since first dose.ITT analysis set: all enrolled participants with documented ALK or ROS1 rearrangement & received at least 1 dose of PF-06463922.

End point type	Secondary

End point timeframe:

From first dose of study treatment until progression (maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

End point values	Phase 2 ITT Population			
Subject group type	Subject analysis set			
Number of subjects analysed	274			
Units: Probability of events				
number (not applicable)				
CNS progression	0.179			
Non CNS progression	0.325			
Death	0.055			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) (Phase 2 and DDI Substudy)

End point title	Progression-Free Survival (PFS) (Phase 2 and DDI

End point description:

PFS was defined as time from first dose of study treatment to first documentation of objective disease progression or to death on study due to any cause, whichever came first. Progressive disease was defined by a 20% or more increase in SLD of target lesions relative to baseline or smallest SLD (nadir) recorded since first dose. In addition to relative increase of 20%, SLD must also demonstrate an absolute increase of at least 5 mm (>= 5 mm) relative to baseline or smallest SLD (nadir) recorded since first dose. Results presented here were based on independent central review. PFS analysis set included all participants with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922. 99999: Upper limit could not be calculated due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From first dose of study treatment to first documentation of objective disease progression or death due to any cause, whichever came first(maximum of 89.65 month of treatment exposure-Phase 2, maximum of 68.69 month of treatment exposure-DDI participant)

Notes:

[33] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	27	60	65
Units: Months				
median (confidence interval 95%)	16.6 (11.8 to 28.3)	20.6 (5.5 to 99999)	6.9 (5.5 to 11.0)	7.3 (4.2 to 11.1)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)	DDI Substudy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	47	32	
Units: Months				
median (confidence interval 95%)	5.5 (3.9 to 8.2)	9.9 (5.5 to 21.0)	5.7 (4.0 to 7.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (Phase 2 and DDI Substudy)

End point title	Overall Survival (Phase 2 and DDI Substudy)[34]

End point description:

OS was defined as the time from first dose to the date of death due to any cause. For participants still alive at the time of analysis, the OS time was censored on the last date the participants were known to be alive. Estimates of OS and its 95% confidence interval were determined using Kaplan-Meier method. ITT analysis set: all enrolled participants with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922. 99999: Median and upper limit could not be calculated due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From first dose of study treatment until date of death (maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[34] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	27	60	65
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	52.5 (24.4 to 99999)	99999 (38.5 to 99999)	18.7 (15.1 to 34.1)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)	DDI Substudy	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	47	32	
Units: Months				
median (confidence interval 95%)	20.4 (10.5 to 31.6)	49.7 (21.0 to 99999)	19.8 (11.1 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of PF-06463922 (Phase 2)

End point title	Maximum Observed Plasma Concentration (Cmax) of PF-06463922 (Phase 2)

End point description:

Maximum observed plasma concentration (Cmax) of PF-06463922 was observed directly from data. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. Here, "Overall Number Analyzed" signifies participants analyzed for this outcome measure. Here, 'Number Analyzed' signifies participants evaluable for specified rows.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24, 48, 72, 96 and 120 hours post-dose on Day -7 and pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 15

End point values	Phase 2 and Japan LIC PK Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day -7, n=19	695.2 (± 40)			
Cycle 1 Day 15, n=22	576.5 (± 42)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time for Cmax (Tmax) of PF-06463922 (Phase 2)

End point title	Time for Cmax (Tmax) of PF-06463922 (Phase 2)

End point description:

Tmax of PF-06463922 was observed directly from data as time of first occurrence. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. Here, "Number Analyzed" signifies participants analyzed for this outcome measure. Here, 'Number Analyzed' signifies participants evaluable for specified rows.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24, 48, 72, 96 and 120 hours post-dose on Day -7 and pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 15

End point values	Phase 2 and Japan LIC PK Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: Hours				
median (full range (min-max))				
Day -7, n=19 Cycle 1 Day 15, n=22	1.15 (0.50 to 4.02) 1.96 (0.50 to 22.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the Plasma Concentration-Time Profile from Time Zero Extrapolated to Infinite Time (AUCinf) of PF-06463922 (Phase 2)

End point title	Area under the Plasma Concentration-Time Profile from Time Zero Extrapolated to Infinite Time (AUCinf) of PF-06463922 (Phase 2)

End point description:

AUCinf was calculated as AUClast + (Clast*/kel), where AUClast was area under plasma concentration-time profile from time 0 to time of last quantifiable concentration, Clast* was predicted plasma concentration at last quantifiable time point estimated from log-linear regression analysis, and kel was rate constant for terminal phase.PK parameter analysis set for PF-06463922: all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of PK parameters of interest for PF-06463922. Here, 'Overall Number of Participants Analyzed' signifies participants analyzed for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24, 48, 72, 96 and 120 hours post-dose on Day -7

End point values	Phase 2 and Japan LIC PK Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: ng*hour/mL				
geometric mean (geometric coefficient of variation)	9088 (± 35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the Plasma Concentration-Time profile from Time Zero to Time Tau (AUCtau) of PF-06463922 (Phase 2)

End point title	Area under the Plasma Concentration-Time profile from Time Zero to Time Tau (AUCtau) of PF-06463922 (Phase 2)

End point description:

Tau refers to the dosing interval, and it equals to 24 hours for QD dosing which was adopted in Phase 2. AUCtau was determined using linear/log trapezoidal method. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. Here, 'Number Analyzed' signifies participants evaluable for specified row.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Day -7 and pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 15

End point values	Phase 2 and Japan LIC PK Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: ng*hour/mL				
geometric mean (geometric coefficient of variation)				
Day -7, n=19	5308 (± 36)			
Cycle 1 Day 15, n=22	5650 (± 39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution (Vz/F) of PF-06463922 (Phase 2)

End point title	Apparent Volume of Distribution (Vz/F) of PF-06463922 (Phase 2)

End point description:

Vz/F was defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired plasma concentration of a drug, and calculated as dose/(AUCinf*kel), where AUCinf was the area under the plasma concentration-time profile from time 0 extrapolated to infinite time, kel was the rate constant for terminal phase. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. Here, "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24, 48, 72, 96 and 120 hours post-dose on Day -7

End point values	Phase 2 and Japan LIC PK Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: Liters				
geometric mean (geometric coefficient of variation)	351.5 (± 37)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Oral Clearance (CL/F) of PF-06463922 (Phase 2)

End point title	Apparent Oral Clearance (CL/F) of PF-06463922 (Phase 2)

End point description:

Clearance of a drug is a measure of the rate at which a drug is metabolized or eliminated by normal biological processes. CL/F was calculated as dose/AUCinf, where AUCinf was the area under the plasma concentration-time profile from time 0 extrapolated to infinite time.PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. Here, 'Number Analyzed' signifies participants evaluable for specified row.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24, 48, 72, 96 and 120 hours post-dose on Day -7 and pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 15

End point values	Phase 2 and Japan LIC PK Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: Liter/hour				
geometric mean (geometric coefficient of variation)				
Day -7, n=16	11.01 (± 35)			
Cycle 1 Day 15, n=22	17.70 (± 39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Half-Life of PF-06463922 (Phase 2)

End point title	Terminal Half-Life of PF-06463922 (Phase 2)

End point description:

Terminal plasma half-life was defined as the time measured for the plasma concentration to decrease by one half, and calculated as loge(2)/kel, where kel was the rate constant for terminal phase. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. Here, "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9, 24, 48, 72, 96 and 120 hours post-dose on Day -7

End point values	Phase 2 and Japan LIC PK Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: Hours				
arithmetic mean (standard deviation)	23.58 (± 9.3743)			

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Accumulation Ratio (Rac) of PF-06463922 Following Multiple Oral Doses (Phase 2)

End point title	Observed Accumulation Ratio (Rac) of PF-06463922 Following Multiple Oral Doses (Phase 2)

End point description:

Rac was calculated as Day 15 AUCtau/Day -7 AUCtau, where AUCtau was the area under the plasma concentration-time profile from time 0 to time tau (24 hours for QD dosing regimen which was adopted in Phase 2). PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. Here, "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 15

End point values	Phase 2 and Japan LIC PK Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Ratio				
arithmetic mean (standard deviation)	1.082 (± 0.42701)			

Statistical analyses

No statistical analyses for this end point

Secondary: Steady State Accumulation Ratio (Rss) of PF-06463922 Following Multiple Oral Doses (Phase 2)

End point title	Steady State Accumulation Ratio (Rss) of PF-06463922 Following Multiple Oral Doses (Phase 2)

End point description:

Rss was calculated as Day 15 AUCtau/Day -7 AUCinf, where AUCtau was the area under the plasma concentration-time profile from time 0 to time tau (24 hours for QD dosing regimen which was adopted in Phase 2), and AUCinf was the area under the plasma concentration-time profile from time 0 extrapolated to infinite time. PK parameter analysis set for PF-06463922 included all enrolled participants who received at least 1 dose of PF-06463922 and had sufficient information to estimate at least one of the PK parameters of interest for PF-06463922. Here, "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cycle 1 Day 15

End point values	Phase 2 and Japan LIC PK Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: Ratio				
arithmetic mean (standard deviation)	0.6577 (± 0.28627)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with ALK Mutation Based on Tumor Tissue Analysis (Phase 2)

End point title	Number of Participants with ALK Mutation Based on Tumor Tissue Analysis (Phase 2)[35]

End point description:

Tumor tissues from archived tissue specimens and/or a de novo biopsy were analyzed for ALK kinase domain mutations. Number of participants with one or more ALK mutations is presented. Tumor Tissue

analysis set included all participants of the ITT analysis set who had at least 1 molecular tumor biomarker assayed from either the screening archival or screening de novo tumor biopsy sample (or both). Tumor Tissue analysis set included all participants of the ITT analysis set who had at least 1 molecular tumor biomarker assayed from either the screening archival or screening de novo tumor biopsy sample (or both).

End point type	Secondary

End point timeframe:

Screening (up to 28 days)

Notes:

[35] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	26	58	63
Units: Participants	0	7	8	12

End point values	EXP-5 (Phase 2)			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Participants	13			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with ALK Mutation Based on Plasma CNA Analysis (Phase 2)

End point title	Number of Participants with ALK Mutation Based on Plasma CNA Analysis (Phase 2)[36]

End point description:

Plasma CNA samples were analyzed for ALK kinase domain mutations by Next Generation Sequencing (NGS). Number of participants with one or more ALK mutations is presented. CNA peripheral blood analysis set included all participants of the ITT analysis set who had at least 1 molecular biomarker assayed. CNA peripheral blood analysis set included all participants of the ITT analysis set who had at least 1 molecular biomarker assayed. Here, "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Screening (up to 28 days)

Notes:

[36] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	26	59	61
Units: Participants	0	6	8	17

End point values	EXP-5 (Phase 2)			
Subject group type	Reporting group			
Number of subjects analysed	46			
Units: Participants	14			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Improved, Worsened or Remained Stable in EORTC QLQ-C30 (Phase 2 and DDI sub-study)

End point title	Number of Participants Who Improved, Worsened or Remained Stable in EORTC QLQ-C30 (Phase 2 and DDI sub-study)[37]

End point description:

EORTC QLQ-C30 (v3.0) consists of 30 questions assessing 5 functional domains (physical, role, emotional, cognitive and social), global QoL, disease/treatment related symptoms (fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation and diarrhea), and the perceived financial impact of disease. Each scale was transformed to a range of 0 to 100 using standard EORTC algorithm. For global QoL and functional scales, higher score indicate better performance, and improvement: increase of at least 10 points, worsening: decrease of at least 10 points. For symptom scales, higher score indicates worse symptoms, and improvement: decrease of at least 10 points, worsening: increase of at least 10 points. All scales which had not improved nor worsened were considered stable.PRO evaluable analysis set: all enrolled participants who received at least 1 dose of PF-06463922 and completed baseline, at least 1 post-baseline PRO assessment.

End point type	Secondary

End point timeframe:

From first dose of study treatment to end of treatment (maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[37] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	26	55	60
Units: Participants				
Improved in global QoL, n=30,26,55,60,43,41,32	17	11	18	25
Stable in global QoL,n=30,26,55,60,43,41,32	10	12	24	22
Worsened in global QoL,n=30,26,55,60,43,41,32	3	3	13	13

Improved physical function,n=30,26,55,60,43,41,32	11	8	13	24
Stable physical function,n=30,26,55,60,43,41,32	13	17	38	24
Worsened physical function,n=30,26,55,60,43,41,32	6	1	4	12
Improved in role function,n=30,26,55,60,43,39,32	12	7	15	25
Stable role function,n=30,26,55,60,43,39,32	9	16	33	18
Worsened role function,n=30,26,55,60,43,39,32	9	3	7	17
Improved emotional function,n=30,26,55,60,43,41,32	13	12	13	20
Stable emotional function,n=30,26,55,60,43,41,32	13	14	32	34
Worsened emotional function,n=30,26,55,60,43,41,32	4	0	10	6
Improved cognitive function,n=30,26,55,60,43,41,32	9	4	5	12
Stable cognitive function,n=30,26,55,60,43,41,32	12	14	36	34
Worsened cognitive function,n=30,26,55,60,43,41,32	9	8	14	14
Improved social function,n=30,26,55,60,43,41,32	14	7	16	20
Stable in social function,n=30,26,55,60,43,41,32	11	16	33	29
Worsened social function,n=30,26,55,60,43,41,32	5	3	6	11
Improved fatigue,n=30,26,55,60,43,41,32	18	14	22	28
Stable in fatigue,n=30,26,55,60,43,41,32	8	11	25	23
Worsened in fatigue,n=30,26,55,60,43,41,32	4	1	8	9
Improved nausea & vomiting,n=30,26,55,60,43,41,32	8	5	10	16
Stable nausea & vomiting,n=30,26,55,60,43,41,32	22	21	44	39
Worsened nausea & vomiting,n=30,26,55,60,43,41,32	0	0	1	5
Improved in pain,n=30,26,55,60,43,41,32	13	10	20	23
Stable in pain,n=30,26,55,60,43,41,32	10	14	25	28
Worsened in pain,n=30,26,55,60,43,41,32	7	2	10	9
Improved in dyspnea,n=30,26,55,60,43,41,32	16	10	10	23
Stable in dyspnea,n=30,26,55,60,43,41,32	10	14	33	22
Worsened in dyspnea,n=30,26,55,60,43,41,32	4	2	12	15
Improved in insomnia,n=30,26,55,60,43,41,32	20	8	18	30
Stable in insomnia,n=30,26,55,60,43,41,32	9	13	28	22
Worsened in insomnia,n=30,26,55,60,43,41,32	1	5	9	8
Improved in appetite loss,n=30,26,55,60,43,41,32	14	4	18	29

Stable in appetite loss,n=30,26,55,60,43,41,32	16	22	36	26
Worsened in appetite loss,n=30,26,55,60,43,41,32	0	0	1	5
Improved in constipation,n=30,26,55,60,43,41,32	10	5	9	16
Stable in constipation,n=30,26,55,60,43,41,32	14	19	33	33
Worsened in constipation,n=30,26,55,60,43,41,32	6	2	13	11
Improved in diarrhea,n=30,26,55,60,43,41,32	5	3	10	10
Stable in diarrhea,n=30,26,55,60,43,41,32	18	21	40	39
Worsened in diarrhea,n=30,26,55,60,43,41,32	7	2	5	11
Improved finance difficulty,n=30,26,55,60,43,41,32	10	6	11	13
Stable financial difficulty,n=30,26,55,60,43,41,32	17	19	34	38
Worsen financial difficulty,n=30,26,55,60,43,41,32	3	1	10	9

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)	DDI Substudy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43	41	32	
Units: Participants				
Improved in global QoL, n=30,26,55,60,43,41,32	17	19	12	
Stable in global QoL,n=30,26,55,60,43,41,32	16	15	18	
Worsened in global QoL,n=30,26,55,60,43,41,32	10	6	2	
Improved physical function,n=30,26,55,60,43,41,32	8	11	5	
Stable physical function,n=30,26,55,60,43,41,32	25	23	23	
Worsened physical function,n=30,26,55,60,43,41,32	10	6	4	
Improved in role function,n=30,26,55,60,43,39,32	18	17	10	
Stable role function,n=30,26,55,60,43,39,32	13	17	15	
Worsened role function,n=30,26,55,60,43,39,32	12	5	7	
Improved emotional function,n=30,26,55,60,43,41,32	17	16	10	
Stable emotional function,n=30,26,55,60,43,41,32	20	22	20	
Worsened emotional function,n=30,26,55,60,43,41,32	6	2	2	
Improved cognitive function,n=30,26,55,60,43,41,32	12	12	9	
Stable cognitive function,n=30,26,55,60,43,41,32	19	20	11	
Worsened cognitive function,n=30,26,55,60,43,41,32	12	8	12	

Improved social function,n=30,26,55,60,43,41,32	11	13	13	
Stable in social function,n=30,26,55,60,43,41,32	21	18	13	
Worsened social function,n=30,26,55,60,43,41,32	11	9	6	
Improved fatigue,n=30,26,55,60,43,41,32	26	16	17	
Stable in fatigue,n=30,26,55,60,43,41,32	9	20	9	
Worsened in fatigue,n=30,26,55,60,43,41,32	8	4	6	
Improved nausea & vomiting,n=30,26,55,60,43,41,32	13	10	6	
Stable nausea & vomiting,n=30,26,55,60,43,41,32	28	28	24	
Worsened nausea & vomiting,n=30,26,55,60,43,41,32	2	2	2	
Improved in pain,n=30,26,55,60,43,41,32	19	21	14	
Stable in pain,n=30,26,55,60,43,41,32	19	12	13	
Worsened in pain,n=30,26,55,60,43,41,32	5	7	5	
Improved in dyspnea,n=30,26,55,60,43,41,32	14	14	9	
Stable in dyspnea,n=30,26,55,60,43,41,32	18	17	15	
Worsened in dyspnea,n=30,26,55,60,43,41,32	11	9	8	
Improved in insomnia,n=30,26,55,60,43,41,32	21	19	12	
Stable in insomnia,n=30,26,55,60,43,41,32	16	18	15	
Worsened in insomnia,n=30,26,55,60,43,41,32	6	3	5	
Improved in appetite loss,n=30,26,55,60,43,41,32	22	20	10	
Stable in appetite loss,n=30,26,55,60,43,41,32	21	20	20	
Worsened in appetite loss,n=30,26,55,60,43,41,32	0	0	2	
Improved in constipation,n=30,26,55,60,43,41,32	11	13	10	
Stable in constipation,n=30,26,55,60,43,41,32	29	22	12	
Worsened in constipation,n=30,26,55,60,43,41,32	3	5	10	
Improved in diarrhea,n=30,26,55,60,43,41,32	10	8	6	
Stable in diarrhea,n=30,26,55,60,43,41,32	27	28	21	
Worsened in diarrhea,n=30,26,55,60,43,41,32	6	4	5	
Improved finance difficulty,n=30,26,55,60,43,41,32	10	10	9	
Stable financial difficulty,n=30,26,55,60,43,41,32	22	26	16	
Worsen financial difficulty,n=30,26,55,60,43,41,32	11	4	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Improved, Worsened or Remained Stable in EORTC QLQ-LC13 (Phase 2 and DDI sub-study)

