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	

Results information

Result version number	v1 (current)
This version publication date	24 March 2018
First version publication date	24 March 2018

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., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 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	Interim
Date of interim/final analysis	22 November 2017
Is this the analysis of the primary	Yes

completion data?	
Primary completion date	15 March 2017
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the Phase 1 portion of the study was to assess safety and tolerability of lorlatinib as a single agent at increasing dose levels in subjects 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). The primary objective of the Phase 2 portion of the study was to evaluate overall (intra- and extra-cranial) and intra-cranial anti-tumor activity of single-agent lorlatinib at RP2D in subjects 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 subjects.

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	Spain: 30
Country: Number of subjects enrolled	Switzerland: 7
Country: Number of subjects enrolled	Taiwan: 11
Country: Number of subjects enrolled	United States: 121
Country: Number of subjects enrolled	Australia: 23
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: 27
Country: Number of subjects enrolled	Japan: 42
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Singapore: 26
Worldwide total number of subjects	332
EEA total number of subjects	89

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)	270
From 65 to 84 years	61
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 334 subjects were enrolled in this study, and 2 of them (one each in Phase 1 and Phase 2) didn't receive any study treatment.

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 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. Midazolam 2 mg was orally given QD on Day -7 and Cycle 1 Day 15.

Arm type	Experimental
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.

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.

Arm title	50 mg QD (Phase 1)

Arm description:

PF-06463922 50 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 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 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 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 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 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	150 mg QD (Phase 1)

Arm description:

PF-06463922 150 mg was orally given 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. Midazolam 2 mg was orally given QD on Day -7 and Cycle 1 Day 15.

Arm type	Experimental
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.

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.

Arm title	200 mg QD (Phase 1)

Arm description:

PF-06463922 200 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 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 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 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 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 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 subjects with advanced ALK-positive NSCLC with or without asymptomatic central nervous system (CNS) metastases were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for subjects 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:

Subjects with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after only crizotinib therapy were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for subjects 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:

Subjects 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 subjects 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 once daily (QD) on Day -7 (only for subjects 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:

subjects 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 subjects 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:

Subjects 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 subjects 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:

Subjects 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 subjects 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 subjects 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 subjects, in order to support inclusion of Japanese subjects 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.

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
Received treatment	3	3	3
Completed	0	0	0
Not completed	3	3	3
Study ongoing	-	2	-
Adverse event, serious fatal	3	1	3
Unspecified	-	-	-
Consent withdrawn by subject	-	-	-
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
Received treatment	12	17	3
Completed	0	0	0
Not completed	12	17	3
Study ongoing	6	8	-
Adverse event, serious fatal	4	6	3
Unspecified	-	-	-
Consent withdrawn by subject	1	2	-
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
Received treatment	3	3	3
Completed	0	0	0
Not completed	3	3	3
Study ongoing	2	-	1
Adverse event, serious fatal	1	3	2
Unspecified	-	-	-
Consent withdrawn by subject	-	-	-
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
Received treatment	4	30	27
Completed	0	0	0
Not completed	4	30	27
Study ongoing	3	29	22
Adverse event, serious fatal	1	1	4
Unspecified	-	-	-
Consent withdrawn by subject	-	-	1
Lost to follow-up	-	-	-

Number of subjects in period 1	EXP-3 (Phase 2)	EXP-4 (Phase 2)	EXP-5 (Phase 2)
Started	60	65	46
Received treatment	60	65	46
Completed	0	0	0
Not completed	60	65	46
Study ongoing	43	41	29
Adverse event, serious fatal	14	19	15
Unspecified	-	-	-
Consent withdrawn by subject	2	5	2
Lost to follow-up	1	-	-

Number of subjects in period 1	EXP-6 (Phase 2)	Japan Lead-In Cohort (LIC)
Started	47	3
Received treatment	47	3
Completed	0	0
Not completed	47	3
Study ongoing	29	2
Adverse event, serious fatal	10	1
Unspecified	1	-
Consent withdrawn by subject	7	-

Lost to follow-up	-	-

Baseline characteristics

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 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. 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 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	75 mg QD (Phase 1)
Reporting group description:	
PF-06463922 75 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	100 mg QD (Phase 1)
Reporting group description:	
PF-06463922 100 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	150 mg QD (Phase 1)
Reporting group description:	
PF-06463922 150 mg was orally given 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. 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 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	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 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	100 mg BID (Phase 1)
Reporting group description:	
PF-06463922 100 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	EXP-1 (Phase 2)
Reporting group description:	
Treatment-naïve subjects with advanced ALK-positive NSCLC with or without asymptomatic central nervous system (CNS) metastases were given PF-06463922 100 mg orally once daily (QD) on Day -7	

(only for subjects 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:

Subjects with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after only crizotinib therapy were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for subjects 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:

Subjects 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 subjects 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 once daily (QD) on Day -7 (only for subjects 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:

subjects 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 subjects 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:

Subjects 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 subjects 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:

Subjects 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 subjects 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 subjects 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 subjects, in order to support inclusion of Japanese subjects in Phase 2.

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: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0

Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1	2	3
From 65-84 years	2	1	0
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	67.3	53.7	52.7
standard deviation	± 11.2	± 13.0	± 10.0
Sex: Female, Male			
Units: Subjects			
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: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	11	16	2
From 65-84 years	1	1	1
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	48.2	49	55.3
standard deviation	± 13.2	± 11.1	± 14.7
Sex: Female, Male			
Units: Subjects			
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: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	2	2
From 65-84 years	0	1	1
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	44.7	61.3	61.3
standard deviation	± 4.2	± 15.4	± 18.1
Sex: Female, Male Units: Subjects			
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: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	22	18
From 65-84 years	1	8	8
85 years and over	0	0	1
Age Continuous Units: years			
arithmetic mean	50.8	57.4	57.1
standard deviation	± 15.2	± 12.1	± 12.7

Sex: Female, Male Units: Subjects			
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: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	48	56	39
From 65-84 years	12	9	7
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	54	52.2	51.5
standard deviation	± 11.9	± 11.8	± 11.2
Sex: Female, Male Units: Subjects			
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)	Total
Number of subjects	47	3	332
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0

Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	39	3	270
From 65-84 years	8	0	61
85 years and over	0	0	1
Age Continuous			
Units: years			
arithmetic mean	52.8	44.3	
standard deviation	± 12.9	± 6.1	-
Sex: Female, Male			
Units: Subjects			
FEMALE	27	2	191
MALE	20	1	141
Race/Ethnicity, Customized			
Units: Subjects			
White|	25	0	169
Black|	1	0	6
Asian|	16	3	113
Other|	3	0	13
Unspecified|	2	0	31

Subject analysis sets

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 intent-to-treat (ITT) subjects 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 intent-to-treat (ITT) subjects 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 intent-to-treat (ITT) subjects.

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 subjects who received at least 1 dose of PF-06463922 and completed a baseline and at least 1 post-baseline patient reported outcome (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 intent-to-treat (ITT) subjects.

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 subjects and Japan LIC. These subjects 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.

Reporting group values	ALK Positive Population (Phase 1)	ROS1 Positive Population (Phase 1)	Phase 1 ITT Population
Number of subjects	41	12	53
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	36	8	44
From 65-84 years	5	4	9
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	51.0	55.0	51.9
standard deviation	± 11.2	± 18.0	± 13.0
Sex: Female, Male Units: Subjects			
FEMALE	24	7	31
MALE	17	5	22
Race/Ethnicity, Customized Units: Subjects			
White|	32	5	37
Black|	2	1	3
Asian|	5	2	7
Other|	0	1	1
Unspecified|	2	3	5

Reporting group values	Phase 1 PRO Evaluable Population	Phase 2 ITT Population	Phase 2 and Japan LIC PK Analysis Set
Number of subjects	43	274	22
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	36	221	21
From 65-84 years	7	52	1
85 years and over	0	1	0
Age Continuous Units: years			
arithmetic mean	51.4	53.6	50.9

standard deviation	± 13.2	± 12.1	± 9.8

Sex: Female, Male Units: Subjects			
FEMALE	24	157	13
MALE	19	117	9
Race/Ethnicity, Customized Units: Subjects			
White|	31	132	9
Black|	1	3	0
Asian|	5	103	11
Other|	1	11	2
Unspecified|	5	25	0

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 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. 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 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	75 mg QD (Phase 1)
Reporting group description:	
PF-06463922 75 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	100 mg QD (Phase 1)
Reporting group description:	
PF-06463922 100 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	150 mg QD (Phase 1)
Reporting group description:	
PF-06463922 150 mg was orally given 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. 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 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	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 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	100 mg BID (Phase 1)
Reporting group description:	
PF-06463922 100 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	EXP-1 (Phase 2)
Reporting group description:	
Treatment-naïve subjects with advanced ALK-positive NSCLC with or without asymptomatic central nervous system (CNS) metastases were given PF-06463922 100 mg orally once daily (QD) on Day -7	

(only for subjects 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:

Subjects with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after only crizotinib therapy were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for subjects 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:

Subjects 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 subjects 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 once daily (QD) on Day -7 (only for subjects 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:

subjects 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 subjects 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:

Subjects 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 subjects 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:

Subjects 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 subjects 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 subjects 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 subjects, in order to support inclusion of Japanese subjects in Phase 2.

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 intent-to-treat (ITT) subjects 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 intent-to-treat (ITT) subjects 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 intent-to-treat (ITT) subjects.

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 subjects who received at least 1 dose of PF-06463922 and completed a baseline and at least 1 post-baseline patient reported outcome (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 intent-to-treat (ITT) subjects.

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 subjects and Japan LIC. These subjects 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.

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

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

End point description:

DLT was defined as any of the following adverse events (AEs) attributable to PF-06463922: (1) hematologic: grade 4 neutropenia for >7 days; febrile neutropenia; grade >=3 neutropenic infection; grade >=3 thrombocytopenia with bleeding; grade 4 thrombocytopenia; (2) 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 that had been confirmed by repeat testing and re-evaluation by a qualified person, and persisted after correction of reversible causes; >=20% decrease from baseline in left ventricular ejection fraction (LVEF); (3) other: failure to deliver at least 16 out of the 21 prescribed daily total doses due to toxicities attributable to study drug; failure to restart dosing after 21 days (1 cycle) delay due to toxicities attributable to study drug.

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 analyses were planned for this primary end point.

[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: All other reporting arms are not applicable to this end point.

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: subjects				
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: subjects				
With DLT|	0	0	1	0
No DLT|	8	2	1	2
Data missing|	8	1	1	0

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: subjects				
With DLT|	0	0		
No DLT|	3	2		
Data missing|	0	1		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Objective response (OR) refers to confirmed complete response (CR) or partial response (PR) according to Response Evaluation Criteria in Solid Tumor (RECIST) version 1.1. Intracranial OR refers to confirmed CR or PR considering only lesions within brain. Results presented here were based on independent central review. The intent-to-treat (ITT) analysis set was used for overall response assessment, and included all enrolled subjects with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922; subjects with central nervous system (CNS) metastases in the ITT analysis set were used for intracranial response assessment.

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 analyses were planned for this primary end point.

[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: All other reporting arms are not applicable to this end point.

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[5]	27[6]	59[7]	65[8]
Units: percentage of subjects				
number (confidence interval 95%)				

Objective response|	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 objective response|	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)

Notes:

[5] - Number of subjects analyzed for intracranial objective response is 8.

[6] - Number of subjects analyzed for intracranial objective response is 17.

[7] - Number of subjects analyzed for intracranial objective response is 32.

[8] - Number of subjects analyzed for intracranial objective response is 45.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[9]	47[10]		
Units: percentage of subjects				
number (confidence interval 95%)				
Objective response|	34.8 (21.4 to 50.2)	36.2 (22.7 to 51.5)		
Intracranial objective response|	39.5 (24.0 to 56.6)	56.0 (34.9 to 75.6)		

Notes:

[9] - Number of subjects analyzed for intracranial objective response is 38.

[10] - Number of subjects analyzed for intracranial objective response is 25.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Overall and Intracranial Objective Response (Phase 1)

End point title	Percentage of Subjects with Overall and Intracranial Objective Response (Phase 1)

End point description:

Objective response (OR) refers to confirmed complete response (CR) or partial response (PR) according to Response Evaluation Criteria in Solid Tumor (RECIST) version 1.1. Intracranial OR refers to confirmed CR or PR considering only lesions within brain. Results presented here were based on independent central review. The intent-to-treat (ITT) analysis set was used for overall response assessment, and included all enrolled subjects with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922; subjects with CNS metastases in the ITT analysis set was used for intracranial response assessment.

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[11]	12[12]		
Units: percentage of subjects				
number (confidence interval 95%)				
Objective response|	39.0 (24.2 to 55.5)	50.0 (21.1 to 78.9)		

Intracranial objective response|	41.2 (24.6 to 59.3)	50.0 (15.7 to 84.3)		

Notes:

[11] - Number of subjects analyzed for intracranial objective response is 34.

[12] - Number of subjects analyzed for intracranial objective response is 8.

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:

Time to tumor response (TTR) was defined as the time from the first dose of study treatment to the first documentation of objective tumor response (CR or PR). For subjects whose objective response proceeded from PR to CR, the onset of PR was taken as the onset of response. TTR was only calculated for the subgroup of subjects with a confirmed objective tumor response. Intracranial TTR was only calculated for subjects with confirmed intracranial objective response. Results presented here were based on independent central review.

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	16[13]	6[14]		
Units: months				
median (full range (min-max))				
TTR|	1.4 (1.2 to 15.2)	1.4 (1.2 to 2.8)		
Intracranial TTR|	1.4 (1.2 to 20.1)	1.4 (1.1 to 2.8)		

Notes:

[13] - Number of subjects analyzed for intracranial TTR is 14.

[14] - Number of subjects analyzed for intracranial TTR is 4.

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Duration of Response (DOR) was defined as the time from the first documentation of objective tumor response (CR or PR) to the first documentation of disease progression or to death due to any cause, whichever occurred first. DOR was only calculated for the subgroup of subjects with a confirmed objective tumor response. Intracranial DOR was only calculated for subjects with confirmed intracranial objective response. Results presented here were based on independent central review. "99999" represents "not applicable" or "non evaluable" data.

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	16[15]	6[16]		
Units: months				
median (confidence interval 95%)				
DOR|	14.06 (4.17 to 99999)	99999 (9.69 to 99999)		
Intra-cranial DOR|	99999 (14.06 to 99999)	99999 (99999 to 99999)		

Notes:

[15] - Number of subjects analyzed for intracranial DOR is 14.

[16] - Number of subjects analyzed for intracranial DOR is 4.

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Tumor response was evaluated according to RECIST version 1.1, and disease control was defined as confirmed complete response (CR), confirmed partial response (PR), or stable disease (SD). Results presented here were based on independent central review. The intent-to-treat (ITT) analysis set was used for overall response assessment, and included all enrolled subjects with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922; subjects with CNS metastases in the ITT analysis set was used for intracranial response assessment.

End point type	Secondary

End point timeframe:

12 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[17]	12[18]		
Units: percentage of subjects				
number (confidence interval 95%)				
Disease control rate|	53.7 (37.4 to 69.3)	58.3 (27.7 to 84.8)		
Intra-cranial disease control rate|	50.0 (32.4 to 67.6)	37.5 (8.5 to 75.5)		

Notes:

[17] - Number of subjects analyzed for intracranial disease control rate is 34.

[18] - Number of subjects analyzed for intracranial disease control rate is 8.

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:

The probability of the 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. Subjects not known to have any of the Competing Events were censored on the date they were last assessed for disease status for PFS. Subjects 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. The results are based on independent central review.

End point type	Secondary

End point timeframe:

3 years

End point values	Phase 1 ITT Population			
Subject group type	Subject analysis set			
Number of subjects analysed	53			
Units: not applicable				
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. Results presented here were based on independent central review. PFS analysis set included all subjects with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922. "99999" represents "not applicable" or "non evaluable" data.

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[19]	12[20]		
Units: months				
median (confidence interval 95%)	5.3 (2.5 to 11.8)	10.1 (1.6 to 99999)		

Notes:

[19] - Number of subjects with objective progression or death is 29; others were censored.

[20] - Number of subjects with objective progression or death is 7; others were censored.

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 subjects still alive at the time of analysis, the OS time was censored on the last date the subjects were known to be alive. Estimates of OS and its 95% confidence interval were determined using Kaplan-Meier method. ITT population was used for OS analysis, and it included all enrolled subjects with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922. "99999" represents "not applicable" or "non evaluable" data.

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[21]	12[22]		
Units: months				
median (confidence interval 95%)	22.3 (11.4 to 99999)	99999 (4.7 to 99999)		

Notes:

[21] - Number of deaths is 21; others were censored.

[22] - Number of deaths is 5; others were censored.

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)[23]

End point description:

Maximum observed plasma concentration (Cmax) of PF-06463922 was observed directly from data. PK concentration analysis set for PF-06463922 included all subjects treated who had at least 1 concentration of PF-06463922. "99999" represents "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cylce 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:

[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: All other reporting arms are not applicable to this end point.

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: 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: 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: 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)[24]

End point description:

Maximum Observed Plasma Concentration (Cmax) of PF-06463922 was observed directly from data. PK concentration analysis set for PF-06463922 included all subjects treated who had at least 1 concentration of PF-06463922. "99999" represents "not applicable" or "non evaluable" data.

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:

[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: All other reporting arms are not applicable to this end point.

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)[25]

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 subjects 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 Cylce 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:

[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: All other reporting arms are not applicable to this end point.

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)[26]

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 subjects 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:

[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: All other reporting arms are not applicable to this end point.

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)[27]

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 subjects 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 "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cylce 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:

[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: All other reporting arms are not applicable to this end point.

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)[28]

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 subjects 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 "not applicable" or "non evaluable" data.

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:

[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: All other reporting arms are not applicable to this end point.

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)[29]

End point description:

AUCinf was calculated as AUClast + (Clast*/kel), where AUClast was the area under the plasma concentration-time profile from time 0 to the time of the last quantifiable concentration, Clast* was the predicted plasma concentration at the last quantifiable time point estimated from the log-linear regression analysis, and kel was the rate constant for terminal phase. PK parameter analysis set for PF-06463922 included all enrolled subjects 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 "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cylce 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:

[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: All other reporting arms are not applicable to this end point.

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)[30]

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 subjects 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 "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cylce 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:

[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: All other reporting arms are not applicable to this end point.

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)[31]

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 subjects 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 "not applicable" or "non evaluable" data.

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:

[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: All other reporting arms are not applicable to this end point.

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)[32]

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 subjects 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 "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cylce 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:

[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: All other reporting arms are not applicable to this end point.

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)[33]

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 subjects 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 "not applicable" or "non evaluable" data.

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:

[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: All other reporting arms are not applicable to this end point.

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)[34]

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 subjects 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 "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, 9 and 24 hours post-dose on Cylce 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:

[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: All other reporting arms are not applicable to this end point.

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)[35]

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 (12 and 24 hours for BID and QD dosing regimen, respectively), 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 subjects 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 "not applicable" or "non evaluable" data.

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:

[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: All other reporting arms are not applicable to this end point.

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)[36]

End point description:

Renal clearance was calculated as Aetau/AUCtau, where Aetau was the cumulative amount of drug recovered unchanged in urine up to dosing interval tau (24 hours for QD dosing regimen), and AUCtau was the area under the plasma concentration-time profile from time 0 to time tau (24 hours for QD dosing regimen). PK parameter analysis set for PF-06463922 included all enrolled subjects 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. This end point is only applicable to 100 mg QD group.

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:

[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: All other reporting arms are not applicable to this end point.

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)[37]

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 subjects 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. This end point is only applicable to 100 mg QD group.

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:

[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: All other reporting arms are not applicable to this end point.

End point values	100 mg QD (Phase 1)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: percentage				
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)[38]

End point description:

Cmax of midazolam was observed directly from data. Only subjects 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 concentration analysis set for midazolam included all subjects treated with midazolam who had at least 1 concentration of midazolam.

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:

[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: All other reporting arms are not applicable to this end point.

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)[39]

End point description:

Tmax of midazolam was observed directly from data as time of first occurrence. Only subjects 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 included all subjects 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:

[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: All other reporting arms are not applicable to this end point.

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)[40]

End point description:

Area under the plasma concentration-time profile from time 0 to the time of the last quantifiable concentration (AUClast) of midazolam was determined using linear/log trapezoidal method. Only subjects 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 included all subjects 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:

[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: All other reporting arms are not applicable to this end point.

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)[41]

End point description:

AUCinf was calculated as AUClast + (Clast*/kel), where AUClast was the area under the plasma concentration-time profile from time 0 to the time of the last quantifiable concentration, Clast* was the predicted plasma concentration at the last quantifiable time point estimated from the log-linear regression analysis, and kel was the rate constant for terminal phase. Only subjects 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 included all subjects who received at least 1 dose of midazolam and for which at least 1 midazolam PK parameter of interest was available. "99999" represents "not applicable" or "non evaluable" data.

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:

[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: All other reporting arms are not applicable to this end point.

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[42]		
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
Day -7|	54.53 (± 43)	99999 (± 99999)		
Cycle 1 Day 15|	21.32 (± 18)	16.09 (± 29)		

Notes:

[42] - Number of subjects contributing to Day -7 data is 2.

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)[43]

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. Only subjects 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 included all subjects who received at least 1 dose of midazolam and for which at least 1 midazolam PK parameter of interest was available. "99999" represents "not applicable" or "non evaluable" data.

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:

[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: All other reporting arms are not applicable to this end point.

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[44]		
Units: L/hr				
geometric mean (geometric coefficient of variation)				
Day -7|	36.68 (± 43)	99999 (± 99999)		
Cycle 1 Day 15|	93.86 (± 18)	124.2 (± 29)		

Notes:

[44] - Number of subjects contributing to Day -7 data is 2.

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 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. Only subjects 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 included all subjects who received at least 1 dose of midazolam and for which at least 1 midazolam PK parameter of interest was available. "99999" represents "not applicable" or "non evaluable" data.

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:

[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: All other reporting arms are not applicable to this end point.

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[46]		
Units: liter				
geometric mean (geometric coefficient of variation)				
Day -7| Cycle 1 Day 15|	229.0 (± 7) 404.4 (± 51)	99999 (± 99999) 702.2 (± 100)		

Notes:

[46] - Number of subjects contributing to Day -7 data is 2.

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)[47]

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. Only subjects 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 included all subjects who received at least 1 dose of midazolam and for which at least 1 midazolam PK parameter of interest was available. "99999" represents "not applicable" or "non evaluable" data.

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:

[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: All other reporting arms are not applicable to this end point.

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[48]		
Units: hr				
arithmetic mean (standard deviation)				
Day -7|	4.620 (± 1.9328)	5.120 (± 99999)		
Cycle 1 Day 15|	3.343 (± 2.0358)	5.257 (± 5.0639)		

Notes:

[48] - Number of subjects contributing to Day -7 data is 2.

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Subjects 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 subjects with one or more ALK mutations is presented. CNA peripheral blood analysis set included all subjects of the ITT analysis set who had at least 1 molecular biomarker assayed.

End point type	Secondary

End point timeframe:

Screening

End point values	ALK Positive Population (Phase 1)			
Subject group type	Subject analysis set			
Number of subjects analysed	39			
Units: subjects	14			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Subjects 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 subjects with one or more ALK mutations is presented. Tumor Tissue analysis set included all subjects 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

End point values	ALK Positive Population (Phase 1)			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: subjects	7			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

European Organisation for Research and Treatment of Cancer Core Quality of Life Questionaires (EORTC QLQ)-C30 (v3.0) consists of 30 questions for 5 functional domains (physical, role, emotional, cognitive, social), global quality of life (QoL), disease/treatment related symptoms (fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea), and the perceived financial impact of disease. Each scale was transformed to a range of 0 to 100 using EORTC algorithm. For global QoL and functional scales, higher score means better performance, improvement was an increase of at least 10 points, worsening was a decrease of at least 10 points. For symptom scales, higher score means worse symptoms, improvement was a decrease of at least 10 points, worsening was an increase of at least 10 points. Patient reported outcome (PRO) set included all subjects who received at least 1 dose of PF-06463922, completed a baseline and at least 1 post-baseline assessment.