End point title	Number of Participants Who Improved, Worsened or Remained Stable in EORTC QLQ-LC13 (Phase 2 and DDI sub-study)[38]

End point description:

EORTC QLQ-LC13 is the lung cancer module of EORTC QLQ-C30 and includes questions specific to the disease associated symptoms (dyspnea, cough, hemoptysis, and site specific pain), treatment-related symptoms (sore mouth, dysphagia, neuropathy and alopecia), and analgesic use of lung cancer patients. Scale was transformed to a range of 0 to 100 using standard EORTC algorithm. Higher score indicates worse symptoms, and improvement: decrease of at least 10 points, worsening was defined as an increase of at least 10 points. All scales which had not improved nor worsened were considered stable. PRO evaluable analysis set: all enrolled participants who received at least 1 dose of PF-06463922 and completed a baseline and at least 1 post-baseline PRO assessment. Here, "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

From first dose of study treatment to end of treatment (maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[38] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	26	55	60
Units: Participants				
Improved in dyspnea	11	5	9	21
Stable in dyspnea	16	18	36	25
Worsened in dyspnea	3	3	10	14
Improved in coughing	18	9	22	26
Stable in coughing	9	13	26	28
Worsened in coughing	3	4	7	6
Improved in hemoptysis	4	0	7	5
Stable in hemoptysis	24	25	47	52
Worsened in hemoptysis	2	1	1	3
Improved in sore mouth	0	2	4	9
Stable in sore mouth	25	20	44	41
Worsened in sore mouth	5	4	7	10
Improved in dysphagia	3	1	3	7
Stable in dysphagia	23	24	46	48
Worsened in dysphagia	4	1	6	5
Improved in peripheral neuropathy	4	5	9	5

Stable in peripheral neuropathy	10	13	27	33
Worsened in peripheral neuropathy	16	8	19	22
Improved in alopecia	2	1	2	10
Stable in alopecia	18	22	41	40
Worsened in alopecia	10	3	12	10
Improved in chest pain	11	7	13	18
Stable in chest pain	17	17	35	33
Worsened in chest pain	2	2	6	9
Improved in arm or shoulder pain	10	5	14	14
Stable in arm or shoulder pain	15	19	30	36
Worsened in arm or shoulder pain	5	2	11	10
Improved in pain in other parts	9	6	17	20
Stable in pain in other parts	14	15	23	24
Worsened in pain in other parts	7	5	15	16

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)	DDI Substudy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43	41	32	
Units: Participants				
Improved in dyspnea	12	12	6	
Stable in dyspnea	21	23	18	
Worsened in dyspnea	9	6	8	
Improved in coughing	18	17	16	
Stable in coughing	15	18	15	
Worsened in coughing	9	6	1	
Improved in hemoptysis	5	4	1	
Stable in hemoptysis	34	36	31	
Worsened in hemoptysis	3	1	0	
Improved in sore mouth	2	5	4	
Stable in sore mouth	33	28	26	
Worsened in sore mouth	7	8	2	
Improved in dysphagia	4	5	3	
Stable in dysphagia	33	30	27	
Worsened in dysphagia	5	6	2	
Improved in peripheral neuropathy	6	9	9	
Stable in peripheral neuropathy	22	18	16	
Worsened in peripheral neuropathy	14	14	7	
Improved in alopecia	10	9	4	
Stable in alopecia	24	27	21	
Worsened in alopecia	8	5	7	
Improved in chest pain	14	14	13	
Stable in chest pain	25	24	17	
Worsened in chest pain	3	3	2	
Improved in arm or shoulder pain	12	12	9	
Stable in arm or shoulder pain	21	22	19	
Worsened in arm or shoulder pain	9	7	4	
Improved in pain in other parts	15	17	9	
Stable in pain in other parts	9	18	10	

Worsened in pain in other parts	17	6	12	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-Emergent Adverse Events (Phase 1, Phase 2 and DDI sub-study)

End point title	Number of Participants with Treatment-Emergent Adverse Events (Phase 1, Phase 2 and DDI sub-study)[39]

End point description:

AE: any untoward medical occurrence in clinical investigation participant administered product or medical device, regardless of causal relationship to study treatment. Treatment-emergent AEs (TEAE): AE which occurred for first time during effective duration of treatment or AE that increased in severity during treatment. Serious AE (SAE): any untoward medical occurrence at any dose that resulted in death; was life-threatening, required inpatient hospitalization or caused prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity (substantial disruption of ability to conduction normal life function). Severity graded as per National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.03.Grade (G)1: mild, G2:moderate, G3:severe, G4:Life threatening consequences; urgent intervention indicated, G5:death related to AE. Safety analysis set: all enrolled participants who received atleast 1 dose of PF-06463922.

End point type	Secondary

End point timeframe:

From first dose of study treatment to end of treatment (maximum of 96.58 months of treatment exposure for Phase 1, maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[39] - 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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	12
Units: Participants				
AEs (all causality)	3	3	3	12
AEs (treatment-related)	3	3	3	11
SAEs (all causality)	3	2	1	6
SAEs (treatment-related)	1	1	0	1
Grade 3 or 4 (all causality)	3	3	0	6
Grade 3 or 4 (treatment-related)	2	2	0	3
Grade 5 (all causality)	1	1	0	1
Grade 5 (treatment-related)	0	0	0	0

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	3	3	3
Units: Participants				
AEs (all causality)	17	3	3	3
AEs (treatment-related)	16	3	3	1
SAEs (all causality)	10	3	2	2
SAEs (treatment-related)	1	3	0	0
Grade 3 or 4 (all causality)	12	3	2	2
Grade 3 or 4 (treatment-related)	6	2	0	0
Grade 5 (all causality)	4	2	0	0
Grade 5 (treatment-related)	0	0	0	0

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	DDI Substudy	Phase 2
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	3	4	32	275
Units: Participants				
AEs (all causality)	3	4	32	274
AEs (treatment-related)	3	4	31	262
SAEs (all causality)	2	2	13	135
SAEs (treatment-related)	0	1	1	27
Grade 3 or 4 (all causality)	1	4	24	209
Grade 3 or 4 (treatment-related)	1	3	16	137
Grade 5 (all causality)	1	0	5	43
Grade 5 (treatment-related)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Laboratory Abnormalities (Phase 1, Phase 2 and DDI sub-study) – Hematology

End point title	Number of Participants with Laboratory Abnormalities (Phase 1, Phase 2 and DDI sub-study) – Hematology[40]

End point description:

Hematology evaluation included hemoglobin, platelets, white blood cell, absolute neutrophils, absolute lymphocytes, absolute monocytes, absolute eosinophils and absolute basophils. Hematology parameters with any abnormalities were reported in this outcome measure. Safety analysis set included all enrolled participants who received at least 1 dose of PF-06463922. Here, 'Number Analyzed' signifies participants evaluable for specified rows. All participants in Phase 2 received 100 mg of PF-06463922, hence combined data is presented for Phase 2.

End point type	Secondary

End point timeframe:

From first dose of study treatment to end of treatment (maximum of 96.58 months of treatment exposure for Phase 1, maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[40] - 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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	12
Units: Participants				
Anemia, n=3,3,3,12,17,3,3,3,3,4,273,32	3	3	3	10
Hb increased, n=3,3,3,12,17,3,3,3,3,4,273,32	0	0	0	0
LC decreased, n=3,3,3,12,17,3,3,3,3,4,272,32	2	2	2	7
LC increased, n=3,3,3,12,17,3,3,3,3,4,272,32	0	0	0	0
NC decreased, n=3,3,3,12,17,3,3,3,3,4,272,32	1	0	0	4
PC decreased, n=3,3,3,12,17,3,3,3,3,4,273,32	2	2	0	4
WBC decreased, n=3,3,3,12,17,3,3,3,3,4,273,32	2	1	0	4

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	3	3	3
Units: Participants				
Anemia, n=3,3,3,12,17,3,3,3,3,4,273,32	16	3	3	3
Hb increased, n=3,3,3,12,17,3,3,3,3,4,273,32	0	0	0	0
LC decreased, n=3,3,3,12,17,3,3,3,3,4,272,32	4	3	3	0
LC increased, n=3,3,3,12,17,3,3,3,3,4,272,32	3	1	0	0
NC decreased, n=3,3,3,12,17,3,3,3,3,4,272,32	2	0	1	0
PC decreased, n=3,3,3,12,17,3,3,3,3,4,273,32	5	1	0	0
WBC decreased, n=3,3,3,12,17,3,3,3,3,4,273,32	2	2	2	0

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	DDI Substudy	Phase 2
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	3	4	32	275
Units: Participants				
Anemia, n=3,3,3,12,17,3,3,3,3,4,273,32	3	4	25	218
Hb increased, n=3,3,3,12,17,3,3,3,3,4,273,32	0	0	1	7

LC decreased, n=3,3,3,12,17,3,3,3,3,4,272,32	0	2	15	134
LC increased, n=3,3,3,12,17,3,3,3,3,4,272,32	0	0	2	15
NC decreased, n=3,3,3,12,17,3,3,3,3,4,272,32	0	1	3	37
PC decreased, n=3,3,3,12,17,3,3,3,3,4,273,32	0	1	8	74
WBC decreased, n=3,3,3,12,17,3,3,3,3,4,273,32	0	1	4	54

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Laboratory Abnormalities (Phase 1, Phase 2 and DDI sub-study) – Chemistry

End point title	Number of Participants with Laboratory Abnormalities (Phase 1, Phase 2 and DDI sub-study) – Chemistry[41]

End point description:

Chemistry evaluation included alanine aminotransferase (ALT), alkaline phosphatase, aspartate aminotransferase (AST), blood bilirubin, creatine phosphokinase (CPK), creatinine, gamma-glutamyl transferase (GGT), calcium, sodium, potassium, magnesium, albumin, glucose (non-fasted), albumin, phosphorus or phosphate, serum amylase and lipase. The safety analysis set included all enrolled participants who received at least 1 dose of PF-06463922. Here, "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure. Here, 'Number Analyzed' signifies participants evaluable for specified rows. All participants in Phase 2 received 100 mg of PF-06463922, hence combined data is presented for Phase 2.

End point type	Secondary

End point timeframe:

From first dose of study treatment to end of treatment (maximum of 96.58 months of treatment exposure for Phase 1, maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[41] - 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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	12
Units: Participants				
ALT increased, n=3,3,3,12,17,3,3,3,3,4,272,32	2	1	1	6
ALP increased, n=3,3,3,12,17,3,3,3,3,4,272,32	1	1	3	6
AST increased, n=3,3,3,12,17,3,3,3,3,4,272,32	2	2	2	5
Bilirubin increased,n=3,3,3,12,17,3,3,3,3,4,272,	1	0	0	1
CPK increased, n=0,0,0,0,3,1,0,0,1,0,18,2	99999	99999	99999	99999
Creat. increased, n=3,3,3,12,17,3,3,3,3,4,273,32	3	2	3	10

GGT increased, n=1,0,0,0,4,1,1,0,1,2,13,1	0	99999	99999	99999
Hypercalcemia, n=3,3,3,12,17,3,3,3,3,4,273,32	0	0	0	0
Hyperglycemia, n=3,3,3,12,17,3,3,3,3,4,273,32	3	3	2	7
Hyperkalemia, n=3,3,3,12,17,3,3,3,3,4,273,32	0	1	2	3
Hypermagnesemia, n=3,3,3,12,17,3,3,3,3,4,272,32	2	0	0	2
Hypernatremia, n=3,3,3,12,17,3,3,3,3,4,273,32	0	1	0	0
Hypoalbuminemia, n=3,3,3,12,17,3,3,3,3,4,271,32	2	1	3	4
Hypocalcemia, n=3,3,3,12,17,3,3,3,3,4,273,32	1	0	1	4
Hypoglycemia, n=3,3,3,12,17,3,3,3,3,4,273,32	0	0	1	3
Hypokalemia, n=3,3,3,12,17,3,3,3,3,4,273,32	0	0	2	4
Hypomagnesemia, n=3,3,3,12,17,3,3,3,3,4,272,32	0	1	2	4
Hyponatremia, n=3,3,3,12,17,3,3,3,3,4,273,32	2	1	1	2
Hypophosphatemia, n=3,3,3,12,17,3,3,3,3,4,272,32	1	2	0	3
Lipase increased, n=3,3,3,12,17,3,3,3,3,4,270,32	3	0	0	8
S.amylase increased,n=3,3,1,11,16,3,3,3,2,4,265,	3	0	0	2

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	3	3	3
Units: Participants				
ALT increased, n=3,3,3,12,17,3,3,3,3,4,272,32	9	2	2	0
ALP increased, n=3,3,3,12,17,3,3,3,3,4,272,32	10	3	1	0
AST increased, n=3,3,3,12,17,3,3,3,3,4,272,32	8	2	2	0
Bilirubin increased,n=3,3,3,12,17,3,3,3,3,4,272,	0	0	0	0
CPK increased, n=0,0,0,0,3,1,0,0,1,0,18,2	1	1	99999	99999
Creat. increased, n=3,3,3,12,17,3,3,3,3,4,273,32	13	3	3	2
GGT increased, n=1,0,0,0,4,1,1,0,1,2,13,1	1	0	1	99999
Hypercalcemia, n=3,3,3,12,17,3,3,3,3,4,273,32	3	1	0	0
Hyperglycemia, n=3,3,3,12,17,3,3,3,3,4,273,32	8	2	1	1
Hyperkalemia, n=3,3,3,12,17,3,3,3,3,4,273,32	6	1	1	1
Hypermagnesemia, n=3,3,3,12,17,3,3,3,3,4,272,32	2	0	0	0

Hypernatremia, n=3,3,3,12,17,3,3,3,3,4,273,32	4	2	0	0
Hypoalbuminemia, n=3,3,3,12,17,3,3,3,3,4,271,32	7	3	1	1
Hypocalcemia, n=3,3,3,12,17,3,3,3,3,4,273,32	5	2	1	0
Hypoglycemia, n=3,3,3,12,17,3,3,3,3,4,273,32	4	0	1	0
Hypokalemia, n=3,3,3,12,17,3,3,3,3,4,273,32	3	3	1	1
Hypomagnesemia, n=3,3,3,12,17,3,3,3,3,4,272,32	2	3	0	1
Hyponatremia, n=3,3,3,12,17,3,3,3,3,4,273,32	4	1	1	0
Hypophosphatemia, n=3,3,3,12,17,3,3,3,3,4,272,32	3	2	1	1
Lipase increased, n=3,3,3,12,17,3,3,3,3,4,270,32	6	0	1	0
S.amylase increased,n=3,3,1,11,16,3,3,3,2,4,265,	5	0	1	0

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	DDI Substudy	Phase 2
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	3	4	32	273
Units: Participants				
ALT increased, n=3,3,3,12,17,3,3,3,3,4,272,32	0	3	10	109
ALP increased, n=3,3,3,12,17,3,3,3,3,4,272,32	2	3	9	118
AST increased, n=3,3,3,12,17,3,3,3,3,4,272,32	1	3	11	139
Bilirubin increased,n=3,3,3,12,17,3,3,3,3,4,272,	0	1	1	8
CPK increased, n=0,0,0,0,3,1,0,0,1,0,18,2	1	99999	1	9
Creat. increased, n=3,3,3,12,17,3,3,3,3,4,273,32	2	3	20	209
GGT increased, n=1,0,0,0,4,1,1,0,1,2,13,1	0	2	0	8
Hypercalcemia, n=3,3,3,12,17,3,3,3,3,4,273,32	0	1	5	33
Hyperglycemia, n=3,3,3,12,17,3,3,3,3,4,273,32	2	1	23	185
Hyperkalemia, n=3,3,3,12,17,3,3,3,3,4,273,32	1	2	5	71
Hypermagnesemia, n=3,3,3,12,17,3,3,3,3,4,272,32	0	0	0	14
Hypernatremia, n=3,3,3,12,17,3,3,3,3,4,273,32	0	1	3	35
Hypoalbuminemia, n=3,3,3,12,17,3,3,3,3,4,271,32	3	1	18	180
Hypocalcemia, n=3,3,3,12,17,3,3,3,3,4,273,32	0	1	6	53
Hypoglycemia, n=3,3,3,12,17,3,3,3,3,4,273,32	1	0	6	33
Hypokalemia, n=3,3,3,12,17,3,3,3,3,4,273,32	0	2	7	57

Hypomagnesemia, n=3,3,3,12,17,3,3,3,3,4,272,32	1	3	15	89
Hyponatremia, n=3,3,3,12,17,3,3,3,3,4,273,32	2	2	10	78
Hypophosphatemia, n=3,3,3,12,17,3,3,3,3,4,272,32	2	1	9	82
Lipase increased, n=3,3,3,12,17,3,3,3,3,4,270,32	2	2	7	80
S.amylase increased,n=3,3,1,11,16,3,3,3,2,4,265,	0	2	4	83

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Laboratory Abnormalities (Phase 1, Phase 2 and DDI sub-study) – Coagulation, Lipids and Urinalysis

End point title	Number of Participants with Laboratory Abnormalities (Phase 1, Phase 2 and DDI sub-study) – Coagulation, Lipids and Urinalysis[42]

End point description:

Coagulation evaluation included activated partial thromboplastin time, international normalized ratio (INR), and prothrombin time. Lipid evaluation included Cholesterol and triglycerides. The safety analysis set included all enrolled participants who received at least 1 dose of PF-06463922. Here, "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure. Here, 'Number Analyzed' signifies participants evaluable for specified rows. All participants in Phase 2 received 100 mg of PF-06463922, hence combined data is presented for Phase 2.