End point type	Secondary

End point timeframe:

3 years

End point values	Phase 1 PRO Evaluable Population			
Subject group type	Subject analysis set			
Number of subjects analysed	43			
Units: subjects				
Improved in global QoL|	20			
Stable in global QoL|	13			
Worsened in global QoL|	10			
Improved in physical functioning|	6			
Stable in physical functioning|	30			
Worsened in physical functioning|	7			
Improved in role functioning|	15			
Stable in role functioning|	16			

Worsened in role functioning|	12			
Improved in emotional functioning|	15			
Stable in emotional functioning|	20			
Worsened in emotional functioning|	8			
Improved in cognitive functioning|	8			
Stable in cognitive functioning|	21			
Worsened in cognitive functioning|	14			
Improved in social functioning|	13			
Stable in social functioning|	18			
Worsened in social functioning|	12			
Improved in fatigue|	18			
Stable in fatigue|	19			
Worsened in fatigue|	6			
Improved in nausea and vomiting|	10			
Stable in nausea and vomiting|	32			
worsened in nausea and vomiting|	1			
Improved in pain|	18			
Stable in pain|	15			
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|	11			
Stable in constipation|	27			
Worsened in constipation|	5			
Improved in diarrhea|	9			
Stable in diarrhea|	29			
Worsened in diarrhea|	5			
Improved in financial difficulties|	7			
Stable in financial difficulties|	21			
Worsened in financial difficulties|	15			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Subjects 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. Patient reported outcome (PRO) set included all subjects who received at least 1 dose of PF-06463922, completed a baseline and at least 1 post-baseline assessment.

End point type	Secondary

End point timeframe:

3 years

End point values	Phase 1 PRO Evaluable Population			
Subject group type	Subject analysis set			
Number of subjects analysed	43[49]			
Units: subjects				
Improved in dyspnea|	10			
Stable in dyspnea|	22			
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|	19			
Worsened in peripheral neuropathy|	18			
Improved in alopecia|	3			
Stable in alopecia|	30			
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|	28			
Worsened in arm or shoulder pain|	5			
Improved in pain in other parts|	19			
Stable in pain in other parts|	14			
Worsened in pain in other parts|	10			

Notes:

[49] - Number of subjects analyzed for alopecia is 42.

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)[50]

End point description:

In Phase 1, the MMSE was collected to assess mental status. The MMSE is a 30 item questionnaire that tests 5 areas of cognitive function: orientation, registration, attention and calculation, recall and language. The maximum score is 30. A score of 23 or lower is indicative of cognitive impairment. The MMSE was removed under Amendment 6 of the study protocol, and not required for Phase 2, as the tool was not considered meaningful for assessment of cognitive function. MMSE assessment evaluable analysis set included all subjects who received at least 1 dose of PF-06463922 and completed a baseline and at least 1 post-baseline assessment. "99999" represents "not applicable" or "non evaluable data".

End point type	Secondary

End point timeframe:

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: All other reporting arms are not applicable to this end point.

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[51]	3[52]	3[53]	9[54]
Units: units on a score				
arithmetic mean (standard deviation)				
Cycle 1 Day 1|	1.0 (± 1.41)	99999 (± 99999)	-0.5 (± 0.71)	-0.9 (± 2.27)
Cycle 2 Day 1|	2.0 (± 99999)	-0.3 (± 0.58)	2.0 (± 99999)	0.3 (± 1.41)
Cycle 3 Day 1|	2.0 (± 0.00)	0.3 (± 0.58)	-0.5 (± 0.71)	-0.6 (± 1.85)
Cycle 4 Day 1|	5.0 (± 99999)	0.5 (± 0.71)	1.5 (± 2.12)	-1.1 (± 1.81)
Cycle 5 Day 1|	0.5 (± 3.54)	0.5 (± 0.71)	1.5 (± 2.12)	0.3 (± 1.25)
Cycle 6 Day 1|	2.5 (± 2.12)	0.5 (± 0.71)	1.0 (± 1.41)	-0.4 (± 2.70)
Cycle 7 Day 1|	2.0 (± 99999)	0.5 (± 0.71)	1.5 (± 2.12)	-0.1 (± 1.21)
Cycle 8 Day 1|	-4.0 (± 99999)	0.5 (± 0.71)	1.5 (± 2.12)	-0.1 (± 2.34)
Cycle 9 Day 1|	99999 (± 99999)	0.0 (± 0.00)	0.0 (± 99999)	-1.0 (± 2.31)
Cycle 10 Day 1|	-5.0 (± 99999)	0.5 (± 0.71)	0.0 (± 99999)	0.0 (± 0.00)
Cycle 11 Day 1|	99999 (± 99999)	-0.5 (± 0.71)	0.0 (± 99999)	0.3 (± 1.70)
Cycle 12 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	-0.6 (± 2.19)
Cycle 13 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	0.8 (± 1.79)
Cycle 14 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	-0.3 (± 3.20)
Cycle 15 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	-1.7 (± 5.43)
Cycle 16 Day 1|	99999 (± 99999)	0.0 (± 1.41)	99999 (± 99999)	-0.2 (± 2.49)
Cycle 17 Day 1|	99999 (± 99999)	-2.0 (± 2.83)	99999 (± 99999)	0.6 (± 1.95)
Cycle 18 Day 1|	99999 (± 99999)	-0.5 (± 0.71)	99999 (± 99999)	0.8 (± 1.79)
Cycle 19 Day 1|	99999 (± 99999)	-0.5 (± 0.71)	99999 (± 99999)	0.8 (± 1.79)

Cycle 20 Day 1|	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.0 (± 1.41)
Cycle 21 Day 1|	99999 (± 99999)	-0.5 (± 0.71)	99999 (± 99999)	0.0 (± 1.41)
Cycle 22 Day 1|	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.4 (± 1.52)
Cycle 23 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	0.0 (± 1.41)
Cycle 24 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	-0.4 (± 0.89)
Cycle 25 Day 1|	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.8 (± 1.79)
Cycle 26 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	0.8 (± 1.79)
Cycle 27 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	0.8 (± 1.79)
Cycle 28 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	1.0 (± 2.00)
Cycle 29 Day 1|	99999 (± 99999)	-1.5 (± 2.12)	99999 (± 99999)	0.5 (± 1.73)
Cycle 30 Day 1|	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.8 (± 1.50)
Cycle 31 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	1.0 (± 2.65)
Cycle 32 Day 1|	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	1.3 (± 2.31)
Cycle 33 Day 1|	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	1.3 (± 2.31)
Cycle 34 Day 1|	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.0 (± 0.00)
Cycle 35 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	0.0 (± 99999)
Cycle 36 Day 1|	99999 (± 99999)	-0.5 (± 0.71)	99999 (± 99999)	0.0 (± 99999)
Cycle 37 Day 1|	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	-1.0 (± 99999)
Cycle 38 Day 1|	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.0 (± 99999)
Cycle 39 Day 1|	99999 (± 99999)	0.0 (± 99999)	99999 (± 99999)	0.0 (± 99999)
Cycle 40 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	-1.0 (± 99999)
Cycle 41 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	0.0 (± 99999)
Cycle 42 Day 1|	99999 (± 99999)	-0.5 (± 0.71)	99999 (± 99999)	0.0 (± 99999)
Cycle 43 Day 1|	99999 (± 99999)	0.0 (± 0.00)	99999 (± 99999)	0.0 (± 99999)
Cycle 44 Day 1|	99999 (± 99999)	1.0 (± 99999)	99999 (± 99999)	-1.0 (± 99999)
Cycle 45 Day 1|	99999 (± 99999)	1.0 (± 99999)	99999 (± 99999)	0.0 (± 99999)
Cycle 46 Day 1|	99999 (± 99999)	0.0 (± 99999)	99999 (± 99999)	-1.0 (± 99999)
Cycle 47 Day 1|	99999 (± 99999)	0.0 (± 99999)	99999 (± 99999)	0.0 (± 99999)
Cycle 48 Day 1|	99999 (± 99999)	-3.0 (± 99999)	99999 (± 99999)	0.0 (± 99999)
Cycle 49 Day 1|	99999 (± 99999)	0.5 (± 0.71)	99999 (± 99999)	99999 (± 99999)
Cycle 50 Day 1|	99999 (± 99999)	-3.0 (± 99999)	99999 (± 99999)	99999 (± 99999)

Cycle 51 Day 1|	99999 (± 99999)	-0.5 (± 0.71)	99999 (± 99999)	99999 (± 99999)
Cycle 52 Day 1|	99999 (± 99999)	1.0 (± 99999)	99999 (± 99999)	99999 (± 99999)
End of treatment|	-8.0 (± 99999)	99999 (± 99999)	0.7 (± 1.15)	-2.0 (± 99999)

Notes:

[51] - Not all subjects had evaluable data at each time point.

[52] - Not all subjects had evaluable data at each time point.

[53] - Not all subjects had evaluable data at each time point.

[54] - Not all subjects had evaluable data at each time point.

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[55]	3[56]	2[57]	2[58]
Units: units on a score				
arithmetic mean (standard deviation)				
Cycle 1 Day 1|	0.8 (± 1.39)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 2 Day 1|	0.0 (± 1.79)	4.7 (± 8.08)	4.0 (± 4.24)	0.0 (± 0.00)
Cycle 3 Day 1|	0.2 (± 1.52)	5.0 (± 8.49)	3.0 (± 2.83)	99999 (± 99999)
Cycle 4 Day 1|	0.0 (± 1.47)	2.0 (± 6.24)	-0.5 (± 3.54)	99999 (± 99999)
Cycle 5 Day 1|	-0.2 (± 1.72)	4.7 (± 8.14)	0.5 (± 6.36)	99999 (± 99999)
Cycle 6 Day 1|	0.3 (± 0.90)	4.3 (± 5.86)	2.0 (± 4.24)	99999 (± 99999)
Cycle 7 Day 1|	0.4 (± 0.90)	4.7 (± 8.33)	3.0 (± 4.24)	99999 (± 99999)
Cycle 8 Day 1|	0.2 (± 1.34)	3.0 (± 7.81)	4.0 (± 4.24)	99999 (± 99999)
Cycle 9 Day 1|	0.3 (± 2.10)	6.0 (± 8.49)	6.0 (± 99999)	99999 (± 99999)
Cycle 10 Day 1|	-0.1 (± 0.88)	6.5 (± 9.19)	6.0 (± 99999)	99999 (± 99999)
Cycle 11 Day 1|	-0.2 (± 1.53)	7.0 (± 8.49)	3.5 (± 3.54)	99999 (± 99999)
Cycle 12 Day 1|	-0.2 (± 2.33)	6.5 (± 9.19)	3.5 (± 3.54)	99999 (± 99999)
Cycle 13 Day 1|	0.5 (± 2.22)	5.5 (± 7.78)	3.0 (± 4.24)	99999 (± 99999)
Cycle 14 Day 1|	0.3 (± 0.79)	6.0 (± 8.49)	2.5 (± 3.54)	99999 (± 99999)
Cycle 15 Day 1|	0.1 (± 1.36)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 16 Day 1|	-0.2 (± 1.99)	1.0 (± 99999)	1.5 (± 6.36)	99999 (± 99999)
Cycle 17 Day 1|	0.1 (± 1.17)	-3.0 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 18 Day 1|	0.0 (± 1.73)	-2.0 (± 99999)	3.0 (± 4.24)	99999 (± 99999)
Cycle 19 Day 1|	-0.6 (± 2.65)	0.0 (± 99999)	3.5 (± 4.95)	99999 (± 99999)
Cycle 20 Day 1|	0.7 (± 2.12)	0.0 (± 99999)	3.5 (± 3.54)	99999 (± 99999)
Cycle 21 Day 1|	0.1 (± 2.09)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)

Cycle 22 Day 1|	0.1 (± 1.45)	0.0 (± 99999)	3.5 (± 3.54)	99999 (± 99999)
Cycle 23 Day 1|	0.1 (± 1.81)	-1.0 (± 99999)	1.5 (± 3.54)	99999 (± 99999)
Cycle 24 Day 1|	0.6 (± 0.74)	1.0 (± 99999)	1.5 (± 4.95)	99999 (± 99999)
Cycle 25 Day 1|	-0.9 (± 2.27)	-2.0 (± 99999)	2.5 (± 4.95)	99999 (± 99999)
Cycle 26 Day 1|	-0.4 (± 2.77)	-1.0 (± 99999)	2.0 (± 4.24)	99999 (± 99999)
Cycle 27 Day 1|	-0.1 (± 2.67)	-1.0 (± 99999)	3.5 (± 3.54)	99999 (± 99999)
Cycle 28 Day 1|	0.7 (± 0.76)	-2.0 (± 99999)	3.0 (± 2.83)	99999 (± 99999)
Cycle 29 Day 1|	0.1 (± 1.81)	0.0 (± 99999)	3.5 (± 3.54)	99999 (± 99999)
Cycle 30 Day 1|	0.4 (± 0.55)	0.0 (± 99999)	3.0 (± 2.83)	99999 (± 99999)
Cycle 31 Day 1|	0.7 (± 0.82)	0.0 (± 99999)	3.0 (± 4.24)	99999 (± 99999)
Cycle 32 Day 1|	0.4 (± 0.55)	99999 (± 99999)	3.5 (± 3.54)	99999 (± 99999)
Cycle 33 Day 1|	0.5 (± 0.58)	99999 (± 99999)	3.5 (± 3.54)	99999 (± 99999)
Cycle 34 Day 1|	0.3 (± 0.50)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 35 Day 1|	0.3 (± 0.50)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 36 Day 1|	0.0 (± 0.00)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 37 Day 1|	0.0 (± 0.00)	99999 (± 99999)	3.5 (± 4.95)	99999 (± 99999)
Cycle 38 Day 1|	0.0 (± 0.00)	99999 (± 99999)	3.0 (± 2.83)	99999 (± 99999)
Cycle 39 Day 1|	-0.5 (± 0.71)	99999 (± 99999)	3.5 (± 4.95)	99999 (± 99999)
Cycle 40 Day 1|	0.0 (± 99999)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 41 Day 1|	0.0 (± 99999)	99999 (± 99999)	1.5 (± 6.36)	99999 (± 99999)
Cycle 42 Day 1|	0.0 (± 99999)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 43 Day 1|	99999 (± 99999)	99999 (± 99999)	4.0 (± 4.24)	99999 (± 99999)
Cycle 44 Day 1|	99999 (± 99999)	99999 (± 99999)	3.0 (± 4.24)	99999 (± 99999)
Cycle 45 Day 1|	99999 (± 99999)	99999 (± 99999)	1.0 (± 99999)	99999 (± 99999)
Cycle 46 Day 1|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 47 Day 1|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 48 Day 1|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 49 Day 1|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 50 Day 1|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 51 Day 1|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 52 Day 1|	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End of treatment|	-2.3 (± 5.19)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Notes:

[55] - Not all subjects had evaluable data at each time point.

[56] - Not all subjects had evaluable data at each time point.

[57] - Not all subjects had evaluable data at each time point.

[58] - Not all subjects had evaluable data at each time point.

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[59]	4[60]		
Units: units on a score				
arithmetic mean (standard deviation)				
Cycle 1 Day 1|	0.0 (± 99999)	0.0 (± 99999)		
Cycle 2 Day 1|	0.0 (± 0.00)	-0.3 (± 1.15)		
Cycle 3 Day 1|	0.0 (± 99999)	-1.0 (± 1.00)		
Cycle 4 Day 1|	0.0 (± 99999)	-0.7 (± 1.15)		
Cycle 5 Day 1|	0.0 (± 99999)	-0.5 (± 0.71)		
Cycle 6 Day 1|	0.0 (± 99999)	-1.3 (± 2.31)		
Cycle 7 Day 1|	0.0 (± 99999)	-0.7 (± 1.15)		
Cycle 8 Day 1|	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 9 Day 1|	99999 (± 99999)	-0.3 (± 0.58)		
Cycle 10 Day 1|	0.0 (± 99999)	-1.7 (± 1.53)		
Cycle 11 Day 1|	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 12 Day 1|	0.0 (± 99999)	-0.7 (± 0.58)		
Cycle 13 Day 1|	0.0 (± 99999)	-0.5 (± 0.71)		
Cycle 14 Day 1|	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 15 Day 1|	0.0 (± 99999)	-0.3 (± 0.58)		
Cycle 16 Day 1|	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 17 Day 1|	0.0 (± 99999)	-1.3 (± 1.53)		
Cycle 18 Day 1|	99999 (± 99999)	0.0 (± 0.00)		
Cycle 19 Day 1|	0.0 (± 99999)	-0.5 (± 0.71)		
Cycle 20 Day 1|	0.0 (± 99999)	-0.5 (± 0.71)		
Cycle 21 Day 1|	0.0 (± 99999)	-0.5 (± 0.71)		
Cycle 22 Day 1|	-1.0 (± 99999)	-0.3 (± 0.58)		
Cycle 23 Day 1|	0.0 (± 99999)	-2.3 (± 4.04)		
Cycle 24 Day 1|	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 25 Day 1|	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 26 Day 1|	0.0 (± 99999)	-0.3 (± 0.58)		
Cycle 27 Day 1|	0.0 (± 99999)	-1.0 (± 1.41)		
Cycle 28 Day 1|	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 29 Day 1|	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 30 Day 1|	0.0 (± 99999)	-1.0 (± 1.00)		
Cycle 31 Day 1|	99999 (± 99999)	0.0 (± 0.00)		
Cycle 32 Day 1|	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 33 Day 1|	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 34 Day 1|	0.0 (± 99999)	0.0 (± 0.00)		
Cycle 35 Day 1|	0.0 (± 99999)	0.0 (± 99999)		
Cycle 36 Day 1|	0.0 (± 99999)	0.0 (± 99999)		

Cycle 37 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 38 Day 1|	0.0 (± 99999)	99999 (± 99999)		
Cycle 39 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 40 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 41 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 42 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 43 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 44 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 45 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 46 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 47 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 48 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 49 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 50 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 51 Day 1|	99999 (± 99999)	99999 (± 99999)		
Cycle 52 Day 1|	99999 (± 99999)	99999 (± 99999)		
End of treatment|	-15.0 (± 99999)	0.0 (± 99999)		

Notes:

[59] - Not all subjects had evaluable data at each time point.

[60] - Not all subjects had evaluable data at each time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Tumor Response (TTR) and Intracranial TTR (Phase 2)

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

End point description:

Time to tumor response (TTR) was defined as the time from the first dose of study treatment to the first documentation of objective tumor response (CR or PR). For subjects whose objective response proceeded from PR to CR, the onset of PR was taken as the onset of response. TTR was only calculated for the subgroup of subjects with a confirmed objective tumor response. Intracranial TTR was only calculated for subjects with confirmed intracranial objective response. Results presented here were based on independent central review.

End point type	Secondary

End point timeframe:

3 years

Notes:

[61] - 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: All other reporting arms are not applicable to this end point.

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[62]	20[63]	30[64]	27[65]
Units: months				
median (full range (min-max))				
TTR|	1.4 (1.2 to 5.4)	1.4 (1.2 to 11.0)	1.4 (1.1 to 5.7)	2.6 (1.2 to 9.9)
Intracranial TTR|	2.1 (1.2 to 2.8)	1.4 (1.2 to 1.5)	1.4 (1.1 to 5.7)	1.5 (1.2 to 6.2)

Notes:

[62] - Number of subjects analyzed for intracranial TTR is 6.

[63] - Number of subjects analyzed for intracranial TTR is 10.

[64] - Number of subjects analyzed for intracranial TTR is 20.

[65] - Number of subjects analyzed for intracranial TTR is 25.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16[66]	17[67]		
Units: months				
median (full range (min-max))				
TTR|	1.4 (1.2 to 4.0)	1.4 (1.3 to 4.2)		
Intracranial TTR|	1.4 (1.2 to 3.3)	1.4 (1.2 to 5.5)		

Notes:

[66] - Number of subjects analyzed for intracranial TTR is 15.

[67] - Number of subjects analyzed for intracranial TTR is 14.

Statistical analyses

No statistical analyses for this end point

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

End point title	Duration of Response (DOR) and Intracranial DOR (Phase 2)[68]

End point description:

Duration of Response (DOR) was defined as the time from the first documentation of objective tumor response (CR or PR) to the first documentation of disease progression or to death due to any cause, whichever occurred first. DOR was only calculated for the subgroup of subjects with a confirmed objective tumor response. Intracranial DOR was only calculated for subjects with confirmed intracranial objective response. Results presented here were based on independent central review. "99999" and "-99999" represent "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

3 years

Notes:

[68] - 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: All other reporting arms are not applicable to this end point.

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[69]	20[70]	30[71]	27[72]
Units: months				
median (confidence interval 95%)				
DOR|	99999 (10.02 to 99999)	99999 (99999 to 99999)	99999 (6.80 to 99999)	6.93 (5.22 to 99999)
Intra-cranial DOR|	9.15 (8.28 to 10.02)	99999 (99999 to 99999)	99999 (8.38 to 99999)	14.52 (-99999 to 99999)

Notes:

[69] - Number of subjects analyzed for intracranial DOR is 6.

[70] - Number of subjects analyzed for intracranial DOR is 10.

[71] - Number of subjects analyzed for intracranial DOR is 20.

[72] - Number of subjects analyzed for intracranial DOR is 25.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16[73]	17[74]		
Units: months				
median (confidence interval 95%)				
DOR|	99999 (4.17 to 99999)	13.83 (11.10 to 99999)		
Intra-cranial DOR|	8.31 (6.93 to 99999)	99999 (4.99 to 99999)		

Notes:

[73] - Number of subjects analyzed for intracranial DOR is 15.

[74] - Number of subjects analyzed for intracranial DOR is 14.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Disease Control and Intracranial Disease Control at 12 Weeks (Phase 2)

End point title	Percentage of Subjects Achieving Disease Control and Intracranial Disease Control at 12 Weeks (Phase 2)[75]

End point description:

Tumor response was evaluated according to RECIST version 1.1, and disease control was defined as confirmed complete response (CR), confirmed partial response (PR), or stable disease (SD). Intracranial assessment was only performed for subjects with CNS metastases. Results presented here were based on independent central review.

End point type	Secondary

End point timeframe:

12 weeks

Notes:

[75] - 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: All other reporting arms are not applicable to this end point.

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[76]	27[77]	59[78]	65[79]
Units: percentage of subjects				
number (confidence interval 95%)				
Disease control rate|	93.3 (77.9 to 99.2)	85.2 (66.3 to 95.8)	67.8 (54.4 to 79.4)	63.1 (50.2 to 74.7)
Intra-cranial disease control rate|	87.5 (47.3 to 99.7)	94.1 (71.3 to 99.9)	75.0 (56.6 to 88.5)	77.8 (62.9 to 88.8)

Notes:

[76] - Number of subjects analyzed for intracranial disease control is 8.

[77] - Number of subjects analyzed for intracranial disease control is 17.

[78] - Number of subjects analyzed for intracranial disease control is 32.

[79] - Number of subjects analyzed for intracranial disease control is 45.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[80]	47[81]		
Units: percentage of subjects				
number (confidence interval 95%)				
Disease control rate|	52.2 (36.9 to 67.1)	63.8 (48.5 to 77.3)		
Intra-cranial disease control rate|	68.4 (51.3 to 82.5)	72.0 (50.6 to 87.9)		

Notes:

[80] - Number of subjects analyzed for intracranial disease control is 38.

[81] - Number of subjects analyzed for intracranial disease control is 25.

Statistical analyses

No statistical analyses for this end point

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

End point title	Time to Progression (TTP) on the Last Prior Therapy (Phase

End point description:

TTP on the last prior therapy was defined as time from the first dose date of the last prior treatment regimen to the date of progression.

End point type	Secondary

End point timeframe:

3 years

Notes:

[82] - 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: All other reporting arms are not applicable to this end point.

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	59	65	46
Units: months				
median (confidence interval 95%)				

Prior systemic therapy before PF-06463922|	11.5 (7.2 to 19.6)	12.8 (9.2 to 16.9)	10.2 (7.6 to 14.9)	3.7 (2.1 to 6.4)
Prior ALK+/ROS1+ TKI treatment|	11.5 (7.2 to 19.6)	12.9 (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 30.7)	8.5 (5.0 to 12.6)	5.0 (3.1 to 10.8)	5.6 (4.7 to 11.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Tumor Progression (Phase 2)

End point title	Time to Tumor Progression (Phase 2)[83]

End point description:

Time to progression (TTP) was defined as the time from the first dose of study treatment to the first documentation of objective disease progression. Intracranial TTP was defined as the time from the first dose of study treatment to the date of the first documentation of objective progression of intracranial disease, based on either new brain metastases or progression of existing brain metastases. Results presented here were based on independent central review. ITT analysis set was used for TTP determination and included all enrolled subjects with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922; ITT subjects with CNS metastases were analyzed for intracranial TTP. "99999" represents "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

3 years

Notes:

[83] - 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: All other reporting arms are not applicable to this end point.