End point type	Secondary

End point timeframe:

From first dose of study treatment to end of treatment (maximum of 96.58 months of treatment exposure for Phase 1, maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[42] - 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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	12
Units: Participants				
APTT prolonged, n=3,3,3,11,14,3,3,3,3,3,82,21	1	0	1	3
Cholesterol high, n=2,2,12,17,2,3,3,3,4,272,32	2	2	2	10
Hypertriglyceridemia, n=1,2,12,17,2,3,3,3,4,272,32	0	2	2	11
INR increased, n=3,3,3,11,14,3,3,3,3,3,113,24	2	1	1	2
Prothrombin time, n=3,3,3,11,14,3,3,3,3,3,103,21	2	1	1	3

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	3	3	3
Units: Participants				
APTT prolonged, n=3,3,3,11,14,3,3,3,3,3,82,21	2	0	0	0
Cholesterol high, n=2,2,12,17,2,3,3,3,4,272,32	16	2	3	3
Hypertriglyceridemia, n=1,2,12,17,2,3,3,3,4,272,32	16	2	3	2
INR increased, n=3,3,3,11,14,3,3,3,3,3,113,24	2	1	0	0
Prothrombin time, n=3,3,3,11,14,3,3,3,3,3,103,21	3	1	0	0

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	DDI Substudy	Phase 2
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	3	4	32	272
Units: Participants				
APTT prolonged, n=3,3,3,11,14,3,3,3,3,3,82,21	0	0	2	14
Cholesterol high, n=2,2,12,17,2,3,3,3,4,272,32	2	3	31	267
Hypertriglyceridemia, n=1,2,12,17,2,3,3,3,4,272,32	1	3	31	261
INR increased, n=3,3,3,11,14,3,3,3,3,3,113,24	0	0	3	21
Prothrombin time, n=3,3,3,11,14,3,3,3,3,3,103,21	1	1	6	25

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Vital Signs Data Meeting Pre-defined Criteria (Phase 1, Phase 2 and DDI sub-study)

End point title	Number of Participants with Vital Signs Data Meeting Pre-defined Criteria (Phase 1, Phase 2 and DDI sub-study)[43]

End point description:

Blood pressure (BP), including systolic BP (SBP) and diastolic BP (DBP), and pulse rate were recorded in sitting position. Body weight was also measured. The safety analysis set included all enrolled participants who received at least 1 dose of PF-06463922. Here, "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure. 'Number Analyzed' signifies participants evaluable for specified row. All participants in Phase 2 received 100 mg of PF-06463922, hence combined data is presented for Phase 2.

End point type	Secondary

End point timeframe:

From first dose of study treatment to end of treatment (maximum of 96.58 months of treatment exposure for Phase 1, maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[43] - 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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	12
Units: Participants				
Increa.SBP>=40mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	0
Increa.SBP>=60mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	0
Decrea.SBP>=40mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	3
Decrea.SBP>=60mmHg, n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	0
Increa.DBP>=20mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	0	2	0	0
Increa.DBP>=40mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	0
Decrea.DBP>=20mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	2	1	0	5
Decrea.DBP>=40mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	0
PR <50 bpm, n=3,3,3,12,17,3,3,3,3,4,273,32	0	1	0	0
PR>120 bpm,n=3,3,3,12,17,3,3,3,3,4,273,32	0	0	1	1
Increase PR>=30 bpm,n=3,3,3,12,17,3,3,3,3,4,269,32	0	1	0	2
Decrease PR>=30bpm,n=3,3,3,12,17,3,3,3,3,4,2	0	0	1	2
Increase W:10-<20%,n=3,3,3,12,17,3,3,3,3,4,262,32	1	0	0	8
Increased W:>=20%,n=3,3,3,12,17,3,3,3,3,4,262	0	2	1	1
Decreased W>=10%,n=3,3,3,12,17,3,3,3,3,4,262,	0	0	0	0

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	3	3	3
Units: Participants				
Increa.SBP>=40mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	3	2	0	0
Increa.SBP>=60mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	0
Decrea.SBP>=40mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	2	1	0	0
Decrea.SBP>=60mmHg, n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	0
Increa.DBP>=20mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	7	3	1	0

Increa.DBP>=40mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	0
Decrea.DBP>=20mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	3	2	2	0
Decrea.DBP>=40mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	0
PR <50 bpm, n=3,3,3,12,17,3,3,3,3,4,273,32	0	0	0	0
PR>120 bpm,n=3,3,3,12,17,3,3,3,3,4,273,32	2	2	0	0
Increase PR>=30 bpm,n=3,3,3,12,17,3,3,3,3,4,269,32	7	1	0	0
Decrease PR>=30bpm,n=3,3,3,12,17,3,3,3,3,4,2	0	1	0	1
Increase W:10-<20%,n=3,3,3,12,17,3,3,3,3,4,262,32	6	2	2	0
Increased W:>=20%,n=3,3,3,12,17,3,3,3,3,4,262	5	1	0	0
Decreased W>=10%,n=3,3,3,12,17,3,3,3,3,4,262,	0	0	0	0

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	DDI Substudy	Phase 2
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	3	4	32	273
Units: Participants				
Increa.SBP>=40mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	1	0	4	45
Increa.SBP>=60mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	2
Decrea.SBP>=40mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	1	14
Decrea.SBP>=60mmHg, n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	0
Increa.DBP>=20mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	1	0	7	86
Increa.DBP>=40mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	8
Decrea.DBP>=20mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	1	2	8	58
Decrea.DBP>=40mmHg,n=3,3,3,12,17,3,3,3,3,4,270,32	0	0	0	1
PR <50 bpm, n=3,3,3,12,17,3,3,3,3,4,273,32	0	0	2	11
PR>120 bpm,n=3,3,3,12,17,3,3,3,3,4,273,32	0	0	3	23
Increase PR>=30 bpm,n=3,3,3,12,17,3,3,3,3,4,269,32	0	1	8	74
Decrease PR>=30bpm,n=3,3,3,12,17,3,3,3,3,4,2	1	2	4	36
Increase W:10-<20%,n=3,3,3,12,17,3,3,3,3,4,262,32	0	0	9	80
Increased W:>=20%,n=3,3,3,12,17,3,3,3,3,4,262	1	1	3	58
Decreased W>=10%,n=3,3,3,12,17,3,3,3,3,4,262,	0	2	1	14

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Maximum Decrease from Baseline Greater than or Equal to 20 Percent in Left Ventricular Ejection Fraction (LVEF) (Phase 1, Phase 2 and DDI sub-study)

End point title	Number of Participants with Maximum Decrease from Baseline Greater than or Equal to 20 Percent in Left Ventricular Ejection Fraction (LVEF) (Phase 1, Phase 2 and DDI sub-study)[44]

End point description:

Left Ventricular Ejection Fraction (LVEF) was determined by echocardiogram. Baseline was defined as the measurement prior to the first dose of study treatment. The safety analysis set included all enrolled participants who received at least 1 dose of PF-06463922.

End point type	Secondary

End point timeframe:

From first dose of study treatment to end of treatment (maximum of 96.58 months of treatment exposure for Phase 1, maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[44] - 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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	12
Units: Participants	1	0	1	3

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	3	3	3
Units: Participants	5	2	1	0

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	DDI Substudy	Phase 2
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	3	4	32	275
Units: Participants	0	2	2	41

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Absolute Values and Change from Baseline in QTcF Meeting Pre-defined Criteria (Phase 1, Phase 2 and DDI sub-study)

End point title	Number of Participants with Absolute Values and Change from Baseline in QTcF Meeting Pre-defined Criteria (Phase 1, Phase 2 and DDI sub-study)[45]

End point description:

Triplicate 12-lead electrocardiograms (ECGs) were performed approximately 2 minutes apart to determine mean QTc interval (QT interval corrected for heart rate). QT interval was corrected for heart rate using Fridericia's formula to provide QTcF. Absolute values and changes from baseline were summarized according to pre-defined criteria. Baseline was defined as the last evaluation on or prior to the first dose of study treatment. The safety analysis set included all enrolled participants who received at least 1 dose of PF-06463922.

End point type	Secondary

End point timeframe:

From first dose of study treatment to end of treatment (maximum of 96.58 months of treatment exposure for Phase 1, maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[45] - 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: This endpoint is reporting statistics for the arms specified

End point values	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)	75 mg QD (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	12
Units: Participants				
QTcF: 450 to <480 msec	1	0	0	2
QTcF: 480 to <500 msec	1	0	0	0
QTcF: >=500 msec	0	0	0	0
QTcF Increase: 30 to <60 msec	0	0	1	3
QTcF: >=60 msec	0	0	0	0

End point values	100 mg QD (Phase 1)	150 mg QD (Phase 1)	200 mg QD (Phase 1)	35 mg BID (Phase 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	3	3	3
Units: Participants				
QTcF: 450 to <480 msec	1	1	0	2
QTcF: 480 to <500 msec	0	0	0	0
QTcF: >=500 msec	0	0	0	0
QTcF Increase: 30 to <60 msec	3	0	0	1

QTcF: >=60 msec	0	0	0	0

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	DDI Substudy	Phase 2
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	3	4	32	275
Units: Participants				
QTcF: 450 to <480 msec	0	1	7	55
QTcF: 480 to <500 msec	0	1	1	7
QTcF: >=500 msec	0	0	1	3
QTcF Increase: 30 to <60 msec	0	1	7	75
QTcF: >=60 msec	0	1	1	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Suicidal Ideation and Suicidal Behavior (Phase 2)

End point title	Number of Participants with Suicidal Ideation and Suicidal Behavior (Phase 2)[46]

End point description:

The Columbia Suicide Severity Rating Scale (C-SSRS) was used to analyze participants' suicidal ideation and behavior, and it is a unique, simple and short method of assessing both behavior and ideation that tracks all suicidal events and provides a summary of suicidality. It assesses the lethality of attempts and other features of ideation (frequency, duration, controllability, reasons for ideation and deterrents), all of which are significantly predictive of completed suicide. Maximum score of 4 or 5 indicates maximum suicidal ideation and minimum score of "0" indicates no suicidal ideation. The safety analysis set included all enrolled participants who received at least 1 dose of PF-06463922.

End point type	Secondary

End point timeframe:

From first dose of study treatment to end of treatment (maximum of 96.58 months of treatment exposure for Phase 1, maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[46] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	24	52	43
Units: Participants				
Suicidal ideation	1	0	2	1
Suicidal behavior	0	0	0	0

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	25		
Units: Participants				
Suicidal ideation	1	2		
Suicidal behavior	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Total Scores for Beck Depression Inventory (BDI)-II (Mood Assessment) (Phase 2)

End point title	Change from Baseline in Total Scores for Beck Depression Inventory (BDI)-II (Mood Assessment) (Phase 2)[47]

End point description:

Beck Depression Inventory (BDI)-II is a 21-item self-report scale, with each item rated by participants on a 4-point scale (ranging from 0-3, where 0 indicated lowest depression and 3 indicated severe depression). Scale includes items capturing mood, (loss of pleasure, sadness, and irritability), suicidal ideation, and cognitive signs (punitive thoughts, self-criticism, self-dislike, pessimism, and poor concentration) as well as somatic signs (appetite, sleep, fatigue and libido). Scores were obtained by adding up the total points from the series of answers. Higher total scores indicate more severe depressive symptoms. The standardized cutoffs are as follows: 0-13: minimal depression; 14-19: mild depression; 20-28: moderate depression; 29-63: severe depression. PRO evaluable analysis set: all enrolled participants who received study treatment, had baseline test assessment and at least 1 on-study test assessment. 'Number Analyzed' signifies participants evaluable for specified row.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 2-5, Day 1 of every other cycle from Cycle 6, and end of treatment (up to 3 years)

Notes:

[47] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	24	53	41
Units: Units on scale				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1, n=24,24,53,41,28,26	-2.59 (-4.82 to -0.37)	-3.27 (-5.52 to -1.01)	-2.26 (-3.77 to -0.76)	-2.17 (-3.89 to -0.46)
Cycle 3 Day 1, n=24,24,53,41,28,26	-3.34 (-5.57 to -1.12)	-3.18 (-5.43 to -0.93)	-3.03 (-4.55 to -1.51)	-3.10 (-4.85 to -1.35)
Cycle 4 Day 1, n=24,24,53,41,28,26	-3.84 (-6.07 to -1.62)	-4.10 (-6.38 to -1.82)	-2.59 (-4.14 to -1.05)	-1.95 (-3.72 to -0.19)
Cycle 5 Day 1, n=24,24,53,41,28,26	-4.47 (-6.69 to -2.24)	-3.96 (-6.27 to -1.66)	-2.75 (-4.33 to -1.16)	-3.03 (-4.82 to -1.25)
Cycle 6 Day 1, n=24,24,53,41,28,26	-3.51 (-5.73 to -1.28)	-4.25 (-6.56 to -1.94)	-3.31 (-4.90 to -1.72)	-3.79 (-5.61 to -1.98)
Cycle 8 Day 1, n=24,24,53,41,28,26	-4.17 (-6.41 to -1.92)	-4.86 (-7.23 to -2.50)	-2.26 (-3.86 to -0.66)	-4.06 (-5.90 to -2.22)

Cycle 10 Day 1, n=24,24,53,41,28,26	-3.09 (-5.38 to -0.80)	-4.92 (-7.28 to -2.55)	-1.94 (-3.54 to -0.34)	-4.27 (-6.14 to -2.39)
Cycle 12 Day 1, n=24,24,53,41,28,26	-3.95 (-6.30 to -1.61)	-5.60 (-7.97 to -3.24)	-0.72 (-2.40 to 0.95)	-4.80 (-6.83 to -2.77)
Cycle 14 Day 1, n=24,24,53,41,28,26	-3.81 (-6.18 to -1.43)	-5.80 (-8.35 to -3.25)	-2.58 (-4.41 to -0.76)	-4.29 (-6.41 to -2.17)
Cycle 16 Day 1, n=24,24,53,41,28,26	-1.75 (-4.40 to 0.89)	-4.61 (-7.51 to -1.71)	-2.15 (-4.35 to 0.06)	-4.65 (-6.90 to -2.41)
Cycle 18 Day 1, n=24,24,53,41,28,26	-4.49 (-7.49 to -1.49)	-7.02 (-10.59 to -3.46)	-1.96 (-4.22 to 0.31)	-2.86 (-5.21 to -0.51)
Cycle 20 Day 1, n=24,24,53,41,0,26	-5.01 (-8.55 to -1.46)	-5.17 (-9.06 to -1.29)	-1.82 (-4.70 to 1.06)	-3.63 (-6.31 to -0.95)
Cycle 22 Day 1, n=24,24,53,41,0,26	-2.93 (-6.79 to 0.94)	-4.63 (-9.00 to -0.26)	-2.36 (-5.68 to 0.96)	-5.50 (-8.87 to -2.12)
Cycle 24 Day 1, n=24,24,53,41,0,26	-7.31 (-11.66 to -2.96)	-5.63 (-10.00 to -1.26)	-2.88 (-7.04 to 1.28)	-3.89 (-8.10 to 0.32)
Cycle 26 Day 1, n=24,24,53,41,0,0	-5.50 (-10.67 to -0.33)	99999 (99999 to 99999)	-3.03 (-10.01 to 3.95)	-4.30 (-11.31 to 2.70)
End of treatment, n=24,24,53,41,28,26	-4.77 (-9.23 to -0.32)	-0.73 (-5.61 to 4.15)	-2.55 (-5.28 to 0.18)	-3.22 (-5.49 to -0.95)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	26		
Units: Units on scale				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1, n=24,24,53,41,28,26	-1.52 (-3.60 to 0.56)	-2.43 (-4.57 to -0.29)		
Cycle 3 Day 1, n=24,24,53,41,28,26	-0.46 (-2.61 to 1.69)	-1.24 (-3.37 to 0.90)		
Cycle 4 Day 1, n=24,24,53,41,28,26	-1.19 (-3.38 to 1.01)	-1.94 (-4.12 to 0.24)		
Cycle 5 Day 1, n=24,24,53,41,28,26	-1.51 (-3.74 to 0.72)	-1.25 (-3.46 to 0.95)		
Cycle 6 Day 1, n=24,24,53,41,28,26	-0.42 (-2.64 to 1.81)	-0.29 (-2.54 to 1.96)		
Cycle 8 Day 1, n=24,24,53,41,28,26	-1.09 (-3.34 to 1.17)	0.17 (-2.10 to 2.45)		
Cycle 10 Day 1, n=24,24,53,41,28,26	-2.97 (-5.29 to -0.66)	-0.19 (-2.60 to 2.22)		
Cycle 12 Day 1, n=24,24,53,41,28,26	-1.94 (-4.29 to 0.42)	-1.40 (-3.81 to 1.01)		
Cycle 14 Day 1, n=24,24,53,41,28,26	-1.73 (-4.40 to 0.94)	-0.08 (-2.59 to 2.42)		
Cycle 16 Day 1, n=24,24,53,41,28,26	-2.22 (-5.50 to 1.07)	0.03 (-2.65 to 2.71)		
Cycle 18 Day 1, n=24,24,53,41,28,26	-1.11 (-8.25 to 6.03)	1.88 (-1.66 to 5.41)		
Cycle 20 Day 1, n=24,24,53,41,0,26	99999 (99999 to 99999)	1.88 (-1.66 to 5.41)		
Cycle 22 Day 1, n=24,24,53,41,0,26	99999 (99999 to 99999)	-2.39 (-6.73 to 1.94)		
Cycle 24 Day 1, n=24,24,53,41,0,26	99999 (99999 to 99999)	2.27 (-2.06 to 6.61)		
Cycle 26 Day 1, n=24,24,53,41,0,0	99999 (99999 to 99999)	99999 (99999 to 99999)		

End of treatment, n=24,24,53,41,28,26	0.74 (-2.70 to 4.17)	-2.08 (-5.65 to 1.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Total Scores for Detection Test (Cognitive Function Assessment) (Phase 2)

End point title	Change from Baseline in Total Scores for Detection Test (Cognitive Function Assessment) (Phase 2)[48]

End point description:

Detection Test is measure of psychomotor function, uses well validated simple reaction time paradigm with playing card stimuli. In this test, on-screen instructions ask: "Has the card turned over?".Playing card is presented face down in center of screen. Card flips over so it is face up. As soon as card flips over participant must press "Yes". Participant is encouraged to work as quickly as they can, be as accurate as possible. Speed and accuracy of each response are recorded, mean of log10 transformed reaction times for correct responses is calculated. Lower values of least square mean change from baseline indicate performance decline. Upper limit of 95% confidence interval of -0.00 or lower indicate statistically significant decline of performance over baseline. PRO evaluable analysis set: all enrolled participants who received study treatment, had baseline test assessment, at least 1 on-study test assessment. 'Number Analyzed': participants evaluable for specified row.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 2-5, Day 1 of every other cycle from Cycle 6, and end of treatment (up to 3 years)

Notes:

[48] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	26	50	46
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1, n=24,26,50,46,38,29	0.01 (-0.04 to 0.05)	0.04 (-0.01 to 0.08)	-0.01 (-0.04 to 0.02)	0.02 (-0.01 to 0.05)
Cycle 3 Day 1, n=24,26,50,46,38,29	-0.01 (-0.05 to 0.03)	0.01 (-0.03 to 0.05)	0.01 (-0.02 to 0.04)	-0.01 (-0.04 to 0.02)
Cycle 4 Day 1, n=24,26,50,46,38,29	0.03 (-0.02 to 0.07)	0.00 (-0.04 to 0.04)	-0.03 (-0.06 to 0.00)	-0.02 (-0.05 to 0.01)
Cycle 5 Day 1, n=24,26,50,46,38,29	-0.01 (-0.05 to 0.03)	-0.01 (-0.06 to 0.03)	-0.00 (-0.03 to 0.03)	0.00 (-0.03 to 0.03)
Cycle 6 Day 1, n=24,26,50,46,38,29	-0.03 (-0.07 to 0.01)	0.01 (-0.03 to 0.06)	-0.02 (-0.05 to 0.01)	-0.00 (-0.04 to 0.03)
Cycle 8 Day 1, n=24,26,50,46,38,29	-0.02 (-0.06 to 0.02)	0.00 (-0.04 to 0.05)	-0.02 (-0.05 to 0.01)	-0.03 (-0.06 to 0.01)
Cycle 10 Day 1, n=24,26,50,46,38,29	-0.02 (-0.06 to 0.02)	0.03 (-0.01 to 0.08)	-0.02 (-0.06 to 0.01)	-0.01 (-0.05 to 0.02)
Cycle 12 Day 1, n=24,26,50,46,38,29	-0.04 (-0.08 to 0.01)	-0.00 (-0.05 to 0.04)	-0.02 (-0.06 to 0.02)	-0.03 (-0.06 to 0.01)

Cycle 14 Day 1, n=24,26,50,46,38,29	0.02 (-0.04 to 0.07)	0.02 (-0.03 to 0.08)	-0.05 (-0.09 to -0.01)	-0.04 (-0.08 to -0.00)
Cycle 16 Day 1, n=24,26,50,46,38,29	-0.03 (-0.09 to 0.03)	0.01 (-0.05 to 0.07)	0.02 (-0.03 to 0.07)	-0.03 (-0.08 to 0.01)
Cycle 18 Day 1, n=24,26,50,46,38,29	0.09 (0.01 to 0.18)	-0.02 (-0.09 to 0.05)	-0.03 (-0.09 to 0.02)	-0.06 (-0.11 to -0.01)
Cycle 20 Day 1, n=24,26,50,46,0,29	0.07 (-0.03 to 0.17)	0.02 (-0.06 to 0.09)	0.01 (-0.06 to 0.08)	-0.09 (-0.16 to -0.03)
Cycle 22 Day 1, n=24,26,50,46,0,29	-0.02 (-0.12 to 0.08)	-0.02 (-0.10 to 0.07)	0.00 (-0.08 to 0.08)	-0.08 (-0.16 to 0.00)
Cycle 24 Day 1, n=24,26,50,46,0,29	0.03 (-0.11 to 0.16)	99999 (99999 to 99999)	99999 (99999 to 99999)	-0.06 (-0.20 to 0.07)
End of treatment, n=24,26,50,46,38,29	-0.04 (-0.13 to 0.04)	-0.01 (-0.10 to 0.08)	-0.02 (-0.08 to 0.04)	-0.05 (-0.10 to -0.00)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	29		
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1, n=24,26,50,46,38,29	-0.02 (-0.05 to 0.02)	0.01 (-0.03 to 0.05)		
Cycle 3 Day 1, n=24,26,50,46,38,29	-0.01 (-0.05 to 0.02)	-0.01 (-0.05 to 0.03)		
Cycle 4 Day 1, n=24,26,50,46,38,29	-0.04 (-0.07 to -0.00)	-0.01 (-0.06 to 0.03)		
Cycle 5 Day 1, n=24,26,50,46,38,29	-0.04 (-0.08 to -0.01)	-0.04 (-0.08 to 0.00)		
Cycle 6 Day 1, n=24,26,50,46,38,29	-0.01 (-0.05 to 0.02)	-0.02 (-0.07 to 0.02)		
Cycle 8 Day 1, n=24,26,50,46,38,29	-0.04 (-0.07 to 0.00)	0.00 (-0.04 to 0.05)		
Cycle 10 Day 1, n=24,26,50,46,38,29	-0.05 (-0.09 to -0.01)	-0.04 (-0.08 to 0.01)		
Cycle 12 Day 1, n=24,26,50,46,38,29	-0.08 (-0.13 to -0.04)	-0.01 (-0.05 to 0.04)		
Cycle 14 Day 1, n=24,26,50,46,38,29	-0.02 (-0.07 to 0.04)	0.01 (-0.05 to 0.06)		
Cycle 16 Day 1, n=24,26,50,46,38,29	-0.04 (-0.14 to 0.06)	-0.01 (-0.07 to 0.06)		
Cycle 18 Day 1, n=24,26,50,46,38,29	-0.09 (-0.23 to 0.04)	-0.01 (-0.08 to 0.05)		
Cycle 20 Day 1, n=24,26,50,46,0,29	99999 (99999 to 99999)	-0.03 (-0.11 to 0.04)		
Cycle 22 Day 1, n=24,26,50,46,0,29	99999 (99999 to 99999)	-0.05 (-0.13 to 0.03)		
Cycle 24 Day 1, n=24,26,50,46,0,29	99999 (99999 to 99999)	99999 (99999 to 99999)		
End of treatment, n=24,26,50,46,38,29	-0.07 (-0.14 to -0.01)	-0.05 (-0.12 to 0.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Total Scores for Identification Test (Cognitive Function Assessment) (Phase 2)

End point title	Change from Baseline in Total Scores for Identification Test (Cognitive Function Assessment) (Phase 2)[49]

End point description:

Identification Test: measure of visual attention and uses well validated choice reaction time paradigm with playing card stimuli. In this, playing cards are all red or black jokers. On-screen instructions ask: "Is card red?". Playing card is presented face down in center of screen. Card flips over so it is face up. As soon as it flips over participant must decide whether card is red or not. If it is red participant should press "Yes", if it is not red participant should press "No". Speed and accuracy of each response are recorded.Mean of log10 transformed reaction time for correct response is calculated. Lower value of least square mean change from baseline=performance decline. Upper limit of 95% CI of -0.00/lower=statistically significant decline of performance over baseline. PRO evaluable analysis set: all enrolled participants who received study treatment, had baseline test assessment, atleast 1 on-study test assessment. Number Analyzed: participants evaluable for specified row.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 2-5, Day 1 of every other cycle from Cycle 6, and end of treatment (up to 3 years)

Notes:

[49] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	26	50	46
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1, n=24,26,50,46,38,29	-0.02 (-0.05 to 0.01)	-0.02 (-0.05 to 0.01)	-0.01 (-0.03 to 0.00)	-0.01 (-0.03 to 0.01)
Cycle 3 Day 1, n=24,26,50,46,38,29	-0.01 (-0.04 to 0.02)	-0.01 (-0.04 to 0.02)	-0.02 (-0.04 to 0.00)	-0.02 (-0.04 to 0.00)
Cycle 4 Day 1, n=24,26,50,46,38,29	-0.02 (-0.05 to 0.01)	-0.01 (-0.04 to 0.01)	-0.02 (-0.04 to 0.00)	-0.03 (-0.05 to -0.01)
Cycle 5 Day 1, n=24,26,50,46,38,29	-0.03 (-0.06 to -0.00)	-0.02 (-0.05 to 0.01)	-0.03 (-0.05 to -0.00)	-0.02 (-0.04 to 0.01)
Cycle 6 Day 1, n=24,26,50,46,38,29	-0.04 (-0.07 to -0.01)	-0.02 (-0.05 to 0.01)	-0.02 (-0.04 to 0.00)	-0.03 (-0.06 to -0.01)
Cycle 8 Day 1, n=24,26,50,46,38,29	-0.03 (-0.06 to -0.00)	-0.02 (-0.05 to 0.01)	-0.03 (-0.05 to -0.01)	-0.03 (-0.05 to -0.01)
Cycle 10 Day 1, n=24,26,50,46,38,29	-0.03 (-0.06 to 0.00)	-0.01 (-0.04 to 0.02)	-0.03 (-0.05 to -0.01)	-0.02 (-0.05 to 0.00)
Cycle 12 Day 1, n=24,26,50,46,38,29	-0.05 (-0.08 to -0.02)	-0.04 (-0.07 to -0.01)	-0.04 (-0.06 to -0.01)	-0.04 (-0.07 to -0.01)
Cycle 14 Day 1, n=24,26,50,46,38,29	-0.04 (-0.08 to 0.00)	-0.04 (-0.07 to -0.00)	-0.03 (-0.06 to -0.00)	-0.04 (-0.07 to -0.01)
Cycle 16 Day 1, n=24,26,50,46,38,29	-0.09 (-0.13 to -0.05)	-0.00 (-0.04 to 0.04)	-0.03 (-0.07 to 0.01)	-0.03 (-0.06 to 0.01)
Cycle 18 Day 1, n=24,26,50,46,38,29	-0.01 (-0.06 to 0.05)	-0.05 (-0.09 to 0.00)	-0.04 (-0.08 to 0.00)	-0.07 (-0.10 to -0.03)
Cycle 20 Day 1, n=24,26,50,46,0,29	-0.03 (-0.10 to 0.04)	-0.01 (-0.06 to 0.04)	-0.03 (-0.08 to 0.02)	-0.10 (-0.15 to -0.06)
Cycle 22 Day 1, n=24,26,50,46,0,29	0.04 (-0.03 to 0.11)	-0.01 (-0.07 to 0.05)	-0.06 (-0.11 to 0.00)	-0.05 (-0.11 to 0.00)

Cycle 24 Day 1, n=24,26,50,46,0,0	0.08 (-0.01 to 0.18)	99999 (99999 to 99999)	99999 (99999 to 99999)	-0.06 (-0.15 to 0.04)
End of treatment, n=24,26,50,46,38,29	-0.07 (-0.13 to -0.02)	-0.03 (-0.10 to 0.03)	-0.02 (-0.06 to 0.02)	-0.03 (-0.06 to 0.01)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	29		
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1, n=24,26,50,46,38,29	-0.02 (-0.04 to 0.01)	-0.01 (-0.04 to 0.02)		
Cycle 3 Day 1, n=24,26,50,46,38,29	-0.02 (-0.05 to 0.00)	-0.01 (-0.04 to 0.02)		
Cycle 4 Day 1, n=24,26,50,46,38,29	-0.05 (-0.08 to -0.03)	-0.02 (-0.04 to 0.01)		
Cycle 5 Day 1, n=24,26,50,46,38,29	-0.05 (-0.07 to -0.02)	-0.02 (-0.05 to 0.00)		
Cycle 6 Day 1, n=24,26,50,46,38,29	-0.03 (-0.06 to -0.01)	-0.03 (-0.06 to -0.00)		
Cycle 8 Day 1, n=24,26,50,46,38,29	-0.05 (-0.07 to -0.02)	-0.03 (-0.06 to 0.00)		
Cycle 10 Day 1, n=24,26,50,46,38,29	-0.05 (-0.08 to -0.02)	-0.03 (-0.06 to 0.00)		
Cycle 12 Day 1, n=24,26,50,46,38,29	-0.06 (-0.09 to -0.03)	-0.03 (-0.06 to 0.00)		
Cycle 14 Day 1, n=24,26,50,46,38,29	-0.04 (-0.08 to -0.00)	-0.02 (-0.06 to 0.02)		
Cycle 16 Day 1, n=24,26,50,46,38,29	-0.07 (-0.13 to 0.00)	-0.06 (-0.10 to -0.01)		
Cycle 18 Day 1, n=24,26,50,46,38,29	-0.19 (-0.29 to -0.09)	-0.01 (-0.05 to 0.04)		
Cycle 20 Day 1, n=24,26,50,46,0,29	99999 (99999 to 99999)	-0.03 (-0.08 to 0.02)		
Cycle 22 Day 1, n=24,26,50,46,0,29	99999 (99999 to 99999)	-0.08 (-0.14 to -0.03)		
Cycle 24 Day 1, n=24,26,50,46,0,0	99999 (99999 to 99999)	99999 (99999 to 99999)		
End of treatment, n=24,26,50,46,38,29	-0.09 (-0.14 to -0.05)	-0.06 (-0.11 to -0.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Total Scores for One Back Test (Cognitive Function Assessment) (Phase 2)

End point title	Change from Baseline in Total Scores for One Back Test (Cognitive Function Assessment) (Phase 2)[50]

End point description:

One Back Test: measure of working memory and uses well validated n back paradigm with playing cards. In this task, the on-screen instructions ask: "Is previous card same?". Playing card is presented

in center of screen. Participant must decide whether card is same as previous card. If it is same participant should press "Yes", and if not press "No". Speed and accuracy of each response are recorded, mean of log10 transformed reaction time for correct response is used to demonstrate speed of performance, arcsine transformation of square root of proportion of correct responses is for demonstrate accuracy. Lower value of least square mean change from baseline= performance decline. Upper limit of 95%CI of -0.00/ lower:statistically significant decline of performance over baseline. PRO evaluable analysis set: all enrolled participants who received study treatment, had baseline test assessment, at least 1 on-study test assessment. Number Analyzed:participants evaluable for specified row.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 2-5, Day 1 of every other cycle from Cycle 6, and end of treatment (up to 3 years)

Notes:

[50] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	26	50	46
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1, n=24,26,50,46,38,29	0.01 (-0.02 to 0.05)	0.02 (-0.01 to 0.05)	0.02 (0.00 to 0.05)	0.01 (-0.01 to 0.04)
Cycle 3 Day 1, n=24,26,50,46,38,29	0.06 (0.02 to 0.09)	0.01 (-0.02 to 0.05)	0.01 (-0.01 to 0.04)	0.01 (-0.02 to 0.03)
Cycle 4 Day 1, n=24,26,50,46,38,29	0.04 (0.01 to 0.08)	0.03 (-0.00 to 0.06)	0.02 (-0.01 to 0.04)	-0.01 (-0.04 to 0.01)
Cycle 5 Day 1, n=24,26,50,46,38,29	0.02 (-0.01 to 0.06)	0.03 (-0.00 to 0.07)	0.03 (0.00 to 0.05)	-0.01 (-0.04 to 0.02)
Cycle 6 Day 1, n=24,26,50,46,38,29	0.03 (-0.01 to 0.06)	0.03 (-0.00 to 0.07)	0.03 (0.01 to 0.06)	0.01 (-0.02 to 0.04)
Cycle 8 Day 1, n=24,26,50,46,38,29	0.03 (-0.01 to 0.06)	0.02 (-0.02 to 0.06)	0.03 (0.00 to 0.05)	0.01 (-0.02 to 0.03)
Cycle 10 Day 1, n=24,26,50,46,38,29	0.07 (0.03 to 0.11)	0.03 (-0.00 to 0.07)	0.03 (0.00 to 0.05)	0.02 (-0.01 to 0.05)
Cycle 12 Day 1, n=24,26,50,46,38,29	0.05 (0.01 to 0.08)	0.01 (-0.03 to 0.05)	0.02 (-0.01 to 0.05)	0.01 (-0.02 to 0.04)
Cycle 14 Day 1, n=24,26,50,46,38,29	0.00 (-0.05 to 0.05)	0.03 (-0.01 to 0.07)	0.03 (-0.01 to 0.07)	-0.00 (-0.04 to 0.03)
Cycle 16 Day 1, n=24,26,50,46,38,29	0.03 (-0.03 to 0.08)	0.05 (-0.01 to 0.10)	0.05 (0.00 to 0.09)	-0.02 (-0.05 to 0.02)
Cycle 18 Day 1, n=24,26,50,46,38,29	0.02 (-0.06 to 0.09)	0.01 (-0.04 to 0.07)	0.06 (0.02 to 0.11)	-0.02 (-0.06 to 0.03)
Cycle 20 Day 1, n=24,26,50,46,0,29	-0.06 (-0.15 to 0.03)	0.07 (0.00 to 0.13)	0.02 (-0.05 to 0.08)	-0.01 (-0.06 to 0.05)
Cycle 22 Day 1, n=24,26,50,46,0,29	0.02 (-0.07 to 0.11)	0.05 (-0.02 to 0.12)	0.04 (-0.03 to 0.11)	-0.07 (-0.14 to 0.00)
Cycle 24 Day 1, n=24,26,50,46,0,0	0.09 (-0.03 to 0.21)	99999 (99999 to 99999)	99999 (99999 to 99999)	0.01 (-0.11 to 0.13)
End of treatment, n=24,26,50,46,0,29	-0.03 (-0.10 to 0.05)	0.03 (-0.05 to 0.11)	0.03 (-0.02 to 0.07)	0.01 (-0.04 to 0.05)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	29		
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1, n=24,26,50,46,38,29	0.02 (-0.01 to 0.05)	0.01 (-0.02 to 0.04)		
Cycle 3 Day 1, n=24,26,50,46,38,29	-0.01 (-0.04 to 0.02)	-0.00 (-0.04 to 0.03)		
Cycle 4 Day 1, n=24,26,50,46,38,29	-0.02 (-0.05 to 0.01)	-0.01 (-0.05 to 0.02)		
Cycle 5 Day 1, n=24,26,50,46,38,29	-0.02 (-0.05 to 0.01)	0.02 (-0.01 to 0.05)		
Cycle 6 Day 1, n=24,26,50,46,38,29	-0.00 (-0.03 to 0.03)	0.01 (-0.03 to 0.04)		
Cycle 8 Day 1, n=24,26,50,46,38,29	-0.01 (-0.04 to 0.02)	0.01 (-0.02 to 0.05)		
Cycle 10 Day 1, n=24,26,50,46,38,29	-0.01 (-0.05 to 0.02)	0.01 (-0.02 to 0.05)		
Cycle 12 Day 1, n=24,26,50,46,38,29	-0.00 (-0.04 to 0.03)	0.03 (-0.01 to 0.07)		
Cycle 14 Day 1, n=24,26,50,46,38,29	0.01 (-0.04 to 0.06)	0.02 (-0.03 to 0.07)		
Cycle 16 Day 1, n=24,26,50,46,38,29	-0.01 (-0.10 to 0.08)	0.03 (-0.03 to 0.08)		
Cycle 18 Day 1, n=24,26,50,46,38,29	-0.18 (-0.30 to -0.06)	0.05 (-0.01 to 0.10)		
Cycle 20 Day 1, n=24,26,50,46,0,29	99999 (99999 to 99999)	0.02 (-0.04 to 0.09)		
Cycle 22 Day 1, n=24,26,50,46,0,29	99999 (99999 to 99999)	0.03 (-0.04 to 0.11)		
Cycle 24 Day 1, n=24,26,50,46,0,0	99999 (99999 to 99999)	99999 (99999 to 99999)		
End of treatment, n=24,26,50,46,0,29	-0.03 (-0.08 to 0.02)	0.02 (-0.05 to 0.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Total Scores for International Shopping List Test (Cognitive Function Assessment) (Phase 2)