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[84]	27[85]	59[86]	65[87]
Units: months				
median (confidence interval 95%)				
TTP|	99999 (11.4 to 99999)	99999 (99999 to 99999)	9.0 (5.5 to 99999)	8.4 (5.6 to 13.7)
Intracranial|	11.4 (9.6 to 11.4)	99999 (99999 to 99999)	99999 (6.9 to 99999)	15.7 (11.0 to 15.7)

Notes:

[84] - Number of subjects analyzed for intracranial TTP is 8.

[85] - Number of subjects analyzed for intracranial TTP is 17.

[86] - Number of subjects analyzed for intracranial TTP is 32.

[87] - Number of subjects analyzed for intracranial TTP is 45.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[88]	47[89]		
Units: months				
median (confidence interval 95%)				

TTP| Intracranial|	7.1 (4.1 to 12.5) 99999 (8.3 to 99999)	12.5 (8.2 to 99999) 99999 (99999 to 99999)		

Notes:

[88] - Number of subjects analyzed for intracranial TTP is 38.

[89] - Number of subjects analyzed for intracranial TTP is 25.

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:

The probability of the 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. Subjects not known to have any of the Competing Events were censored on the date they were last assessed for disease status for PFS. Subjects 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. The results are based on independent central review.

End point type	Secondary

End point timeframe:

3 years

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

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) (Phase 2)

End point title	Progression-Free Survival (PFS) (Phase 2)[90]

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. Results presented here were based on independent central review. PFS analysis set included all subjects with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922. "99999"

represents "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

3 years

Notes:

[90] - 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: All other reporting arms are not applicable to this end point.

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[91]	27[92]	59[93]	65[94]
Units: months				
median (confidence interval 95%)	99999 (11.4 to 99999)	99999 (99999 to 99999)	8.2 (5.5 to 99999)	7.3 (5.4 to 11.0)

Notes:

[91] - Number of subjects with objective progression or death is 7; others were censored.

[92] - Number of subjects with objective progression or death is 8; others were censored.

[93] - Number of subjects with objective progression or death is 30; others were censored.

[94] - Number of subjects with objective progression or death is 36; others were censored.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[95]	47[96]		
Units: months				
median (confidence interval 95%)	5.6 (4.0 to 12.5)	9.6 (4.7 to 99999)		

Notes:

[95] - Number of subjects with objective progression or death is 26; others were censored.

[96] - Number of subjects with objective progression or death is 21; others were censored.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (Phase 2)

End point title	Overall Survival (Phase 2)[97]

End point description:

OS was defined as the time from first dose to the date of death due to any cause. For subjects still alive at the time of analysis, the OS time was censored on the last date the subjects were known to be alive. Estimates of OS and its 95% confidence interval were determined using Kaplan-Meier method. ITT set was used for OS analysis, and it included all enrolled subjects with documented ALK or ROS1 rearrangement who received at least 1 dose of PF-06463922. "99999" represents "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

3 years

Notes:

[97] - 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: All other reporting arms are not applicable to this end point.

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[98]	27[99]	59[100]	65[101]
Units: months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (12.1 to 99999)	99999 (14.4 to 99999)	99999 (14.7 to 99999)

Notes:

[98] - Number of death is 1; others were censored.

[99] - Number of death is 4; others were censored.

[100] - Number of death is 14; others were censored.

[101] - Number of death is 20; others were censored.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[102]	47[103]		
Units: months				
median (confidence interval 95%)	99999 (9.7 to 99999)	99999 (99999 to 99999)		

Notes:

[102] - Number of death is 15; others were censored.

[103] - Number of death is 10; others were censored.

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 concentration analysis set of PF-06463922 included all subjects treated who had at least 1 concentration of PF-06463922.

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[104]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day -7| Cycle 1 Day 15|	695.2 (± 40) 576.5 (± 42)			

Notes:

[104] - Number of subjects contributing to Day -7 data is 19.

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 subjects 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, 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[105]			
Units: hours				
median (full range (min-max))				
Day -7|	1.15 (0.50 to 4.02)			
Cycle 1 Day 15|	1.96 (0.50 to 22.7)			

Notes:

[105] - Number of subjects contributing to Day -7 data is 19.

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 the area under the plasma concentration-time profile from time 0 to the time of the last quantifiable concentration, Clast* was the predicted plasma concentration at the last quantifiable time point estimated from the log-linear regression analysis, and kel was the rate constant for terminal phase. PK parameter analysis set for PF-06463922 included all enrolled subjectswho 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, 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 subjects 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 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[106]			
Units: ng*hour/mL				
geometric mean (geometric coefficient of variation)				
Day -7| Cycle 1 Day 15|	5308 (± 36) 5650 (± 39)			

Notes:

[106] - Number of subjects contributing to Day -7 data is 19.

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 subjects 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, 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[107]			
Units: liter/hour				
geometric mean (geometric coefficient of variation)				
Day -7|	11.01 (± 35)			
Cycle 1 Day 15|	17.70 (± 39)			

Notes:

[107] - Number of subjects contributing to Day -7 data is 16.

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 subjects 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, 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: 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 subjects 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, 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 subjects 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 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 subjects 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 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 Subjects with ALK Mutation Based on Plasma CNA Analysis (Phase 2)

End point title	Number of Subjects with ALK Mutation Based on Plasma CNA Analysis (Phase 2)[108]

End point description:

Plasma CNA samples were analyzed for ALK kinase domain mutations by Next Generation Sequencing (NGS). Number of subjects with one or more ALK mutations is presented. CNA peripheral blood analysis set included all subjects of the ITT analysis set who had at least 1 molecular biomarker assayed.

End point type	Secondary

End point timeframe:

Screening

Notes:

[108] - 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: All other reporting arms are not applicable to this end point.

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	58	61
Units: subjects	1	6	8	17

End point values	EXP-5 (Phase 2)			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: subjects	14			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Subjects with ALK Mutation Based on Tumor Tissue Analysis (Phase 2)[109]

End point description:

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

Notes:

[109] - 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: All other reporting arms are not applicable to this end point.

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	26	52	48
Units: subjects	0	7	8	11

End point values	EXP-5 (Phase 2)			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: subjects	13			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Improved, Worsened or Remained Stable in EORTC QLQ-C30 (Phase 2)

End point title	Number of Subjects Who Improved, Worsened or Remained Stable in EORTC QLQ-C30 (Phase 2)[110]

End point description:

European Organisation for Research and Treatment of Cancer Core Quality of Life Questionaires (EORTC QLQ)-C30 (v3.0) consists of 30 questions for 5 functional domains (physical, role, emotional, cognitive, social), global quality of life (QoL), disease/treatment related symptoms (fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea), and the perceived financial impact of disease. Each scale was transformed to a range of 0 to 100 using EORTC algorithm. For global QoL and functional scales, higher score means better performance, improvement was an increase of at least 10 points, worsening was a decrease of at least 10 points. For symptom scales, higher score means worse symptoms, improvement was a decrease of at least 10 points, worsening was an increase of at least 10 points. Patient reported outcome (PRO) set included all subjects who received at least 1 dose of PF-06463922, completed a baseline and at least 1 post-baseline assessment.

End point type	Secondary

End point timeframe:

3 years

Notes:

[110] - 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: All other reporting arms are not applicable to this end point.

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: subjects				
Improved in global QoL|	17	11	18	25
Stable in global QoL|	10	13	26	22
Worsened in global QoL|	3	2	11	13
Improved in physical functioning|	10	7	14	23
Stable in physical functioning|	14	19	37	27
Worsened in physical functioning|	6	0	4	10

Improved in role functioning|	12	8	18	25
Stable in role functioning|	11	15	31	19
Worsened in role functioning|	7	3	6	16
Improved in emotional functioning|	12	12	18	21
Stable in emotional functioning|	14	14	29	32
Worsened in emotional functioning|	4	0	8	7
Improved in cognitive functioning|	10	3	11	13
Stable in cognitive functioning|	12	15	31	35
Worsened in cognitive functioning|	8	8	13	12
Improved in social functioning|	14	7	18	22
Stable in social functioning|	13	17	32	28
Worsened in social functioning|	3	2	5	10
Improved in fatigue|	17	14	22	29
Stable in fatigue|	9	11	25	22
Worsened in fatigue|	4	1	8	9
Improved in nausea and vomiting|	8	4	11	16
Stable in nausea and vomiting|	22	22	43	38
Worsened in nausea and vomiting|	0	0	1	6
Improved in pain|	14	9	19	23
Stable in pain|	11	15	27	26
Worsened in pain|	5	2	9	11
Improved in dyspnea|	15	9	10	21
Stable in dyspnea|	11	14	34	22
Worsened in dyspnea|	4	3	11	17
Improved in insomnia|	19	8	19	28
Stable in insomnia|	10	14	28	23
Worsened in insomnia|	1	4	8	9
Improved in appetite loss|	14	4	17	29
Stable in appetite loss|	16	22	37	26
Worsened in appetite loss|	0	0	1	5
Improved in constipation|	10	6	9	15
Stable in constipation|	13	18	36	33
Worsened in constipation|	7	2	10	12
Improved in diarrhea|	5	3	8	9
Stable in diarrhea|	19	22	42	40
Worsened in diarrhea|	6	1	5	11
Improved in financial difficulties|	10	6	11	13
Stable in financial difficulties|	18	18	33	38
Worsened in financial difficulties|	2	2	11	9

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	40[111]		
Units: subjects				
Improved in global QoL|	18	20		
Stable in global QoL|	17	13		
Worsened in global QoL|	8	7		
Improved in physical functioning|	8	11		

Stable in physical functioning|	25	24		
Worsened in physical functioning|	10	5		
Improved in role functioning|	16	17		
Stable in role functioning|	16	19		
Worsened in role functioning|	11	3		
Improved in emotional functioning|	18	17		
Stable in emotional functioning|	20	20		
Worsened in emotional functioning|	5	3		
Improved in cognitive functioning|	13	12		
Stable in cognitive functioning|	16	22		
Worsened in cognitive functioning|	14	6		
Improved in social functioning|	12	13		
Stable in social functioning|	23	22		
Worsened in social functioning|	8	5		
Improved in fatigue|	26	17		
Stable in fatigue|	11	19		
Worsened in fatigue|	6	4		
Improved in nausea and vomiting|	14	10		
Stable in nausea and vomiting|	28	28		
Worsened in nausea and vomiting|	1	2		
Improved in pain|	18	21		
Stable in pain|	20	12		
Worsened in pain|	5	7		
Improved in dyspnea|	14	13		
Stable in dyspnea|	21	19		
Worsened in dyspnea|	8	8		
Improved in insomnia|	22	19		
Stable in insomnia|	14	18		
Worsened in insomnia|	7	3		
Improved in appetite loss|	22	20		
Stable in appetite loss|	21	20		
Worsened in appetite loss|	0	0		
Improved in constipation|	11	13		
Stable in constipation|	28	23		
Worsened in constipation|	4	4		
Improved in diarrhea|	11	8		
Stable in diarrhea|	26	28		
Worsened in diarrhea|	6	4		
Improved in financial difficulties|	11	10		
Stable in financial difficulties|	22	26		
Worsened in financial difficulties|	10	4		

Notes:

[111] - Number of subjects analyzed for role functioning is 39.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Improved, Worsened or Remained Stable in EORTC QLQ-LC13 (Phase 2)

End point title	Number of Subjects Who Improved, Worsened or Remained Stable in EORTC QLQ-LC13 (Phase 2)[112]

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. Patient reported outcome (PRO) set included all subjects who received at least 1 dose of PF-06463922, completed a baseline and at least 1 post-baseline assessment.

End point type	Secondary

End point timeframe:

3 years

Notes:

[112] - 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: All other reporting arms are not applicable to this end point.