End point title	Change from Baseline in Total Scores for International Shopping List Test (Cognitive Function Assessment) (Phase 2)[51]

End point description:

International Shopping List task: measure of verbal learning,uses well validated list learning paradigm administered using computer. High frequencies, high imagery, concrete nouns (items from a shopping list) were read to participant at rate of one word every 2 seconds. Once all 12 words had been read, participant was asked to recall as many of words as quickly as possible. Words recalled by participant were marked on computer screen. When participant could recall no more words, same list was read again. Words recalled by participant were recorded. This was repeated third time. Total number of correct responses on 3 consecutive trials at single assessment was recorded. Upper limit of 95% CI of -0.00 or lower indicate statistically significant decline of performance over baseline. PRO evaluable analysis set: all enrolled participants who received study treatment, had baseline test assessment, atleast 1 on-study test assessment. Number Analyzed: participant evaluable for specified row.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 2-5, Day 1 of every other cycle from Cycle 6, and end of treatment (up to 3 years)

Notes:

[51] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	26	50	46
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1, n=24,26,50,46,0,29	-0.02 (-1.89 to 1.84)	-1.13 (-2.90 to 0.64)	0.25 (-1.01 to 1.52)	-0.45 (-1.76 to 0.86)
Cycle 3 Day 1, n=24,26,50,46,0,29	0.19 (-1.66 to 2.03)	-0.81 (-2.58 to 0.96)	0.14 (-1.15 to 1.43)	-1.04 (-2.36 to 0.29)
Cycle 4 Day 1, n=24,26,50,46,0,29	0.58 (-1.26 to 2.42)	0.26 (-1.54 to 2.05)	0.28 (-1.05 to 1.61)	0.24 (-1.12 to 1.60)
Cycle 5 Day 1, n=24,26,50,46,0,29	1.30 (-0.51 to 3.12)	-0.66 (-2.53 to 1.21)	0.59 (-0.77 to 1.95)	-0.94 (-2.33 to 0.45)
Cycle 6 Day 1, n=24,26,50,46,0,29	0.18 (-1.64 to 1.99)	0.81 (-1.06 to 2.68)	0.50 (-0.87 to 1.87)	0.08 (-1.31 to 1.47)
Cycle 8 Day 1, n=24,26,50,46,0,29	0.84 (-1.00 to 2.68)	0.60 (-1.30 to 2.50)	1.69 (0.29 to 3.08)	0.15 (-1.27 to 1.57)
Cycle 10 Day 1, n=24,26,50,46,0,29	0.26 (-1.68 to 2.21)	2.59 (0.65 to 4.52)	0.86 (-0.56 to 2.27)	0.13 (-1.46 to 1.72)
Cycle 12 Day 1, n=24,26,50,46,0,29	2.87 (0.86 to 4.88)	0.02 (-2.06 to 2.10)	0.11 (-1.52 to 1.73)	0.69 (-0.98 to 2.35)
Cycle 14 Day 1, n=24,26,50,46,0,29	1.91 (-0.71 to 4.53)	1.46 (-0.85 to 3.78)	2.27 (0.36 to 4.17)	0.94 (-0.86 to 2.73)
Cycle 16 Day 1, n=24,26,50,46,0,29	4.52 (1.58 to 7.46)	0.87 (-2.06 to 3.79)	1.36 (-1.11 to 3.84)	1.04 (-0.99 to 3.07)
Cycle 18 Day 1, n=24,26,50,46,0,29	4.77 (0.82 to 8.73)	0.66 (-2.50 to 3.81)	-0.27 (-2.89 to 2.36)	-0.52 (-2.77 to 1.73)
Cycle 20 Day 1, n=24,26,50,46,0,29	-2.72 (-7.47 to 2.03)	-1.44 (-4.91 to 2.03)	0.56 (-2.81 to 3.92)	1.20 (-1.84 to 4.24)
Cycle 22 Day 1, n=24,26,50,46,0,29	-5.72 (-10.47 to -0.97)	-0.28 (-4.22 to 3.66)	2.17 (-1.68 to 6.01)	-0.36 (-4.21 to 3.48)
Cycle 24 Day 1, n=24,26,50,46,0,0	-8.49 (-15.06 to -1.92)	99999 (99999 to 99999)	99999 (99999 to 99999)	-3.35 (-9.86 to 3.16)
End of treatment, n=24,26,50,46,38,29	1.02 (-2.99 to 5.04)	-1.62 (-5.95 to 2.71)	0.80 (-1.80 to 3.40)	-0.27 (-2.47 to 1.92)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	29		
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1, n=24,26,50,46,0,29	0.96 (-0.50 to 2.43)	0.16 (-1.51 to 1.83)		

Cycle 3 Day 1, n=24,26,50,46,0,29	-0.08 (-1.59 to 1.44)	-0.56 (-2.21 to 1.09)		
Cycle 4 Day 1, n=24,26,50,46,0,29	1.30 (-0.26 to 2.86)	-0.87 (-2.59 to 0.84)		
Cycle 5 Day 1, n=24,26,50,46,0,29	1.23 (-0.36 to 2.82)	0.74 (-0.97 to 2.45)		
Cycle 6 Day 1, n=24,26,50,46,0,29	0.82 (-0.83 to 2.46)	-0.51 (-2.31 to 1.29)		
Cycle 8 Day 1, n=24,26,50,46,0,29	0.44 (-1.23 to 2.11)	1.70 (-0.11 to 3.50)		
Cycle 10 Day 1, n=24,26,50,46,0,29	2.29 (0.53 to 4.05)	0.97 (-0.99 to 2.93)		
Cycle 12 Day 1, n=24,26,50,46,0,29	1.74 (-0.25 to 3.72)	3.10 (1.06 to 5.14)		
Cycle 14 Day 1, n=24,26,50,46,0,29	-4.43 (-7.11 to -1.75)	2.67 (0.09 to 5.25)		
Cycle 16 Day 1, n=24,26,50,46,0,29	3.46 (-1.26 to 8.18)	1.97 (-0.93 to 4.87)		
Cycle 18 Day 1, n=24,26,50,46,0,29	-0.35 (-6.90 to 6.21)	3.13 (0.00 to 6.27)		
Cycle 20 Day 1, n=24,26,50,46,0,29	99999 (99999 to 99999)	0.56 (-2.89 to 4.01)		
Cycle 22 Day 1, n=24,26,50,46,0,29	99999 (99999 to 99999)	3.99 (0.07 to 7.91)		
Cycle 24 Day 1, n=24,26,50,46,0,0	99999 (99999 to 99999)	99999 (99999 to 99999)		
End of treatment, n=24,26,50,46,38,29	2.37 (-0.54 to 5.27)	-0.60 (-4.09 to 2.89)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Total Scores for International Shopping List Test-Delayed Recall (Cognitive Function Assessment) (Phase 2)

End point title	Change from Baseline in Total Scores for International Shopping List Test-Delayed Recall (Cognitive Function Assessment) (Phase 2)[52]

End point description:

This test was performed in same way as the International Shopping List Test, with exception that, delayed recall condition required participant to recall words from list 15 30 minutes later without having list read again. During recognition condition, qualified personnel read a shopping list item that may or may not have been on original list and participant had to respond either affirmatively (if item was on original list) or negatively (if it was not). Total number of correct responses made in remembering word list after a delay was recorded. Lower values of least square mean change from baseline indicate performance decline. Upper limit of 95% CI of -0.00 or lower indicate statistically significant decline of performance over baseline at that cycle. PRO evaluable analysis: all enrolled participants who received study treatment, had a baseline test assessment and at least 1 on-study test assessment. Here, 'Number Analyzed' signifies participants evaluable for specified row.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 2-5, Day 1 of every other cycle from Cycle 6, and end of treatment (up to 3 years)

Notes:

[52] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	26	50	46
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1, n=24,26,50,46,38,29	0.10 (-0.85 to 1.06)	-0.84 (-1.76 to 0.08)	-0.12 (-0.77 to 0.53)	-0.59 (-1.28 to 0.09)
Cycle 3 Day 1,n=24,26,50,46,38,29	-0.33 (-1.28 to 0.62)	-1.32 (-2.24 to -0.40)	-0.14 (-0.81 to 0.52)	-0.77 (-1.46 to -0.07)
Cycle 4 Day 1,n=24,26,50,46,38,29	-0.44 (-1.38 to 0.50)	-0.91 (-1.86 to 0.03)	0.03 (-0.66 to 0.72)	-0.25 (-0.97 to 0.47)
Cycle 5 Day 1,n=24,26,50,46,38,29	-0.35 (-1.29 to 0.59)	-0.57 (-1.54 to 0.40)	0.02 (-0.69 to 0.73)	-0.46 (-1.20 to 0.27)
Cycle 6 Day 1,n=24,26,50,46,38,29	0.48 (-0.46 to 1.42)	-0.38 (-1.35 to 0.59)	0.12 (-0.59 to 0.84)	-0.22 (-0.95 to 0.52)
Cycle 8 Day 1,n=24,26,50,46,38,29	0.56 (-0.38 to 1.50)	-0.24 (-1.23 to 0.75)	0.02 (-0.70 to 0.74)	-0.49 (-1.24 to 0.25)
Cycle 10 Day 1, n=24,26,50,46,38,29	0.29 (-0.74 to 1.31)	0.80 (-0.22 to 1.82)	0.54 (-0.20 to 1.28)	0.23 (-0.61 to 1.08)
Cycle 12 Day 1,n=24,26,50,46,38,29	0.90 (-0.15 to 1.95)	0.13 (-0.95 to 1.21)	0.22 (-0.63 to 1.07)	0.19 (-0.70 to 1.07)
Cycle 14 Day 1, n=24,26,50,46,38,29	0.38 (-0.99 to 1.75)	0.06 (-1.15 to 1.27)	1.06 (0.06 to 2.06)	0.11 (-0.85 to 1.07)
Cycle 16 Day 1, n=24,26,50,46,38,29	0.89 (-0.66 to 2.43)	0.52 (-1.02 to 2.05)	0.68 (-0.62 to 1.98)	-0.12 (-1.22 to 0.98)
Cycle 18 Day 1, n=24,26,50,46,38,29	1.06 (-1.02 to 3.14)	0.68 (-0.98 to 2.34)	0.38 (-1.00 to 1.76)	-0.24 (-1.54 to 1.07)
Cycle 20 Day 1,n=24,26,50,46,0,29	-1.22 (-3.73 to 1.28)	0.16 (-1.67 to 1.98)	-0.24 (-2.01 to 1.53)	-0.18 (-1.78 to 1.43)
Cycle 22 Day 1, n=24,26,50,46,0,29	-3.22 (-5.73 to -0.72)	0.68 (-1.40 to 2.76)	0.80 (-1.23 to 2.83)	-0.64 (-2.67 to 1.39)
Cycle 24 Day 1, n=24,0,0,46,0,0	-2.43 (-5.89 to 1.04)	99999 (99999 to 99999)	99999 (99999 to 99999)	-0.80 (-4.25 to 2.64)
End of treatment,n=24,26,50,46,38,29	-0.87 (-2.99 to 1.24)	-2.31 (-4.58 to -0.04)	0.52 (-0.84 to 1.89)	-0.85 (-2.06 to 0.35)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	29		
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1, n=24,26,50,46,38,29	-0.22 (-0.96 to 0.53)	-0.25 (-1.11 to 0.62)		
Cycle 3 Day 1,n=24,26,50,46,38,29	-0.87 (-1.64 to -0.10)	-0.30 (-1.15 to 0.56)		
Cycle 4 Day 1,n=24,26,50,46,38,29	-0.02 (-0.82 to 0.78)	-1.06 (-1.95 to -0.18)		
Cycle 5 Day 1,n=24,26,50,46,38,29	0.09 (-0.74 to 0.92)	0.17 (-0.72 to 1.05)		
Cycle 6 Day 1,n=24,26,50,46,38,29	0.30 (-0.55 to 1.15)	-0.28 (-1.21 to 0.66)		
Cycle 8 Day 1,n=24,26,50,46,38,29	-1.08 (-1.94 to -0.22)	-0.16 (-1.10 to 0.77)		

Cycle 10 Day 1, n=24,26,50,46,38,29	0.25 (-0.67 to 1.16)	-0.00 (-1.02 to 1.02)		
Cycle 12 Day 1,n=24,26,50,46,38,29	0.60 (-0.43 to 1.64)	0.42 (-0.64 to 1.49)		
Cycle 14 Day 1, n=24,26,50,46,38,29	-1.80 (-3.31 to -0.30)	0.35 (-1.00 to 1.71)		
Cycle 16 Day 1, n=24,26,50,46,38,29	0.40 (-2.09 to 2.88)	-0.22 (-1.75 to 1.30)		
Cycle 18 Day 1, n=24,26,50,46,38,29	-0.39 (-3.85 to 3.07)	-0.33 (-1.97 to 1.32)		
Cycle 20 Day 1,n=24,26,50,46,0,29	99999 (99999 to 99999)	-0.70 (-2.52 to 1.11)		
Cycle 22 Day 1, n=24,26,50,46,0,29	99999 (99999 to 99999)	0.37 (-1.70 to 2.43)		
Cycle 24 Day 1, n=24,0,0,46,0,0	99999 (99999 to 99999)	99999 (99999 to 99999)		
End of treatment,n=24,26,50,46,38,29	-0.19 (-1.71 to 1.34)	0.11 (-1.72 to 1.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Absolute Values and Change from Baseline in PR Interval Meeting Pre-defined Criteria (Phase 2 and DDI Substudy)

End point title	Number of Participants with Absolute Values and Change from Baseline in PR Interval Meeting Pre-defined Criteria (Phase 2 and DDI Substudy)[53]

End point description:

PR Interval was determined by ECG measurement. Baseline was defined as the average of the triplicate measurements prior to the first dose of study drug. The safety analysis set included all enrolled participants who received at least 1 dose of PF-06463922. Here, "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

From first dose of study treatment to end of treatment (maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[53] - 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: This endpoint is reporting statistics for the arms specified

End point values	DDI Substudy	Phase 2		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	32	272		
Units: Participants				
40-<60 msec	2	19		
60-<80 msec	0	9		
>=80 msec	0	5		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants with Overall and Intracranial Objective Response (Phase 2 and DDI sub-study)

End point title	Percentage of Participants with Overall and Intracranial Objective Response (Phase 2 and DDI sub-study)[54]

End point description:

ITT analysis set was used for overall response assessment and included all enrolled participants with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922; participants with central nervous system (CNS) metastases in the ITT analysis set were used for intracranial response assessment. Here, "Number Analyzed" signifies participants evaluable for specified rows.

End point type	Other pre-specified

End point timeframe:

From first dose of study treatment to end of treatment (maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Notes:

[54] - 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: This endpoint is reporting statistics for the arms specified

End point values	EXP-1 (Phase 2)	EXP-2 (Phase 2)	EXP-3 (Phase 2)	EXP-4 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	27	60	65
Units: Percentage of participants				
number (confidence interval 95%)				
OR, n=30,27,60,65,46,47,32	90.0 (73.5 to 97.9)	77.8 (57.7 to 91.4)	56.7 (43.2 to 69.4)	40.0 (28.0 to 52.9)
Intracranial OR, n=8,17,33,45,37,25,16	75.0 (34.9 to 96.8)	58.8 (32.9 to 81.6)	66.7 (48.2 to 82.0)	53.3 (37.9 to 68.3)

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)	DDI Substudy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	47	32	
Units: Percentage of participants				
number (confidence interval 95%)				
OR, n=30,27,60,65,46,47,32	37.0 (23.2 to 52.5)	38.3 (24.5 to 53.6)	40.6 (23.7 to 59.4)	
Intracranial OR, n=8,17,33,45,37,25,16	43.2 (27.1 to 60.5)	56.0 (34.9 to 75.6)	25.0 (7.3 to 52.4)	

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

From first dose of study treatment to end of treatment (maximum of 96.58 months of treatment exposure for Phase 1, maximum of 89.65 months of treatment exposure for Phase 2 and maximum of 68.69 months of treatment exposure for DDI participants)

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one participant and as non-serious in another participant, or one participant may have experienced both a serious and non-serious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	50 mg QD (Phase 1)

Reporting group description:

PF-06463922 50 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	25 mg QD (Phase 1)

Reporting group description:

PF-06463922 25 mg was orally given QD in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal. Midazolam 2 mg was orally given QD on Day -7 and Cycle 1 Day 15.