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[113]	60
Units: subjects				
Improved in dyspnea|	11	5	11	20
Stable in dyspnea|	16	19	36	26
Worsened in dyspnea|	3	2	8	14
Improved in coughing|	18	9	22	27
Stable in coughing|	9	14	26	27
Worsened in coughing|	3	3	7	6
Improved in hemoptysis|	4	0	7	5
Stable in hemoptysis|	24	26	47	53
Worsened in hemoptysis|	2	0	1	2
Improved in sore mouth|	0	2	4	10
Stable in sore mouth|	24	21	45	39
Worsened in sore mouth|	6	3	6	11
Improved in dysphagia|	3	1	5	7
Stable in dysphagia|	24	25	44	47
Worsened in dysphagia|	3	0	6	6
Improved in peripheral neuropathy|	2	4	9	5
Stable in peripheral neuropathy|	10	13	25	32
Worsened in peripheral neuropathy|	18	9	21	23
Improved in alopecia|	1	1	2	10
Stable in alopecia|	19	22	41	38
Worsened in alopecia|	10	3	12	12
Improved in chest pain|	11	5	14	18
Stable in chest pain|	15	19	36	33
Worsened in chest pain|	4	2	4	9
Improved in arm or shoulder pain|	9	4	13	14
Stable in arm or shoulder pain|	16	18	33	37
Worsened in arm or shoulder pain|	5	4	9	9
Improved in pain in other parts|	10	5	18	19
Stable in pain in other parts|	14	12	23	25
Worsened in pain in other parts|	6	9	14	16

Notes:
[113] - Number of subjects analyzed for chest pain is 54.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	41		
Units: subjects				
Improved in dyspnea|	12	13		
Stable in dyspnea|	22	22		
Worsened in dyspnea|	8	6		
Improved in coughing|	18	17		
Stable in coughing|	15	17		
Worsened in coughing|	9	7		
Improved in hemoptysis|	5	4		
Stable in hemoptysis|	34	36		
Worsened in hemoptysis|	3	1		
Improved in sore mouth|	2	5		
Stable in sore mouth|	32	28		
Worsened in sore mouth|	8	8		
Improved in dysphagia|	4	5		
Stable in dysphagia|	33	30		
Worsened in dysphagia|	5	6		
Improved in peripheral neuropathy|	6	8		
Stable in peripheral neuropathy|	23	19		
Worsened in peripheral neuropathy|	13	14		
Improved in alopecia|	8	9		
Stable in alopecia|	27	26		
Worsened in alopecia|	7	6		
Improved in chest pain|	14	14		
Stable in chest pain|	25	22		
Worsened in chest pain|	3	5		
Improved in arm or shoulder pain|	12	12		
Stable in arm or shoulder pain|	21	21		
Worsened in arm or shoulder pain|	9	8		
Improved in pain in other parts|	14	17		
Stable in pain in other parts|	11	17		
Worsened in pain in other parts|	16	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-Emergent Adverse Events (Phase 1 and Phase 2)

End point title	Number of Subjects with Treatment-Emergent Adverse Events (Phase 1 and Phase 2)[114]

End point description:

AE was any untoward medical occurrence in a clinical investigation subject administered a product or medical device, regardless of the causal relationship to study treatment. Treatment-emergent AEs

(TEAEs) were AEs which occurred for the first time during the effective duration of treatment or AEs that increased in severity during treatment. Serious AEs (SAEs) were 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. AEs included SAEs and non-serious AEs. Causality to study treatment was determined by the investigator. Severity was graded according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v4.03. The safety analysis set included all enrolled subjects who received at least 1 dose of PF-06463922.

End point type	Secondary

End point timeframe:

3 years

Notes:

[114] - 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: All other reporting arms are not applicable to this end point.

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: subjects				
AEs (all causality)|	3	3	3	12
AEs (treatment-related)|	3	3	3	11
SAEs (all causality)|	3	1	1	4
SAEs (treatment-related)|	1	0	0	1
Grade 1 (all causality)|	0	0	1	1
Grade 2 (all causality)|	0	1	2	4
Grade 3 (all causality)|	2	0	0	5
Grade 4 (all causality)|	0	1	0	1
Grade 5 (all causality)|	1	1	0	1

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: subjects				
AEs (all causality)|	17	3	3	3
AEs (treatment-related)|	16	3	3	1
SAEs (all causality)|	9	3	1	2
SAEs (treatment-related)|	1	3	0	0
Grade 1 (all causality)|	0	0	0	0
Grade 2 (all causality)|	5	0	1	1
Grade 3 (all causality)|	8	0	2	1
Grade 4 (all causality)|	1	1	0	1
Grade 5 (all causality)|	3	2	0	0

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	EXP-1 (Phase 2)	EXP-2 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group

Number of subjects analysed	3	4	30	27
Units: subjects				
AEs (all causality)|	3	4	30	27
AEs (treatment-related)|	3	4	30	27
SAEs (all causality)|	2	2	8	5
SAEs (treatment-related)|	0	1	3	0
Grade 1 (all causality)|	0	0	3	0
Grade 2 (all causality)|	1	0	12	11
Grade 3 (all causality)|	0	1	12	12
Grade 4 (all causality)|	1	3	3	3
Grade 5 (all causality)|	1	0	0	1

End point values	EXP-3 (Phase 2)	EXP-4 (Phase 2)	EXP-5 (Phase 2)	EXP-6 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	65	46	47
Units: subjects				
AEs (all causality)|	59	65	46	47
AEs (treatment-related)|	55	61	43	45
SAEs (all causality)|	18	24	18	16
SAEs (treatment-related)|	5	4	5	2
Grade 1 (all causality)|	5	3	3	0
Grade 2 (all causality)|	20	19	11	12
Grade 3 (all causality)|	24	28	20	26
Grade 4 (all causality)|	3	7	4	3
Grade 5 (all causality)|	7	8	8	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Laboratory Abnormalities (Phase 1 and Phase 2) – Hematology

End point title	Number of Subjects with Laboratory Abnormalities (Phase 1 and Phase 2) – Hematology[115]

End point description:

Hematology evaluation included hemoglobin, platelets, white blood cell, absolute neutrophils, absolute lymphocytes, absolute monocytes, absolute eosinophils and absolute basophils. The safety analysis set included all enrolled subjects who received at least 1 dose of PF-06463922.

End point type	Secondary

End point timeframe:

3 years

Notes:

[115] - 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: All other reporting arms are not applicable to this end point.

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[116]	3[117]	3[118]	12[119]
Units: subjects				
Anemia|	3	3	3	8
Hemoglobin increased|	0	0	0	0
Lymphocyte count decreased|	2	2	2	6
Lymphocyte count increased|	1	0	0	0
Neutrophil count decreased|	1	0	0	4
Platelet count decreased|	2	2	0	4
White blood cell decreased|	2	0	0	4

Notes:

[116] - Not all subjects had evaluable data for each parameter.

[117] - Not all subjects had evaluable data for each parameter.

[118] - Not all subjects had evaluable data for each parameter.

[119] - Not all subjects had evaluable data for each parameter.

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[120]	3[121]	3[122]	3[123]
Units: subjects				
Anemia|	16	3	3	3
Hemoglobin increased|	0	0	0	0
Lymphocyte count decreased|	4	3	3	0
Lymphocyte count increased|	3	1	0	0
Neutrophil count decreased|	2	0	0	0
Platelet count decreased|	5	1	0	0
White blood cell decreased|	2	2	1	0

Notes:

[120] - Not all subjects had evaluable data for each parameter.

[121] - Not all subjects had evaluable data for each parameter.

[122] - Not all subjects had evaluable data for each parameter.

[123] - Not all subjects had evaluable data for each parameter.

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	EXP-1 (Phase 2)	EXP-2 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[124]	4[125]	30[126]	27[127]
Units: subjects				
Anemia|	3	4	20	14
Hemoglobin increased|	0	0	0	0
Lymphocyte count decreased|	0	2	9	9
Lymphocyte count increased|	0	0	3	3
Neutrophil count decreased|	0	1	5	2
Platelet count decreased|	0	1	6	9
White blood cell decreased|	0	1	6	3

Notes:

[124] - Not all subjects had evaluable data for each parameter.

[125] - Not all subjects had evaluable data for each parameter.

[126] - Not all subjects had evaluable data for each parameter.

[127] - Not all subjects had evaluable data for each parameter.

End point values	EXP-3 (Phase 2)	EXP-4 (Phase 2)	EXP-5 (Phase 2)	EXP-6 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60[128]	64[129]	45[130]	47[131]
Units: subjects				
Anemia|	50	48	35	32
Hemoglobin increased|	1	3	1	1
Lymphocyte count decreased|	21	29	18	21
Lymphocyte count increased|	6	4	2	1
Neutrophil count decreased|	7	6	1	5
Platelet count decreased|	13	9	10	11
White blood cell decreased|	6	9	5	8

Notes:

[128] - Not all subjects had evaluable data for each parameter.

[129] - Not all subjects had evaluable data for each parameter.

[130] - Not all subjects had evaluable data for each parameter.

[131] - Not all subjects had evaluable data for each parameter.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Laboratory Abnormalities (Phase 1 and Phase 2) – Chemistry

End point title	Number of Subjects with Laboratory Abnormalities (Phase 1 and Phase 2) – Chemistry[132]

End point description:

Chemistry evaluation included alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, sodium, potassium, magnesium, chloride, total calcium, total bilirubin, blood urea nitrogen (BUN) or urea, creatinine, uric acid, glucose (non-fasted), albumin, phosphorus or phosphate, serum total amylase and serum lipase. The safety analysis set included all enrolled subjects who received at least 1 dose of PF-06463922.

End point type	Secondary

End point timeframe:

3 years

Notes:

[132] - 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: All other reporting arms are not applicable to this end point.

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[133]	3[134]	3[135]	12[136]
Units: subjects				
ALT increased|	2	1	1	4
Alkaline phosphatase increased|	1	1	3	4
AST increased|	2	2	2	3
Blood bilirubin increased|	1	0	0	1
CPK increased|	0	0	0	0

Creatinine increased|	3	2	3	9
GGT increased|	0	0	0	0
Hypercalcemia|	0	0	0	0
Hyperglycemia|	3	2	2	6
Hyperkalemia|	0	1	2	2
Hypermagnesemia|	2	0	0	1
Hypernatremia|	0	1	0	0
Hypoalbuminemia|	2	1	3	4
Hypocalcemia|	1	0	1	3
Hypoglycemia|	0	0	1	3
Hypokalemia|	0	0	2	3
Hypomagnesemia|	0	1	2	4
Hyponatremia|	2	1	1	1
Hypophosphatemia|	1	2	0	3
Lipase increased|	3	1	0	8
Serum amylase increased|	3	0	0	2

Notes:

[133] - Not all subjects had evaluable data for each parameter.

[134] - Not all subjects had evaluable data for each parameter.

[135] - Not all subjects had evaluable data for each parameter.

[136] - Not all subjects had evaluable data for each parameter.

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[137]	3[138]	3[139]	3[140]
Units: subjects				
ALT increased|	7	2	2	0
Alkaline phosphatase increased|	9	3	1	0
AST increased|	7	2	2	0
Blood bilirubin increased|	0	0	0	0
CPK increased|	1	1	0	0
Creatinine increased|	13	3	3	2
GGT increased|	1	0	1	0
Hypercalcemia|	1	1	0	0
Hyperglycemia|	8	2	1	1
Hyperkalemia|	6	1	1	1
Hypermagnesemia|	2	0	0	0
Hypernatremia|	4	2	0	0
Hypoalbuminemia|	6	3	1	1
Hypocalcemia|	3	2	1	0
Hypoglycemia|	4	0	1	0
Hypokalemia|	3	3	1	1
Hypomagnesemia|	1	3	0	1
Hyponatremia|	4	1	1	0
Hypophosphatemia|	3	2	1	1
Lipase increased|	6	0	1	0
Serum amylase increased|	5	0	1	0

Notes:

[137] - Not all subjects had evaluable data for each parameter.

[138] - Not all subjects had evaluable data for each parameter.

[139] - Not all subjects had evaluable data for each parameter.
[140] - Not all subjects had evaluable data for each parameter.

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	EXP-1 (Phase 2)	EXP-2 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[141]	4[142]	30[143]	27[144]
Units: subjects				
ALT increased|	0	3	11	11
Alkaline phosphatase increased|	2	3	6	8
AST increased|	1	3	15	12
Blood bilirubin increased|	0	1	0	0
CPK increased|	1	0	0	0
Creatinine increased|	2	3	26	21
GGT increased|	0	2	0	1
Hypercalcemia|	0	1	4	3
Hyperglycemia|	2	0	11	16
Hyperkalemia|	1	2	8	7
Hypermagnesemia|	0	0	2	1
Hypernatremia|	0	1	3	1
Hypoalbuminemia|	3	1	16	15
Hypocalcemia|	0	1	2	4
Hypoglycemia|	1	0	1	2
Hypokalemia|	0	2	6	1
Hypomagnesemia|	1	3	4	8
Hyponatremia|	2	2	8	6
Hypophosphatemia|	2	1	3	6
Lipase increased|	2	2	9	5
Serum amylase increased|	0	2	9	5

Notes:
[141] - Not all subjects had evaluable data for each parameter.
[142] - Not all subjects had evaluable data for each parameter.
[143] - Not all subjects had evaluable data for each parameter.
[144] - Not all subjects had evaluable data for each parameter.

End point values	EXP-3 (Phase 2)	EXP-4 (Phase 2)	EXP-5 (Phase 2)	EXP-6 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60[145]	64[146]	45[147]	47[148]
Units: subjects				
ALT increased|	23	17	12	13
Alkaline phosphatase increased|	21	21	21	14
AST increased|	31	27	17	17
Blood bilirubin increased|	2	0	1	1
CPK increased|	3	0	0	2
Creatinine increased|	37	44	32	34
GGT increased|	2	1	0	1
Hypercalcemia|	4	4	3	1
Hyperglycemia|	30	41	31	29
Hyperkalemia|	14	11	5	5
Hypermagnesemia|	2	2	1	3
Hypernatremia|	2	4	2	4

Hypoalbuminemia|	34	42	29	27
Hypocalcemia|	11	9	3	9
Hypoglycemia|	8	7	5	3
Hypokalemia|	9	9	6	13
Hypomagnesemia|	20	17	13	11
Hyponatremia|	10	19	9	6
Hypophosphatemia|	17	14	7	14
Lipase increased|	11	15	14	16
Serum amylase increased|	14	18	10	13

Notes:

[145] - Not all subjects had evaluable data for each parameter.

[146] - Not all subjects had evaluable data for each parameter.

[147] - Not all subjects had evaluable data for each parameter.

[148] - Not all subjects had evaluable data for each parameter.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Laboratory Abnormalities (Phase 1 and Phase 2) – Coagulation, Lipids and Urinalysis

End point title	Number of Subjects with Laboratory Abnormalities (Phase 1 and Phase 2) – Coagulation, Lipids and Urinalysis[149]

End point description:

Coagulation evaluation included activated partial thromboplastin time, international normalized ratio (INR), and prothrombin time. Lipid evaluation included total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL) and triglycerides. Urinalysis included urine protein and urine blood. The safety analysis set included all enrolled subjects who received at least 1 dose of PF-06463922.

End point type	Secondary

End point timeframe:

3 years

Notes:

[149] - 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: All other reporting arms are not applicable to this end point.

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[150]	3[151]	3[152]	12[153]
Units: subjects				
Activated partial thromboplastin time prolonged|	1	0	1	3
Cholesterol high|	2	2	2	10
Hypertriglyceridemia|	0	2	2	10
INR increased|	2	0	1	2
Proteinuria|	2	0	0	0
Prothrombin time|	2	0	1	3

Notes:

[150] - Not all subjects had evaluable data for each parameter.

[151] - Not all subjects had evaluable data for each parameter.

[152] - Not all subjects had evaluable data for each parameter.

[153] - Not all subjects had evaluable data for each parameter.

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[154]	3[155]	3[156]	3[157]
Units: subjects				
Activated partial thromboplastin time prolonged|	2	0	0	0
Cholesterol high|	16	2	3	3
Hypertriglyceridemia|	16	2	3	2
INR increased|	2	1	0	0
Proteinuria|	4	3	0	0
Prothrombin time|	3	1	0	0

Notes:

[154] - Not all subjects had evaluable data for each parameter.

[155] - Not all subjects had evaluable data for each parameter.

[156] - Not all subjects had evaluable data for each parameter.

[157] - Not all subjects had evaluable data for each parameter.

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	EXP-1 (Phase 2)	EXP-2 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[158]	4[159]	30[160]	27[161]
Units: subjects				
Activated partial thromboplastin time prolonged|	0	0	1	0
Cholesterol high|	2	3	30	26
Hypertriglyceridemia|	1	3	30	25
INR increased|	0	0	0	0
Proteinuria|	1	0	1	0
Prothrombin time|	1	1	0	1

Notes:

[158] - Not all subjects had evaluable data for each parameter.

[159] - Not all subjects had evaluable data for each parameter.

[160] - Not all subjects had evaluable data for each parameter.

[161] - Not all subjects had evaluable data for each parameter.

End point values	EXP-3 (Phase 2)	EXP-4 (Phase 2)	EXP-5 (Phase 2)	EXP-6 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60[162]	65[163]	46[164]	47[165]
Units: subjects				
Activated partial thromboplastin time prolonged|	1	0	1	4
Cholesterol high|	57	64	45	44
Hypertriglyceridemia|	56	60	45	42
INR increased|	1	4	0	6
Proteinuria|	2	2	2	4
Prothrombin time|	4	4	2	5

Notes:

[162] - Not all subjects had evaluable data for each parameter.

[163] - Not all subjects had evaluable data for each parameter.

[164] - Not all subjects had evaluable data for each parameter.

[165] - Not all subjects had evaluable data for each parameter.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Vital Signs Data Meeting Pre-defined Criteria (Phase 1 and Phase 2)

End point title	Number of Subjects with Vital Signs Data Meeting Pre-defined Criteria (Phase 1 and Phase 2)[166]

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 subjects who received at least 1 dose of PF-06463922.

End point type	Secondary

End point timeframe:

3 years

Notes:

[166] - 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: All other reporting arms are not applicable to this end point.

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: subjects				
Sitting pulse rate <50 bpm|	0	1	0	0
Sitting pulse rate >120 bpm|	0	0	1	1
Increase in weight: 10% to <20%|	1	1	0	6
Increase in weight: >=20%|	0	1	1	1
Increase in sitting SBP >=40 mmHg|	0	0	0	0
Increase in sitting SBP >=60 mmHg|	0	0	0	0
Increase in sitting DBP >=20 mmHg|	0	2	0	0
Increase in sitting DBP >=40 mmHg|	0	0	0	0
Increase in sitting pulse rate >=30 bpm|	0	1	0	1
Decrease in weight >=10%|	0	0	0	0
Decrease in SBP >=40 mmHg|	0	0	0	3
Decrease in SBP >=60 mmHg|	0	0	0	0
Decrease in DBP >=20 mmHg|	2	1	0	4
Decrease in DBP >=40 mmHg|	0	0	0	0
Decrease in sitting pulse rate >=30 bpm|	0	0	1	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: subjects				
Sitting pulse rate <50 bpm|	0	0	0	0
Sitting pulse rate >120 bpm|	2	2	0	0
Increase in weight: 10% to <20%|	6	2	2	0

Increase in weight: >=20%|	4	1	0	0
Increase in sitting SBP >=40 mmHg|	1	2	0	0
Increase in sitting SBP >=60 mmHg|	0	0	0	0
Increase in sitting DBP >=20 mmHg|	7	3	1	0
Increase in sitting DBP >=40 mmHg|	0	0	0	0
Increase in sitting pulse rate >=30 bpm|	3	1	0	0
Decrease in weight >=10%|	0	0	0	0
Decrease in SBP >=40 mmHg|	2	1	0	0
Decrease in SBP >=60 mmHg|	0	0	0	0
Decrease in DBP >=20 mmHg|	3	2	2	0
Decrease in DBP >=40 mmHg|	0	0	0	0
Decrease in sitting pulse rate >=30 bpm|	0	1	0	1

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	EXP-1 (Phase 2)	EXP-2 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	30	26
Units: subjects				
Sitting pulse rate <50 bpm|	0	0	0	0
Sitting pulse rate >120 bpm|	0	0	0	0
Increase in weight: 10% to <20%|	1	0	9	12
Increase in weight: >=20%|	0	1	8	1
Increase in sitting SBP >=40 mmHg|	0	0	5	3
Increase in sitting SBP >=60 mmHg|	0	0	0	0
Increase in sitting DBP >=20 mmHg|	0	0	9	9
Increase in sitting DBP >=40 mmHg|	0	0	0	1
Increase in sitting pulse rate >=30 bpm|	0	1	0	2
Decrease in weight >=10%|	0	1	1	0
Decrease in SBP >=40 mmHg|	0	0	0	1
Decrease in SBP >=60 mmHg|	0	0	0	0
Decrease in DBP >=20 mmHg|	1	2	5	3
Decrease in DBP >=40 mmHg|	0	0	0	0
Decrease in sitting pulse rate >=30 bpm|	1	1	7	2

End point values	EXP-3 (Phase 2)	EXP-4 (Phase 2)	EXP-5 (Phase 2)	EXP-6 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	65	45	46
Units: subjects				
Sitting pulse rate <50 bpm|	3	1	0	2
Sitting pulse rate >120 bpm|	4	8	3	2
Increase in weight: 10% to <20%|	14	18	15	12
Increase in weight: >=20%|	4	9	3	8
Increase in sitting SBP >=40 mmHg|	4	5	5	3

Increase in sitting SBP >=60 mmHg|	0	1	0	0
Increase in sitting DBP >=20 mmHg|	16	12	10	11
Increase in sitting DBP >=40 mmHg|	0	0	0	2
Increase in sitting pulse rate >=30 bpm|	10	15	12	13
Decrease in weight >=10%|	6	4	1	1
Decrease in SBP >=40 mmHg|	2	1	1	3
Decrease in SBP >=60 mmHg|	0	0	0	0
Decrease in DBP >=20 mmHg|	12	8	5	6
Decrease in DBP >=40 mmHg|	0	0	0	0
Decrease in sitting pulse rate >=30 bpm|	4	5	3	5

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Subjects with Maximum Decrease from Baseline Greater than or Equal to 20 Percent in Left Ventricular Ejection Fraction (LVEF) (Phase 1 and Phase 2)[167]

End point description:

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

End point type	Secondary

End point timeframe:

3 years

Notes:

[167] - 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: All other reporting arms are not applicable to this end point.

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: subjects	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: subjects	4	2	1	0

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	EXP-1 (Phase 2)	EXP-2 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	30	27
Units: subjects	0	2	3	1

End point values	EXP-3 (Phase 2)	EXP-4 (Phase 2)	EXP-5 (Phase 2)	EXP-6 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	65	46	47
Units: subjects	9	11	3	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Absolute Values and Change from Baseline in QTcF Meeting Pre-defined Criteria (Phase 1 and Phase 2)

End point title	Number of Subjects with Absolute Values and Change from Baseline in QTcF Meeting Pre-defined Criteria (Phase 1 and Phase 2)[168]

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 subjects who received at least 1 dose of PF-06463922.

End point type	Secondary

End point timeframe:

3 years

Notes:

[168] - 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: All other reporting arms are not applicable to this end point.

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: subjects				
QTcF: 450 to <480 ms|	1	0	0	2
QTcF: 480 to <500 ms|	1	0	0	0
QTcF: >=500 ms|	0	0	0	0
QTcF Increase: 30 to <60 ms|	0	0	1	3
QTcF: >=60 ms|	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: subjects				
QTcF: 450 to <480 ms|	1	1	0	2
QTcF: 480 to <500 ms|	0	0	0	0
QTcF: >=500 ms|	0	0	0	0
QTcF Increase: 30 to <60 ms|	3	0	0	1
QTcF: >=60 ms|	0	0	0	0

End point values	75 mg BID (Phase 1)	100 mg BID (Phase 1)	EXP-1 (Phase 2)	EXP-2 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	30	27
Units: subjects				
QTcF: 450 to <480 ms|	0	0	4	7
QTcF: 480 to <500 ms|	0	1	1	1
QTcF: >=500 ms|	0	0	0	0
QTcF Increase: 30 to <60 ms|	0	0	8	8
QTcF: >=60 ms|	0	1	0	0

End point values	EXP-3 (Phase 2)	EXP-4 (Phase 2)	EXP-5 (Phase 2)	EXP-6 (Phase 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	65	46	47
Units: subjects				
QTcF: 450 to <480 ms|	11	9	13	8
QTcF: 480 to <500 ms|	3	0	1	1
QTcF: >=500 ms|	0	1	1	0
QTcF Increase: 30 to <60 ms|	17	20	7	11
QTcF: >=60 ms|	0	1	3	1

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Subjects with Suicidal Ideation and Suicidal Behavior (Phase 2)[169]

End point description:

The Columbia Suicide Severity Rating Scale (C-SSRS) was used to analyze subjects' 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. The analysis set included all enrolled subjects

who received study treatment, had a baseline test assessment and at least 1 on-study test assessment.

End point type	Secondary

End point timeframe:

3 years

Notes:

[169] - 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: All other reporting arms are not applicable to this end point.

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: subjects				
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: subjects				
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)[170]

End point description:

The Beck Depression Inventory (BDI)-II is a 21-item self-report scale, with each item rated by subjects on a 4-point scale (ranging from 0-3). The 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. The analysis set included all enrolled subjects who received study treatment, had a baseline test assessment and at least 1 on-study test assessment. "99999" represents "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

3 years

Notes:

[170] - 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: All other reporting arms are not applicable to this end point.

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[171]	24[172]	53[173]	41[174]
Units: units on score				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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)

Notes:

[171] - Not all subjects had evaluable data at each time point.

[172] - Not all subjects had evaluable data at each time point.

[173] - Not all subjects had evaluable data at each time point.

[174] - Not all subjects had evaluable data at each time point.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28[175]	26[176]		
Units: units on score				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1|	-1.52 (-3.60 to 0.56)	-2.43 (-4.57 to -0.29)		

Cycle 3 Day 1|	-0.46 (-2.61 to 1.69)	-1.24 (-3.37 to 0.90)		
Cycle 4 Day 1|	-1.19 (-3.38 to 1.01)	-1.94 (-4.12 to 0.24)		
Cycle 5 Day 1|	-1.51 (-3.74 to 0.72)	-1.25 (-3.46 to 0.95)		
Cycle 6 Day 1|	-0.42 (-2.64 to 1.81)	-0.29 (-2.54 to 1.96)		
Cycle 8 Day 1|	-1.09 (-3.34 to 1.17)	0.17 (-2.10 to 2.45)		
Cycle 10 Day 1|	-2.97 (-5.29 to -0.66)	-0.19 (-2.60 to 2.22)		
Cycle 12 Day 1|	-1.94 (-4.29 to 0.42)	-1.40 (-3.81 to 1.01)		
Cycle 14 Day 1|	-1.73 (-4.40 to 0.94)	-0.08 (-2.59 to 2.42)		
Cycle 16 Day 1|	-2.22 (-5.50 to 1.07)	0.03 (-2.65 to 2.71)		
Cycle 18 Day 1|	-1.11 (-8.25 to 6.03)	1.88 (-1.66 to 5.41)		
Cycle 20 Day 1|	99999 (99999 to 99999)	1.88 (-1.66 to 5.41)		
Cycle 22 Day 1|	99999 (99999 to 99999)	-2.39 (-6.73 to 1.94)		
Cycle 24 Day 1|	99999 (99999 to 99999)	2.27 (-2.06 to 6.61)		
Cycle 26 Day 1|	99999 (99999 to 99999)	99999 (99999 to 99999)		
End of treatment|	0.74 (-2.70 to 4.17)	-2.08 (-5.65 to 1.50)		

Notes:

[175] - Not all subjects had evaluable data at each time point.

[176] - Not all subjects had evaluable data at each time point.

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)[177]

End point description:

The Detection Test is a measure of psychomotor function and uses a well validated simple reaction time paradigm with playing card stimuli. In this test, the playing cards all depict the same joker. The subject is asked to press the Yes key as soon as the card in the center of the screen turns face up. The speed and accuracy of each response are recorded and mean of the log10 transformed reaction times for correct responses is calculated. Lower scores indicate better performance. The analysis set included all enrolled subjects who received study treatment, had a baseline test assessment and at least 1 on-study test assessment. "99999" represents "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

3 years

Notes:

[177] - 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: All other reporting arms are not applicable to this end point.

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[178]	26[179]	50[180]	46[181]
Units: units on a score				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1|	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|	-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|	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|	-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|	-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|	-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|	-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|	-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|	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|	-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|	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|	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|	-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|	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|	-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)

Notes:

[178] - Not all subjects had evaluable data at each time point.

[179] - Not all subjects had evaluable data at each time point.

[180] - Not all subjects had evaluable data at each time point.

[181] - Not all subjects had evaluable data at each time point.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38[182]	29[183]		
Units: units on a score				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1|	-0.02 (-0.05 to 0.02)	0.01 (-0.03 to 0.05)		
Cycle 3 Day 1|	-0.01 (-0.05 to 0.02)	-0.01 (-0.05 to 0.03)		
Cycle 4 Day 1|	-0.04 (-0.07 to -0.00)	-0.01 (-0.06 to 0.03)		
Cycle 5 Day 1|	-0.04 (-0.08 to -0.01)	-0.04 (-0.08 to 0.00)		
Cycle 6 Day 1|	-0.01 (-0.05 to 0.02)	-0.02 (-0.07 to 0.02)		

Cycle 8 Day 1|	-0.04 (-0.07 to 0.00)	0.00 (-0.04 to 0.05)		
Cycle 10 Day 1|	-0.05 (-0.09 to -0.01)	-0.04 (-0.08 to 0.01)		
Cycle 12 Day 1|	-0.08 (-0.13 to -0.04)	-0.01 (-0.05 to 0.04)		
Cycle 14 Day 1|	-0.02 (-0.07 to 0.04)	0.01 (-0.05 to 0.06)		
Cycle 16 Day 1|	-0.04 (-0.14 to 0.06)	-0.01 (-0.07 to 0.06)		
Cycle 18 Day 1|	-0.09 (-0.23 to 0.04)	-0.01 (-0.08 to 0.05)		
Cycle 20 Day 1|	99999 (99999 to 99999)	-0.03 (-0.11 to 0.04)		
Cycle 22 Day 1|	99999 (99999 to 99999)	-0.05 (-0.13 to 0.03)		
Cycle 24 Day 1|	99999 (99999 to 99999)	99999 (99999 to 99999)		
End of treatment|	-0.07 (-0.14 to -0.01)	-0.05 (-0.12 to 0.03)		

Notes:

[182] - Not all subjects had evaluable data at each time point.

[183] - Not all subjects had evaluable data at each time point.

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)[184]

End point description:

The Identification Test is a measure of visual attention and uses a well validated choice reaction time paradigm with playing card stimuli. In this task, the playing cards are all either red or black jokers. The subject is asked whether the card displayed in the center of the screen is red. The patient responds by pressing the Yes key when the joker card is red and No when it is black. The speed and accuracy of each response are recorded and mean of the log10 transformed reaction times for correct responses is calculated. Lower scores indicate better performance. The analysis set included all enrolled subjects who received study treatment, had a baseline test assessment and at least 1 on-study test assessment. "99999" represents "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

3 years

Notes:

[184] - 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: All other reporting arms are not applicable to this end point.

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[185]	26[186]	50[187]	46[188]
Units: units on a score				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	-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|	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|	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|	-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)

Notes:

[185] - Not all subjects had evaluable data at each time point.

[186] - Not all subjects had evaluable data at each time point.

[187] - Not all subjects had evaluable data at each time point.

[188] - Not all subjects had evaluable data at each time point.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38[189]	29[190]		
Units: units on a score				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1|	-0.02 (-0.04 to 0.01)	-0.01 (-0.04 to 0.02)		
Cycle 3 Day 1|	-0.02 (-0.05 to 0.00)	-0.01 (-0.04 to 0.02)		
Cycle 4 Day 1|	-0.05 (-0.08 to -0.03)	-0.02 (-0.04 to 0.01)		
Cycle 5 Day 1|	-0.05 (-0.07 to -0.02)	-0.02 (-0.05 to 0.00)		
Cycle 6 Day 1|	-0.03 (-0.06 to -0.01)	-0.03 (-0.06 to -0.00)		
Cycle 8 Day 1|	-0.05 (-0.07 to -0.02)	-0.03 (-0.06 to 0.00)		
Cycle 10 Day 1|	-0.05 (-0.08 to -0.02)	-0.03 (-0.06 to 0.00)		
Cycle 12 Day 1|	-0.06 (-0.09 to -0.03)	-0.03 (-0.06 to 0.00)		
Cycle 14 Day 1|	-0.04 (-0.08 to -0.00)	-0.02 (-0.06 to 0.02)		

Cycle 16 Day 1|	-0.07 (-0.13 to 0.00)	-0.06 (-0.10 to -0.01)		
Cycle 18 Day 1|	-0.19 (-0.29 to -0.09)	-0.01 (-0.05 to 0.04)		
Cycle 20 Day 1|	99999 (99999 to 99999)	-0.03 (-0.08 to 0.02)		
Cycle 22 Day 1|	99999 (99999 to 99999)	-0.08 (-0.14 to -0.03)		
Cycle 24 Day 1|	99999 (99999 to 99999)	99999 (99999 to 99999)		
End of treatment|	-0.09 (-0.14 to -0.05)	-0.06 (-0.11 to -0.01)		

Notes:

[189] - Not all subjects had evaluable data at each time point.

[190] - Not all subjects had evaluable data at each time point.

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)[191]

End point description:

The One Back Test is a measure of working memory and uses a well validated n back paradigm with playing card stimuli. In this task, the playing cards are identical to those found in a standard deck of 52 playing cards (without the joker cards). The patient is asked whether the card displayed in the center of the screen is the same as the card presented immediately previously. The patient responds by pressing the Yes or No key. Because no card has been presented yet on the first trial, a correct first response is always No. The speed and accuracy of each response are recorded and mean of the log10 transformed reaction times for correct responses is calculated. Lower scores indicate better performance. The analysis set included all enrolled subjects who received study treatment, had a baseline test assessment and at least 1 on-study test assessment. "99999" represents "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

3 years

Notes:

[191] - 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: All other reporting arms are not applicable to this end point.

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[192]	26[193]	50[194]	46[195]
Units: units on a score				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1|	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|	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|	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|	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|	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|	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|	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|	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|	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|	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|	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|	-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|	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|	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|	-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)

Notes:

[192] - Not all subjects had evaluable data at each time point.

[193] - Not all subjects had evaluable data at each time point.

[194] - Not all subjects had evaluable data at each time point.

[195] - Not all subjects had evaluable data at each time point.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38[196]	29[197]		
Units: units on a score				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1|	0.02 (-0.01 to 0.05)	0.01 (-0.02 to 0.04)		
Cycle 3 Day 1|	-0.01 (-0.04 to 0.02)	-0.00 (-0.04 to 0.03)		
Cycle 4 Day 1|	-0.02 (-0.05 to 0.01)	-0.01 (-0.05 to 0.02)		
Cycle 5 Day 1|	-0.02 (-0.05 to 0.01)	0.02 (-0.01 to 0.05)		
Cycle 6 Day 1|	-0.00 (-0.03 to 0.03)	0.01 (-0.03 to 0.04)		
Cycle 8 Day 1|	-0.01 (-0.04 to 0.02)	0.01 (-0.02 to 0.05)		
Cycle 10 Day 1|	-0.01 (-0.05 to 0.02)	0.01 (-0.02 to 0.05)		
Cycle 12 Day 1|	-0.00 (-0.04 to 0.03)	0.03 (-0.01 to 0.07)		
Cycle 14 Day 1|	0.01 (-0.04 to 0.06)	0.02 (-0.03 to 0.07)		
Cycle 16 Day 1|	-0.01 (-0.10 to 0.08)	0.03 (-0.03 to 0.08)		
Cycle 18 Day 1|	-0.18 (-0.30 to -0.06)	0.05 (-0.01 to 0.10)		
Cycle 20 Day 1|	99999 (99999 to 99999)	0.02 (-0.04 to 0.09)		

Cycle 22 Day 1|	99999 (99999 to 99999)	0.03 (-0.04 to 0.11)		
Cycle 24 Day 1|	99999 (99999 to 99999)	99999 (99999 to 99999)		
End of treatment|	-0.03 (-0.08 to 0.02)	0.02 (-0.05 to 0.08)		

Notes:

[196] - Not all subjects had evaluable data at each time point.

[197] - Not all subjects had evaluable data at each time point.

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)[198]

End point description:

The International Shopping