Reporting group title	10 mg QD (Phase 1)

Reporting group description:

PF-06463922 10 mg was orally given once daily (QD) on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	DDI Substudy

Reporting group description:

Participants with advanced ALK positive or ROS1-positive NSCLC who were treatment naïve or had any number of prior cancer therapies with or without asymptomatic CNS metastases were administered a single dose of a probe substrate alone on Day -2. Participants were given PF-06463922 100 mg orally QD starting on Cycle1 Day 1 and along with probe substrate on Day 15 Cycle 1.

Reporting group title	35 mg BID (Phase 1)

Reporting group description:

PF-06463922 35 mg was orally given twice daily (BID) on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	75 mg BID (Phase 1)

Reporting group description:

PF-06463922 75 mg was orally given BID on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	100 mg BID (Phase 1)

Reporting group description:

PF-06463922 100 mg was orally given BID on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	Phase 2

Reporting group description:

Participants with advanced ROS1-positive NSCLC who were treatment naïve or had any number of prior cancer therapies with or without asymptomatic CNS metastases were given PF-06463922 100 mg orally

once daily (QD) on Day -7 (only for participants scheduled for pharmacokinetic evaluation) and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	Japan Lead-In Cohort (LIC)

Reporting group description:

Few Japanese participants were given PF-06463922 100 mg orally once daily (QD) in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal to evaluate safety of PF-06463922 in Japanese participants, in order to support inclusion of Japanese participants in Phase 2.

Reporting group title	150 mg QD (Phase 1)

Reporting group description:

PF-06463922 150 mg was orally given QD in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal. Midazolam 2 mg was orally given QD on Day -7 and Cycle 1 Day 15.

Reporting group title	100 mg QD (Phase 1)

Reporting group description:

PF-06463922 100 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	75 mg QD (Phase 1)

Reporting group description:

PF-06463922 75 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Reporting group title	200 mg QD (Phase 1)

Reporting group description:

PF-06463922 200 mg was orally given QD on Day -7 and in 21-day cycles from Cycle 1 Day 1 until progression of disease (unless clinical benefit was still achievable), unacceptable toxicity, death or consent withdrawal.

Serious adverse events	50 mg QD (Phase 1)	25 mg QD (Phase 1)	10 mg QD (Phase 1)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	3 / 3 (100.00%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myeloid leukaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 tumour thrombotic microangiopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Embolism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Embolism venous			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic dissection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery occlusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Disease progression			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 physical health deterioration			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			

subjects affected / exposed[1]	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute pulmonary oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			

subjects affected / exposed[2]	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 distress			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asphyxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral bilateral pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Assisted suicide			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impulse-control disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophreniform disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 cholesterol increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ejection fraction decreased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Subdural haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed[3]	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation necrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed[4]	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar stroke			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vagus nerve disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurological symptom			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brainstem compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blepharitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric volvulus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glossitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Terminal ileitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Biloma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stenosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystocholangitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatomyositis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurogenic bladder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 cyst haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethritis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
alternative assessment type: Systematic			
subjects affected / exposed[5]	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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	DDI Substudy	35 mg BID (Phase 1)	75 mg BID (Phase 1)
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 32 (40.63%)	2 / 3 (66.67%)	2 / 3 (66.67%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myeloid leukaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 tumour thrombotic microangiopathy			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm progression			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Embolism			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism venous			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic dissection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery occlusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Disease progression			
subjects affected / exposed	5 / 32 (15.63%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyrexia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 physical health deterioration			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 peripheral			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (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
Hypoxia			
subjects affected / exposed[1]	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute pulmonary oedema			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 exertional			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (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
Epistaxis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed[2]	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 congestion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 distress			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 hypertension			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asphyxia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral bilateral pulmonary embolism			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Assisted suicide			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impulse-control disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophreniform disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Aspartate aminotransferase increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 cholesterol increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ejection fraction decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 creatine phosphokinase increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Subdural haematoma			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (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
Femoral neck fracture			
subjects affected / exposed[3]	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation necrosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Pericardial effusion			

subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Headache			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed[4]	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar stroke			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vagus nerve disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurological symptom			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brainstem compression			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphasia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (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
Hemiparesis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			

Thrombocytopenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blepharitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Abdominal pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 haematoma			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric volvulus			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glossitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Terminal ileitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Biloma			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stenosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (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
Cholecystocholangitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatomyositis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurogenic bladder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 cyst haemorrhage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Influenza			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lower respiratory tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung abscess			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (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
Vestibular neuronitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (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
Dehydration			
alternative assessment type: Systematic			
subjects affected / exposed[5]	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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	100 mg BID (Phase 1)	Phase 2	Japan Lead-In Cohort (LIC)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	135 / 275 (49.09%)	1 / 3 (33.33%)
number of deaths (all causes)	0	32	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Acute myeloid leukaemia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Breast cancer			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Pulmonary tumour thrombotic microangiopathy			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Neoplasm progression			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 4 (0.00%)	5 / 275 (1.82%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Embolism venous			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic dissection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Deep vein thrombosis			

subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Hypertensive crisis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Peripheral artery occlusion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 4 (0.00%)	29 / 275 (10.55%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 29	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 12	0 / 0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	9 / 275 (3.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 10	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
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 physical health deterioration			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Pain			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	1 / 4 (25.00%)	8 / 275 (2.91%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hypoxia			
subjects affected / exposed[1]	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	4 / 275 (1.45%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 4 (0.00%)	3 / 275 (1.09%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute pulmonary oedema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			

subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Asthma			
subjects affected / exposed[2]	0 / 4 (0.00%)	1 / 47 (2.13%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 4 (0.00%)	3 / 275 (1.09%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 4 (0.00%)	3 / 275 (1.09%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Pulmonary congestion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Respiratory distress			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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 hypertension			

subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	4 / 275 (1.45%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asphyxia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Peripheral bilateral pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 4 (0.00%)	4 / 275 (1.45%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	3 / 275 (1.09%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			

subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Assisted suicide			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Impulse-control disorder			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophreniform disorder			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood cholesterol increased			

subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ejection fraction decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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 creatine phosphokinase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 4 (0.00%)	6 / 275 (2.18%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed[3]	0 / 4 (0.00%)	2 / 47 (4.26%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Pelvic fracture			

subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Road traffic accident			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Rib fracture			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Toxicity to various agents			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Ankle fracture			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Traumatic intracranial haemorrhage			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Radiation necrosis			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Pericardial effusion			
subjects affected / exposed	0 / 4 (0.00%)	5 / 275 (1.82%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Supraventricular tachycardia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Coronary artery disease			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 4 (25.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 3	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed[4]	0 / 4 (0.00%)	1 / 47 (2.13%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 4 (25.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Lacunar stroke			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Vagus nerve disorder			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurological symptom			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brainstem compression			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Aphasia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Cerebral infarction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
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%)	1 / 275 (0.36%)	0 / 3 (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
Metabolic encephalopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
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 disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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			
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Eye pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (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
Cataract			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blepharitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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 wall haematoma			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric volvulus			

subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Gastritis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glossitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Pancreatitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	3 / 275 (1.09%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Terminal ileitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biloma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Bile duct stenosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystocholangitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Dermatomyositis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
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%)	1 / 275 (0.36%)	0 / 3 (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
Neurogenic bladder			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cyst haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Spinal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	19 / 275 (6.91%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 33	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	4 / 275 (1.45%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Pyelonephritis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
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%)	4 / 275 (1.45%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung abscess			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			

subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)	3 / 275 (1.09%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Escherichia bacteraemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
COVID-19			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Infectious pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Viral upper respiratory tract infection			

subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Urethritis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (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
Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 4 (25.00%)	1 / 275 (0.36%)	0 / 3 (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
Hypercalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
alternative assessment type:			

Systematic			
subjects affected / exposed[5]	0 / 3 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	150 mg QD (Phase 1)	100 mg QD (Phase 1)	75 mg QD (Phase 1)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	10 / 17 (58.82%)	6 / 12 (50.00%)
number of deaths (all causes)	2	3	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Acute myeloid leukaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Breast cancer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Colon cancer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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 tumour thrombotic microangiopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Neoplasm progression			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (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
Embolism venous			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (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
Aortic dissection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Hypertensive crisis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Peripheral artery occlusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Superior vena cava syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Thrombosis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 3 (33.33%)	4 / 17 (23.53%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 3	0 / 1
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
General physical health deterioration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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			
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	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
Hypoxia			
subjects affected / exposed[1]	1 / 3 (33.33%)	0 / 17 (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 / 1	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	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
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	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
Acute respiratory failure			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Acute pulmonary oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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 exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Asthma			
subjects affected / exposed[2]	0 / 3 (0.00%)	0 / 17 (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
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Interstitial lung disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Lung disorder			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Pleuritic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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 congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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 distress			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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 hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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 / 3 (0.00%)	0 / 17 (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 failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	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
Asphyxia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Peripheral bilateral pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 3 (33.33%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (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
Delirium			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Assisted suicide			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Impulse-control disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Schizophreniform disorder			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Blood cholesterol increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Ejection fraction decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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			
Subdural haematoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	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
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Femoral neck fracture			
subjects affected / exposed[3]	0 / 3 (0.00%)	0 / 17 (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
Hip fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Pelvic fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Humerus fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Road traffic accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Rib fracture			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Toxicity to various agents			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Ankle fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Tendon rupture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Radiation necrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Pericardial effusion			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Atrioventricular block complete			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Sinus node dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Atrial flutter			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Coronary artery disease			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Haemorrhage intracranial			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (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
Presyncope			
subjects affected / exposed[4]	0 / 3 (0.00%)	0 / 17 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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	1 / 3 (33.33%)	0 / 17 (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
Brain oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Cognitive disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Hydrocephalus			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Partial seizures			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Ischaemic stroke			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Lacunar stroke			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Vagus nerve disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Neurological symptom			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Brainstem compression			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Aphasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Cerebral infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Dysarthria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Hemiparesis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Metabolic encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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 disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Blood and lymphatic system disorders			

Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Blepharitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Ileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Large intestinal obstruction			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Intestinal perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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 pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Abdominal wall haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Gastric volvulus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Glossitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Nausea			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Pancreatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Terminal ileitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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			
Biloma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	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
Jaundice			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Bile duct stenosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Cholangitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Cholecystocholangitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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 and subcutaneous tissue disorders			
Dermatomyositis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Neurogenic bladder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Renal cyst haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Renal failure			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Spinal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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			
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	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

Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Pneumonia			
subjects affected / exposed	2 / 3 (66.67%)	2 / 17 (11.76%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	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
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Lung abscess			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Erysipelas			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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 / 3 (0.00%)	0 / 17 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Vestibular neuronitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	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
Escherichia bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
COVID-19			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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 infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Infectious pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Urethritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Hypercalcaemia			

subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (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
Hyperuricaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (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
Hypertriglyceridaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (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
Dehydration			
alternative assessment type: Systematic			
subjects affected / exposed[5]	0 / 3 (0.00%)	0 / 17 (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

Serious adverse events	200 mg QD (Phase 1)		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute myeloid leukaemia			

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Breast cancer				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colon cancer				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary tumour thrombotic microangiopathy				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neoplasm progression				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Embolism				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Embolism venous				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic dissection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive crisis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral artery occlusion				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Superior vena cava syndrome				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombosis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Disease progression				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthenia				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral swelling				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Generalised oedema				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gait disturbance				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed[1]	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute pulmonary oedema				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea exertional				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epistaxis				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed[2]	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung disorder				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleuritic pain				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary congestion				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary hypertension				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wheezing				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asphyxia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral bilateral pulmonary embolism				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Mental status changes				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Delirium				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hallucination				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Assisted suicide				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Impulse-control disorder				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Schizophreniform disorder				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lipase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alanine aminotransferase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood cholesterol increased				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ejection fraction decreased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood creatine phosphokinase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SARS-CoV-2 test positive				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Subdural haematoma				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femoral neck fracture				
subjects affected / exposed[3]	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic fracture				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural haemorrhage				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ankle fracture				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thoracic vertebral fracture				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Traumatic intracranial haemorrhage				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radiation necrosis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiac arrest				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block complete				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus node dysfunction				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Headache				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed[4]	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Brain oedema				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cognitive disorder				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hydrocephalus				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Partial seizures				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lacunar stroke				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral sensory neuropathy				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vagus nerve disorder				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neurological symptom				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Brainstem compression				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aphasia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysarthria				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolic encephalopathy				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorder				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tremor				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Thrombocytopenia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Eye pain				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cataract				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blepharitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestinal obstruction				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal wall haematoma				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric volvulus				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Glossitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Terminal ileitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysphagia				

subjects affected / exposed	0 / 3 (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 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Biloma				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Jaundice				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bile duct stenosis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholangitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystocholangitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				

Dermatomyositis				
subjects affected / exposed	0 / 3 (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 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neurogenic bladder				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal cyst haemorrhage				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal pain				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Musculoskeletal chest pain				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthralgia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Influenza				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				

subjects affected / exposed	1 / 3 (33.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung abscess				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vestibular neuronitis				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infectious pleural effusion				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral upper respiratory tract infection				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urethritis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperuricaemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertriglyceridaemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				
alternative assessment type:				

Systematic			
subjects affected / exposed[5]	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Data is valid

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Data is valid

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Data is valid

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Data is valid

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Data is valid

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

Non-serious adverse events	50 mg QD (Phase 1)	25 mg QD (Phase 1)	10 mg QD (Phase 1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Shock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Raynaud's phenomenon			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	2	2	1
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	3 / 3 (100.00%)
occurrences (all)	1	1	3
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Axillary pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Catheter site extravasation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Disease progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Performance status decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Swelling face			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Social circumstances			
Menopause			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Breast pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erectile dysfunction			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Acute respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis chronic			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laryngeal inflammation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleuritic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rales			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lung disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Snoring			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Affect lability			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abnormal dreams			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mental status changes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hallucination			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bradyphrenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nightmare			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reading disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hallucination, auditory			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mental disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mania			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood cholesterol increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Amylase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	3
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Blood triglycerides increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Blood creatinine increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood phosphorus decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Candida test positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Glucose urine present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Amino acid level increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipids increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Incision site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Limb injury			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Toxicity to various agents			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ventricular dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Aphasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Amnesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Neuropathy peripheral			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	2
Memory impairment			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Presyncope			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Slow speech			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Formication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Dysaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hemiparesis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neurotoxicity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nervous system disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mental impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Partial seizures			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peroneal nerve palsy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Seizure			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Speech disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Sensory disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Brachial plexopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bradykinesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Facial paralysis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Motor dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep deficit			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fine motor skill dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Thrombocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Iron deficiency anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhagic diathesis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Vertigo positional			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Deafness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eye disorders			

Visual impairment			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Diplopia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Astigmatism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Asthenopia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Presbyopia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinal vein occlusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Retinal detachment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Faeces discoloured			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Swollen tongue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Colitis ulcerative			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Terminal ileitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pancreatic disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oesophagitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tooth impacted			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatic cytolysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hyperhidrosis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dermatitis contact			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatomyositis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rosacea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipohypertrophy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hand dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Micturition urgency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chronic kidney disease			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal colic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperparathyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	3
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint swelling			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Bone lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neck pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteoporosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Torticollis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint lock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Synovial cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sacral pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteonecrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Trismus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bacterial infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chronic sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Clostridium difficile colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enteritis infectious			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterococcal bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Soft tissue infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterocolitis infectious			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	2	6	1
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	0	5	1
Hypomagnesaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	4	9	0
Hyperlipidaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cell death			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	DDI Substudy	35 mg BID (Phase 1)	75 mg BID (Phase 1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 32 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 32 (6.25%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	10	1	1
Deep vein thrombosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Haemorrhage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Shock			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Raynaud's phenomenon			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	8 / 32 (25.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	18	1	0
Mucosal inflammation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Gait disturbance			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	4 / 32 (12.50%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	5	0	1
Face oedema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Oedema			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Oedema peripheral			
subjects affected / exposed	14 / 32 (43.75%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	31	0	3
Pyrexia			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Peripheral swelling			
subjects affected / exposed	4 / 32 (12.50%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Axillary pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Catheter site extravasation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Disease progression			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Generalised oedema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Performance status decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Swelling			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Swelling face			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Social circumstances			

Menopause			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Breast pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erectile dysfunction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 32 (21.88%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	9	1	0
Dysphonia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Dyspnoea			
subjects affected / exposed	10 / 32 (31.25%)	3 / 3 (100.00%)	1 / 3 (33.33%)
occurrences (all)	16	4	4
Dyspnoea exertional			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Epistaxis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Haemoptysis			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	1 / 32 (3.13%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Wheezing			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Acute respiratory failure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis chronic			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laryngeal inflammation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pleuritic pain			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Pulmonary oedema			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory tract congestion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lung disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Snoring			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Affect lability			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 32 (3.13%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	2	0

Insomnia			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Irritability			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Abnormal dreams			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mental status changes			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Confusional state			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Bradyphrenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	2 / 32 (6.25%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Nightmare			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Reading disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Depression			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hallucination, auditory			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Mental disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mania			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Investigations			
Blood cholesterol increased			
subjects affected / exposed	17 / 32 (53.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	60	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	5	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
Amylase increased			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	35	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Weight increased			
subjects affected / exposed	9 / 32 (28.13%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	20	0	2
Lipase increased			

subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	4 / 32 (12.50%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	12	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Candida test positive			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Glucose urine present			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Amino acid level increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipids increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 32 (15.63%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	8	0	0
Contusion			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Incision site pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toxicity to various agents			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal fracture			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0

Atrial fibrillation			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ventricular dysfunction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Angina pectoris			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Cognitive disorder			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Aphasia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Amnesia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Dizziness			
subjects affected / exposed	6 / 32 (18.75%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	9	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	8 / 32 (25.00%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	15	2	1
Neuropathy peripheral			

subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	4	0	2
Memory impairment			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Headache			
subjects affected / exposed	4 / 32 (12.50%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	9	1	2
Dysgeusia			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Presyncope			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Slow speech			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Formication			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dysaesthesia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Balance disorder			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Ataxia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hemiparesis			

subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Neurotoxicity			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Nervous system disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mental impairment			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Partial seizures			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peroneal nerve palsy			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Speech disorder			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sensory disturbance			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Brachial plexopathy			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bradykinesia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Facial paralysis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Motor dysfunction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperaesthesia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep deficit			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Fine motor skill dysfunction			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 32 (25.00%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	17	1	4

Thrombocytopenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhagic diathesis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Vertigo positional			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear discomfort			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Deafness			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Visual impairment			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Vision blurred			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival oedema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Astigmatism			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Asthenopia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Presbyopia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Retinal vein occlusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Photopsia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinal detachment			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Abdominal distension			
subjects affected / exposed	7 / 32 (21.88%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	9	0	0
Vomiting			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Nausea			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	3	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Dysphagia			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Dyspepsia			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	5 / 32 (15.63%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
Constipation			
subjects affected / exposed	8 / 32 (25.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	13	1	2
Abdominal discomfort			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Abdominal pain upper			
subjects affected / exposed	3 / 32 (9.38%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	4	1	1
Faeces discoloured			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Intestinal obstruction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Swollen tongue			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Stomatitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Colitis ulcerative			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dental caries			
subjects affected / exposed	10 / 32 (31.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Food poisoning			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Terminal ileitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pancreatic disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oesophagitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth impacted			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	4 / 32 (12.50%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatic cytolysis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			

subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Dry skin			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Rash			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Pruritus			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatomyositis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rosacea			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipohypertrophy			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hand dermatitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chronic kidney disease			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal colic			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperparathyroidism			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 32 (18.75%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	9	0	1
Back pain			
subjects affected / exposed	6 / 32 (18.75%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	7	0	3
Bone pain			
subjects affected / exposed	4 / 32 (12.50%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Joint swelling			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Muscular weakness			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal chest pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Myalgia			
subjects affected / exposed	5 / 32 (15.63%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	7	0	1
Pain in extremity			
subjects affected / exposed	5 / 32 (15.63%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	8	0	4
Arthritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bone lesion			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Osteoarthritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteoporosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Torticollis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint lock			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Synovial cyst			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sacral pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteonecrosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Trismus			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	4
Influenza			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	4 / 32 (12.50%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Rhinitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Sinusitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Bacterial infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chronic sinusitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enteritis infectious			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterococcal bacteraemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Nasopharyngitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Periodontitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Soft tissue infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	4 / 32 (12.50%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Viral rhinitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Ear infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterocolitis infectious			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyelonephritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	3 / 32 (9.38%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
Hypercholesterolaemia			
subjects affected / exposed	15 / 32 (46.88%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	91	1	17
Decreased appetite			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			

subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	3 / 32 (9.38%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	4	1	0
Hyperuricaemia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Hypertriglyceridaemia			
subjects affected / exposed	23 / 32 (71.88%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	137	0	3
Hyperlipidaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fluid retention			
subjects affected / exposed	2 / 32 (6.25%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
Hypocalcaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Increased appetite			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cell death			

subjects affected / exposed	0 / 32 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Hyponatraemia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0

Non-serious adverse events	100 mg BID (Phase 1)	Phase 2	Japan Lead-In Cohort (LIC)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	273 / 275 (99.27%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	35 / 275 (12.73%)	1 / 3 (33.33%)
occurrences (all)	0	82	2
Deep vein thrombosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Haemorrhage			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Raynaud's phenomenon			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	40 / 275 (14.55%)	0 / 3 (0.00%)
occurrences (all)	0	82	0
Mucosal inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 4 (0.00%)	14 / 275 (5.09%)	0 / 3 (0.00%)
occurrences (all)	0	25	0
Fatigue			
subjects affected / exposed	3 / 4 (75.00%)	50 / 275 (18.18%)	0 / 3 (0.00%)
occurrences (all)	5	90	0
Face oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 4 (0.00%)	30 / 275 (10.91%)	0 / 3 (0.00%)
occurrences (all)	0	42	0
Oedema			
subjects affected / exposed	1 / 4 (25.00%)	25 / 275 (9.09%)	0 / 3 (0.00%)
occurrences (all)	1	34	0
Oedema peripheral			

subjects affected / exposed	3 / 4 (75.00%)	127 / 275 (46.18%)	1 / 3 (33.33%)
occurrences (all)	7	238	1
Pyrexia			
subjects affected / exposed	1 / 4 (25.00%)	49 / 275 (17.82%)	0 / 3 (0.00%)
occurrences (all)	1	70	0
Pain			
subjects affected / exposed	0 / 4 (0.00%)	15 / 275 (5.45%)	0 / 3 (0.00%)
occurrences (all)	0	19	0
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	21 / 275 (7.64%)	0 / 3 (0.00%)
occurrences (all)	0	26	0
Axillary pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site extravasation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Disease progression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Generalised oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Performance status decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Swelling			

subjects affected / exposed	0 / 4 (0.00%)	5 / 275 (1.82%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Swelling face			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Social circumstances			
Menopause			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Breast pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erectile dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 4 (50.00%)	68 / 275 (24.73%)	0 / 3 (0.00%)
occurrences (all)	4	134	0

Dysphonia			
subjects affected / exposed	1 / 4 (25.00%)	13 / 275 (4.73%)	0 / 3 (0.00%)
occurrences (all)	1	15	0
Dyspnoea			
subjects affected / exposed	2 / 4 (50.00%)	82 / 275 (29.82%)	1 / 3 (33.33%)
occurrences (all)	5	116	1
Dyspnoea exertional			
subjects affected / exposed	1 / 4 (25.00%)	15 / 275 (5.45%)	0 / 3 (0.00%)
occurrences (all)	4	25	0
Epistaxis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	15 / 275 (5.45%)	0 / 3 (0.00%)
occurrences (all)	0	16	0
Wheezing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Acute respiratory failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis chronic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laryngeal inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Oropharyngeal pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pulmonary hypertension			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 4 (0.00%)	15 / 275 (5.45%)	0 / 3 (0.00%)
occurrences (all)	0	21	0
Pleuritic pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Sinus congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Lung disorder			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Snoring			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Affect lability			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 4 (25.00%)	21 / 275 (7.64%)	0 / 3 (0.00%)
occurrences (all)	1	25	0
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	30 / 275 (10.91%)	0 / 3 (0.00%)
occurrences (all)	0	40	0
Irritability			
subjects affected / exposed	0 / 4 (0.00%)	16 / 275 (5.82%)	0 / 3 (0.00%)
occurrences (all)	0	21	0
Abnormal dreams			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mental status changes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	11 / 275 (4.00%)	0 / 3 (0.00%)
occurrences (all)	0	13	0
Bradyphrenia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	0 / 4 (0.00%)	4 / 275 (1.45%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Nightmare			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reading disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 4 (0.00%)	16 / 275 (5.82%)	0 / 3 (0.00%)
occurrences (all)	0	24	0
Hallucination, auditory			
subjects affected / exposed	0 / 4 (0.00%)	5 / 275 (1.82%)	1 / 3 (33.33%)
occurrences (all)	0	7	2
Mental disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mania			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood cholesterol increased			
subjects affected / exposed	1 / 4 (25.00%)	97 / 275 (35.27%)	3 / 3 (100.00%)
occurrences (all)	3	566	24
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 4 (0.00%)	14 / 275 (5.09%)	2 / 3 (66.67%)
occurrences (all)	0	44	22
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 4 (50.00%)	44 / 275 (16.00%)	1 / 3 (33.33%)
occurrences (all)	8	109	1
Amylase increased			
subjects affected / exposed	1 / 4 (25.00%)	35 / 275 (12.73%)	0 / 3 (0.00%)
occurrences (all)	2	119	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	42 / 275 (15.27%)	2 / 3 (66.67%)
occurrences (all)	5	97	2
Weight increased			
subjects affected / exposed	2 / 4 (50.00%)	77 / 275 (28.00%)	1 / 3 (33.33%)
occurrences (all)	3	175	2
Lipase increased			
subjects affected / exposed	1 / 4 (25.00%)	39 / 275 (14.18%)	1 / 3 (33.33%)
occurrences (all)	2	123	5
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 4 (25.00%)	19 / 275 (6.91%)	0 / 3 (0.00%)
occurrences (all)	1	28	0
Blood triglycerides increased			
subjects affected / exposed	1 / 4 (25.00%)	17 / 275 (6.18%)	0 / 3 (0.00%)
occurrences (all)	6	38	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Candida test positive			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Ejection fraction decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 4 (50.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	12	0	0
Glucose urine present			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Amino acid level increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood glucose increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			

subjects affected / exposed	0 / 4 (0.00%)	10 / 275 (3.64%)	0 / 3 (0.00%)
occurrences (all)	0	10	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipids increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	17 / 275 (6.18%)	1 / 3 (33.33%)
occurrences (all)	0	35	2
Contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Incision site pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toxicity to various agents			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Spinal fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	11 / 275 (4.00%)	0 / 3 (0.00%)
occurrences (all)	0	12	0
Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ventricular dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Angina pectoris			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 4 (0.00%)	13 / 275 (4.73%)	0 / 3 (0.00%)
occurrences (all)	0	28	0
Cognitive disorder			
subjects affected / exposed	1 / 4 (25.00%)	23 / 275 (8.36%)	0 / 3 (0.00%)
occurrences (all)	1	31	0
Aphasia			

subjects affected / exposed	0 / 4 (0.00%)	9 / 275 (3.27%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Amnesia			
subjects affected / exposed	0 / 4 (0.00%)	24 / 275 (8.73%)	0 / 3 (0.00%)
occurrences (all)	0	41	0
Dizziness			
subjects affected / exposed	2 / 4 (50.00%)	51 / 275 (18.55%)	1 / 3 (33.33%)
occurrences (all)	2	90	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 4 (0.00%)	25 / 275 (9.09%)	2 / 3 (66.67%)
occurrences (all)	0	36	2
Paraesthesia			
subjects affected / exposed	2 / 4 (50.00%)	44 / 275 (16.00%)	0 / 3 (0.00%)
occurrences (all)	4	72	0
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)	42 / 275 (15.27%)	0 / 3 (0.00%)
occurrences (all)	0	51	0
Memory impairment			
subjects affected / exposed	1 / 4 (25.00%)	36 / 275 (13.09%)	0 / 3 (0.00%)
occurrences (all)	2	85	0
Headache			
subjects affected / exposed	2 / 4 (50.00%)	57 / 275 (20.73%)	1 / 3 (33.33%)
occurrences (all)	3	98	1
Dysgeusia			
subjects affected / exposed	1 / 4 (25.00%)	11 / 275 (4.00%)	0 / 3 (0.00%)
occurrences (all)	1	11	0
Presyncope			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Slow speech			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Formication			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysarthria			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dysaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	1 / 4 (25.00%)	7 / 275 (2.55%)	0 / 3 (0.00%)
occurrences (all)	1	12	0
Ataxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hemiparesis			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Neurotoxicity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 4 (0.00%)	4 / 275 (1.45%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Nervous system disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mental impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Partial seizures			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peroneal nerve palsy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Speech disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sensory disturbance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Brachial plexopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bradykinesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Facial paralysis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Motor dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperaesthesia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep deficit			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Fine motor skill dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 4 (50.00%)	46 / 275 (16.73%)	0 / 3 (0.00%)
occurrences (all)	2	101	0
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 4 (0.00%)	3 / 275 (1.09%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhagic diathesis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 4 (25.00%)	25 / 275 (9.09%)	1 / 3 (33.33%)
occurrences (all)	3	37	1
Vertigo positional			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Deafness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 4 (0.00%)	15 / 275 (5.45%)	0 / 3 (0.00%)
occurrences (all)	0	23	0
Vision blurred			
subjects affected / exposed	0 / 4 (0.00%)	16 / 275 (5.82%)	0 / 3 (0.00%)
occurrences (all)	0	20	0
Dry eye			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diplopia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Astigmatism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Asthenopia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Presbyopia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinal vein occlusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Photophobia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinal detachment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 4 (50.00%)	22 / 275 (8.00%)	0 / 3 (0.00%)
occurrences (all)	4	32	0
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)	20 / 275 (7.27%)	0 / 3 (0.00%)
occurrences (all)	0	24	0

Vomiting			
subjects affected / exposed	2 / 4 (50.00%)	43 / 275 (15.64%)	0 / 3 (0.00%)
occurrences (all)	6	59	0
Nausea			
subjects affected / exposed	3 / 4 (75.00%)	59 / 275 (21.45%)	1 / 3 (33.33%)
occurrences (all)	5	83	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 4 (0.00%)	20 / 275 (7.27%)	0 / 3 (0.00%)
occurrences (all)	0	22	0
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)	17 / 275 (6.18%)	0 / 3 (0.00%)
occurrences (all)	0	17	0
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	3 / 4 (75.00%)	69 / 275 (25.09%)	0 / 3 (0.00%)
occurrences (all)	5	122	0
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	50 / 275 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	76	0
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	4 / 275 (1.45%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Abdominal pain upper			
subjects affected / exposed	2 / 4 (50.00%)	15 / 275 (5.45%)	0 / 3 (0.00%)
occurrences (all)	2	22	0
Faeces discoloured			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Swollen tongue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 4 (0.00%)	12 / 275 (4.36%)	0 / 3 (0.00%)
occurrences (all)	0	12	0
Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	14 / 275 (5.09%)	0 / 3 (0.00%)
occurrences (all)	0	19	0
Colitis ulcerative			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Terminal ileitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pancreatic disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oesophagitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth impacted			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Flatulence			
subjects affected / exposed	0 / 4 (0.00%)	9 / 275 (3.27%)	0 / 3 (0.00%)
occurrences (all)	0	10	0
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatic cytolysis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 4 (25.00%)	18 / 275 (6.55%)	1 / 3 (33.33%)
occurrences (all)	1	20	1
Dry skin			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Rash			
subjects affected / exposed	0 / 4 (0.00%)	33 / 275 (12.00%)	0 / 3 (0.00%)
occurrences (all)	0	49	0
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	11 / 275 (4.00%)	0 / 3 (0.00%)
occurrences (all)	0	14	0
Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)	19 / 275 (6.91%)	0 / 3 (0.00%)
occurrences (all)	0	20	0
Dermatitis acneiform			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatomyositis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rash pruritic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rosacea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash papular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia			

syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipohypertrophy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hand dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)	14 / 275 (5.09%)	0 / 3 (0.00%)
occurrences (all)	0	20	0
Pollakiuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chronic kidney disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal colic			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperparathyroidism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	84 / 275 (30.55%)	1 / 3 (33.33%)
occurrences (all)	1	138	1
Back pain			
subjects affected / exposed	2 / 4 (50.00%)	45 / 275 (16.36%)	1 / 3 (33.33%)
occurrences (all)	2	63	1
Bone pain			
subjects affected / exposed	0 / 4 (0.00%)	8 / 275 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	8	0
Joint swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 4 (25.00%)	19 / 275 (6.91%)	0 / 3 (0.00%)
occurrences (all)	1	22	0
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	18 / 275 (6.55%)	0 / 3 (0.00%)
occurrences (all)	0	22	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)	11 / 275 (4.00%)	0 / 3 (0.00%)
occurrences (all)	0	12	0
Musculoskeletal pain			

subjects affected / exposed	0 / 4 (0.00%)	7 / 275 (2.55%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Myalgia			
subjects affected / exposed	1 / 4 (25.00%)	38 / 275 (13.82%)	2 / 3 (66.67%)
occurrences (all)	1	50	3
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	50 / 275 (18.18%)	0 / 3 (0.00%)
occurrences (all)	0	64	0
Arthritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bone lesion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 4 (0.00%)	8 / 275 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Osteoarthritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteoporosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pain in jaw			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Torticollis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint lock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Synovial cyst			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sacral pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteonecrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Trismus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 4 (0.00%)	3 / 275 (1.09%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 4 (25.00%)	20 / 275 (7.27%)	0 / 3 (0.00%)
occurrences (all)	4	30	0
Influenza			
subjects affected / exposed	0 / 4 (0.00%)	17 / 275 (6.18%)	0 / 3 (0.00%)
occurrences (all)	0	24	0
Pneumonia			
subjects affected / exposed	1 / 4 (25.00%)	27 / 275 (9.82%)	1 / 3 (33.33%)
occurrences (all)	1	37	1

Rhinitis			
subjects affected / exposed	1 / 4 (25.00%)	16 / 275 (5.82%)	0 / 3 (0.00%)
occurrences (all)	2	26	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	38 / 275 (13.82%)	0 / 3 (0.00%)
occurrences (all)	0	61	0
Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bacterial infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chronic sinusitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enteritis infectious			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterococcal bacteraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Helicobacter infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Laryngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 4 (25.00%)	24 / 275 (8.73%)	2 / 3 (66.67%)
occurrences (all)	1	31	3
Oral candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	2 / 275 (0.73%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Periodontitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Soft tissue infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 4 (25.00%)	20 / 275 (7.27%)	0 / 3 (0.00%)
occurrences (all)	1	28	0

Viral rhinitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterocolitis infectious			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyelonephritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperglycaemia			

subjects affected / exposed	0 / 4 (0.00%)	26 / 275 (9.45%)	0 / 3 (0.00%)
occurrences (all)	0	76	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 4 (25.00%)	153 / 275 (55.64%)	0 / 3 (0.00%)
occurrences (all)	8	789	0
Decreased appetite			
subjects affected / exposed	2 / 4 (50.00%)	18 / 275 (6.55%)	0 / 3 (0.00%)
occurrences (all)	3	20	0
Hypophosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	19 / 275 (6.91%)	0 / 3 (0.00%)
occurrences (all)	0	43	0
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	17 / 275 (6.18%)	0 / 3 (0.00%)
occurrences (all)	0	27	0
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	18 / 275 (6.55%)	0 / 3 (0.00%)
occurrences (all)	0	30	0
Hyperuricaemia			
subjects affected / exposed	1 / 4 (25.00%)	19 / 275 (6.91%)	1 / 3 (33.33%)
occurrences (all)	1	24	1
Hypertriglyceridaemia			
subjects affected / exposed	1 / 4 (25.00%)	179 / 275 (65.09%)	3 / 3 (100.00%)
occurrences (all)	11	1273	33
Hyperlipidaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypercalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	0 / 4 (0.00%)	7 / 275 (2.55%)	0 / 3 (0.00%)
occurrences (all)	0	8	0
Hypocalcaemia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)	16 / 275 (5.82%)	0 / 3 (0.00%)
occurrences (all)	0	26	0
Increased appetite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cell death			
subjects affected / exposed	1 / 4 (25.00%)	0 / 275 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Gout			
subjects affected / exposed	0 / 4 (0.00%)	1 / 275 (0.36%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	10 / 275 (3.64%)	0 / 3 (0.00%)
occurrences (all)	0	14	0

Non-serious adverse events	150 mg QD (Phase 1)	100 mg QD (Phase 1)	75 mg QD (Phase 1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	17 / 17 (100.00%)	12 / 12 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 3 (33.33%)	1 / 17 (5.88%)	2 / 12 (16.67%)
occurrences (all)	1	3	3
Deep vein thrombosis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Shock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Raynaud's phenomenon			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	4 / 17 (23.53%)	4 / 12 (33.33%)
occurrences (all)	0	7	8
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Fatigue			

subjects affected / exposed	2 / 3 (66.67%)	5 / 17 (29.41%)	5 / 12 (41.67%)
occurrences (all)	4	8	6
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	3
Oedema peripheral			
subjects affected / exposed	3 / 3 (100.00%)	10 / 17 (58.82%)	4 / 12 (33.33%)
occurrences (all)	7	17	7
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 17 (17.65%)	1 / 12 (8.33%)
occurrences (all)	1	3	1
Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Axillary pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Catheter site extravasation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Disease progression			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Generalised oedema			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Performance status decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 3 (33.33%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Seasonal allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Social circumstances			
Menopause			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Dysmenorrhoea			

subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Breast pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Erectile dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 3 (0.00%)	2 / 17 (11.76%)	2 / 12 (16.67%)
occurrences (all)	0	2	3
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	4 / 17 (23.53%)	3 / 12 (25.00%)
occurrences (all)	0	0	3
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
Epistaxis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Wheezing			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Acute respiratory failure			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Bronchitis chronic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Laryngeal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 17 (11.76%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Pulmonary hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pleuritic pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Pulmonary oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Rales			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lung disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Snoring			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Affect lability			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	0	5
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Irritability			
subjects affected / exposed	0 / 3 (0.00%)	2 / 17 (11.76%)	2 / 12 (16.67%)
occurrences (all)	0	2	2
Abnormal dreams			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0

Mental status changes			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hallucination			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Confusional state			
subjects affected / exposed	1 / 3 (33.33%)	2 / 17 (11.76%)	0 / 12 (0.00%)
occurrences (all)	1	2	0
Bradyphrenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nightmare			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Reading disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hallucination, auditory			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Mental disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Mania			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood cholesterol increased			
subjects affected / exposed	1 / 3 (33.33%)	4 / 17 (23.53%)	6 / 12 (50.00%)
occurrences (all)	1	13	9
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	7	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	4 / 17 (23.53%)	3 / 12 (25.00%)
occurrences (all)	0	9	6
Amylase increased			
subjects affected / exposed	0 / 3 (0.00%)	5 / 17 (29.41%)	1 / 12 (8.33%)
occurrences (all)	0	18	3
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	4 / 17 (23.53%)	3 / 12 (25.00%)
occurrences (all)	0	8	5
Weight increased			
subjects affected / exposed	1 / 3 (33.33%)	4 / 17 (23.53%)	4 / 12 (33.33%)
occurrences (all)	1	7	9
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	5 / 17 (29.41%)	3 / 12 (25.00%)
occurrences (all)	0	30	6
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Blood triglycerides increased			
subjects affected / exposed	1 / 3 (33.33%)	4 / 17 (23.53%)	2 / 12 (16.67%)
occurrences (all)	1	10	3
Blood alkaline phosphatase increased			

subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Blood creatinine increased			
subjects affected / exposed	2 / 3 (66.67%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	2	2	3
Blood phosphorus decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Candida test positive			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Ejection fraction decreased			
subjects affected / exposed	2 / 3 (66.67%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	3
Glucose urine present			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Transaminases increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Liver function test increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram PR prolongation			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Amino acid level increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Lipids increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Ligament sprain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Joint dislocation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Incision site pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Toxicity to various agents			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Road traffic accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin laceration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Spinal fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ventricular dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Cognitive disorder			
subjects affected / exposed	2 / 3 (66.67%)	1 / 17 (5.88%)	2 / 12 (16.67%)
occurrences (all)	2	1	2
Aphasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Amnesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	2 / 17 (11.76%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	4 / 17 (23.53%)	1 / 12 (8.33%)
occurrences (all)	0	5	4
Neuropathy peripheral			
subjects affected / exposed	1 / 3 (33.33%)	3 / 17 (17.65%)	4 / 12 (33.33%)
occurrences (all)	3	3	6
Memory impairment			
subjects affected / exposed	0 / 3 (0.00%)	3 / 17 (17.65%)	2 / 12 (16.67%)
occurrences (all)	0	3	4
Headache			
subjects affected / exposed	1 / 3 (33.33%)	2 / 17 (11.76%)	4 / 12 (33.33%)
occurrences (all)	1	6	5
Dysgeusia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Slow speech			
subjects affected / exposed	0 / 3 (0.00%)	3 / 17 (17.65%)	1 / 12 (8.33%)
occurrences (all)	0	4	1
Formication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Dysaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Ataxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hemiparesis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Neurotoxicity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	5	0
Neuralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nervous system disorder			

subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Mental impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	3 / 12 (25.00%)
occurrences (all)	0	1	3
Partial seizures			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Peroneal nerve palsy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Speech disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
Sensory disturbance			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Brachial plexopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Bradykinesia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Facial paralysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Motor dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Hyperaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Sleep deficit			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Fine motor skill dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 3 (100.00%)	7 / 17 (41.18%)	3 / 12 (25.00%)
occurrences (all)	5	22	4
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 17 (11.76%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Thrombocytosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	8	0

Leukocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Iron deficiency anaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Haemorrhagic diathesis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 3 (33.33%)	3 / 17 (17.65%)	3 / 12 (25.00%)
occurrences (all)	1	4	4
Vertigo positional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Hypoacusis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	2 / 12 (16.67%)
occurrences (all)	0	1	3
Ear discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Deafness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Tympanic membrane perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	3
Ear pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	3	0	1
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	2 / 17 (11.76%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Conjunctival oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Astigmatism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Asthenopia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Presbyopia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Retinal vein occlusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
Photopsia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

Photophobia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Retinal detachment			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 17 (11.76%)	2 / 12 (16.67%)
occurrences (all)	0	3	2
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	3 / 17 (17.65%)	1 / 12 (8.33%)
occurrences (all)	0	5	1
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	4 / 17 (23.53%)	3 / 12 (25.00%)
occurrences (all)	0	5	3
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	3 / 17 (17.65%)	1 / 12 (8.33%)
occurrences (all)	0	4	1
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	4 / 17 (23.53%)	3 / 12 (25.00%)
occurrences (all)	1	5	7
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	4 / 17 (23.53%)	3 / 12 (25.00%)
occurrences (all)	0	5	3
Abdominal discomfort			

subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Swollen tongue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Colitis ulcerative			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Food poisoning			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Terminal ileitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pancreatic disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Oesophagitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Tooth impacted			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hepatic cytolysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	2 / 17 (11.76%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	3 / 12 (25.00%)
occurrences (all)	0	1	4
Pruritus			

subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dermatomyositis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Photosensitivity reaction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Rash pruritic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Rosacea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin lesion			

subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Lipohypertrophy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hand dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	2 / 17 (11.76%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Micturition urgency			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hydronephrosis			

subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Chronic kidney disease			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	1 / 3 (33.33%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Urinary incontinence			
subjects affected / exposed	1 / 3 (33.33%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Renal colic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Hyperparathyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	6 / 17 (35.29%)	3 / 12 (25.00%)
occurrences (all)	0	12	4
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	6 / 17 (35.29%)	2 / 12 (16.67%)
occurrences (all)	0	11	2
Bone pain			

subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 17 (11.76%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	4 / 17 (23.53%)	0 / 12 (0.00%)
occurrences (all)	0	5	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 17 (11.76%)	2 / 12 (16.67%)
occurrences (all)	0	2	3
Pain in extremity			
subjects affected / exposed	1 / 3 (33.33%)	2 / 17 (11.76%)	2 / 12 (16.67%)
occurrences (all)	1	2	2
Arthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Bone lesion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 17 (17.65%)	0 / 12 (0.00%)
occurrences (all)	0	4	0
Limb discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Musculoskeletal discomfort			

subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 17 (17.65%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
Osteoarthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Osteoporosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 3 (0.00%)	2 / 17 (11.76%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Plantar fasciitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 17 (11.76%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Torticollis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Joint lock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Synovial cyst			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Sacral pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Osteonecrosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Trismus			

subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Spinal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 3 (33.33%)	2 / 17 (11.76%)	2 / 12 (16.67%)
occurrences (all)	1	6	2
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	1 / 3 (33.33%)	4 / 17 (23.53%)	3 / 12 (25.00%)
occurrences (all)	1	8	12
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	2
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Bacterial infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Chronic sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Enteritis infectious			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Enterococcal bacteraemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Helicobacter infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	0 / 3 (0.00%)	3 / 17 (17.65%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Herpes virus infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Periodontitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	3 / 17 (17.65%)	1 / 12 (8.33%)
occurrences (all)	0	4	1
Soft tissue infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Tooth abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	4 / 17 (23.53%)	1 / 12 (8.33%)
occurrences (all)	0	8	2
Viral rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Enterocolitis infectious			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2

Paronychia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	2
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Viral infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	3
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	12	0
Hypercholesterolaemia			
subjects affected / exposed	2 / 3 (66.67%)	12 / 17 (70.59%)	7 / 12 (58.33%)
occurrences (all)	4	68	38
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	4	0	0
Hypomagnesaemia			
subjects affected / exposed	3 / 3 (100.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	5	0	0
Hypokalaemia			
subjects affected / exposed	2 / 3 (66.67%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	7	1	0
Hyperuricaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hypertriglyceridaemia			

subjects affected / exposed	1 / 3 (33.33%)	7 / 17 (41.18%)	5 / 12 (41.67%)
occurrences (all)	1	74	10
Hyperlipidaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Hypocalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	4	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 17 (5.88%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Cell death			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 17 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	200 mg QD (Phase 1)		
Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 3 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Shock			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Raynaud's phenomenon			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Flushing			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Gait disturbance			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	3		
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Peripheral swelling			

subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Axillary pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Catheter site extravasation			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Disease progression			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Performance status decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Swelling			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Swelling face			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

Seasonal allergy subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Social circumstances Menopause subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Reproductive system and breast disorders Menstruation irregular subjects affected / exposed occurrences (all) Vaginal haemorrhage subjects affected / exposed occurrences (all) Dysmenorrhoea subjects affected / exposed occurrences (all) Breast pain subjects affected / exposed occurrences (all) Erectile dysfunction subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dysphonia subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Dyspnoea exertional subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0		

Epistaxis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Haemoptysis				
subjects affected / exposed	2 / 3 (66.67%)			
occurrences (all)	0			
Hypoxia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Pleural effusion				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Wheezing				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Acute respiratory failure				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Bronchitis chronic				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Laryngeal inflammation				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Nasal congestion				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Oropharyngeal pain				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Pulmonary hypertension				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Pulmonary embolism				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			

Productive cough subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Pleuritic pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Pulmonary oedema subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Respiratory tract congestion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Sinus congestion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Rales subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Sleep apnoea syndrome subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Lung disorder subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Snoring subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Psychiatric disorders Affect lability			

subjects affected / exposed	2 / 3 (66.67%)			
occurrences (all)	2			
Anxiety				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Insomnia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Irritability				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	2			
Abnormal dreams				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Mental status changes				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Hallucination				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Depressed mood				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Confusional state				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Bradyphrenia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Agitation				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Nightmare				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Sleep disorder				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Reading disorder			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hallucination, auditory			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Mental disorder			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Mania			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Investigations			
Blood cholesterol increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	3		
Amylase increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Alanine aminotransferase increased			

subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Weight increased				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Lipase increased				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	3			
Electrocardiogram QT prolonged				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blood triglycerides increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blood alkaline phosphatase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blood creatinine increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blood phosphorus decreased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Candida test positive				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Ejection fraction decreased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Glucose urine present				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			

International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Transaminases increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Liver function test increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Amino acid level increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood glucose increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Haemoglobin decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Lipids increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			

Fall				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Contusion				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Ligament sprain				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Joint dislocation				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Incision site pain				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Limb injury				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Toxicity to various agents				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Road traffic accident				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Skin abrasion				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Skin laceration				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Fracture				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Spinal fracture				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			

Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Ventricular dysfunction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Cognitive disorder			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	5		
Aphasia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Amnesia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Paraesthesia			

subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Neuropathy peripheral				
subjects affected / exposed	2 / 3 (66.67%)			
occurrences (all)	6			
Memory impairment				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Headache				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Dysgeusia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Presyncope				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Slow speech				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Formication				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Dysarthria				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Dysaesthesia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Carpal tunnel syndrome				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Balance disorder				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Ataxia				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Hemiparesis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Neurotoxicity				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Neuralgia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Nervous system disorder				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Migraine				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Mental impairment				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Hypoaesthesia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Partial seizures				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Psychomotor hyperactivity				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Peroneal nerve palsy				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Seizure				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Tremor				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Speech disorder			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Sensory disturbance			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Brachial plexopathy			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Bradykinesia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Facial paralysis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Motor dysfunction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hyperaesthesia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Sleep deficit			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Fine motor skill dysfunction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			

Anaemia				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Thrombocytopenia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Thrombocytosis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Neutropenia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Leukocytosis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Iron deficiency anaemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Haemorrhagic diathesis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Febrile neutropenia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Ear and labyrinth disorders				
Tinnitus				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Vertigo positional				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Vertigo				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Hypoacusis				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Ear discomfort			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Deafness			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tympanic membrane perforation			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Vision blurred			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Diplopia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Conjunctival oedema			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Astigmatism			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Asthenopia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

Presbyopia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Retinal vein occlusion			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Visual acuity reduced			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Photopsia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Photophobia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Retinal detachment			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dysphagia			

subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Dyspepsia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Diarrhoea				
subjects affected / exposed	2 / 3 (66.67%)			
occurrences (all)	4			
Constipation				
subjects affected / exposed	2 / 3 (66.67%)			
occurrences (all)	2			
Abdominal discomfort				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Abdominal pain upper				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Faeces discoloured				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Gastrointestinal disorder				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Intestinal obstruction				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Swollen tongue				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Ascites				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Dry mouth				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Stomatitis				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Colitis ulcerative			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dental caries			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Food poisoning			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Terminal ileitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pancreatic disorder			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Oesophagitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tooth impacted			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hepatic cytolysis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dermatitis contact			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dermatomyositis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Photosensitivity reaction			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Rash erythematous			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Rash maculo-papular			

subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Rash pruritic				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Rosacea				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Seborrhoeic dermatitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Skin lesion				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Erythema				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Dermatitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Eczema				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Rash papular				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Palmar-plantar erythrodysaesthesia syndrome				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Lipohypertrophy				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Hand dermatitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			

Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Micturition urgency			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Chronic kidney disease			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Renal colic			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hyperparathyroidism			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypothyroidism			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	4		
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Arthritis			

subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Bone lesion				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Flank pain				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Limb discomfort				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Musculoskeletal discomfort				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Neck pain				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Osteoarthritis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Osteoporosis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Pain in jaw				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Plantar fasciitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Torticollis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Musculoskeletal stiffness				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Joint lock				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Synovial cyst			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Sacral pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Osteonecrosis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Trismus			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Spinal pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	3		
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

Viral upper respiratory tract infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Bacterial infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Candida infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Cellulitis				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Chronic sinusitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Clostridium difficile colitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Enteritis infectious				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Gastroenteritis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Enterococcal bacteraemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Helicobacter infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Laryngitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			

Herpes virus infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Oral candidiasis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Periodontitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Pharyngitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Respiratory tract infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Soft tissue infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Tooth abscess				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Urinary tract infection				
subjects affected / exposed	2 / 3 (66.67%)			
occurrences (all)	3			
Viral rhinitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Conjunctivitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Herpes zoster				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			

Cystitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Ear infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Enterocolitis infectious			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Paronychia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Viral infection			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypercholesterolaemia			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	21		
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			

subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	4			
Hypomagnesaemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Hypokalaemia				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	16			
Hyperuricaemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Hypertriglyceridaemia				
subjects affected / exposed	2 / 3 (66.67%)			
occurrences (all)	11			
Hyperlipidaemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Dehydration				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Hypercalcaemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Fluid retention				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Hypocalcaemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Hypoalbuminaemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Increased appetite				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Hyperkalaemia				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Cell death			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Gout			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2013	Added left ventricular ejection fraction (LVEF) evaluation, exclusion criterion about LVEF, secondary efficacy measures, specific DLT definition and dose modification in case of toxicity.
28 March 2014	Updated Schedule of Activities; revised inclusion and exclusion criteria; updated DLT definition and clarified intra-subject dose escalation.
29 October 2014	Added lipid testing, a food effect substudy, neurological assessment, BID dosing, Japanese LIC; revised inclusion and exclusion criteria.
22 July 2015	Revised inclusion and exclusion criteria; removed midazolam, food effect and some other assessments from Phase 2; added cognition, mood and suicidal ideation and behavior assessment in Phase 2.
11 March 2016	Excluded subjects with PR interval >220 msec, or 2nd or 3rd degree atrioventricular block within 3 months prior to study entry; added dose modification for subjects with PR interval prolongation.
15 July 2016	Added Drug Drug Interaction, Holter Monitoring; updated dose modification for those with 1st, 2nd degree or complete heart block; deleted restriction for taking proton pump inhibitors with study drug.

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.

Participant with ALK/ROS1positive NSCLC were enrolled in EXP-1 to EXP-6 cohort,received 100mg dose.Primary safety population=participant had atleast 1dose of lorlatinib.Sample size N=275 provided more valuable information than single expansion cohort

Notes: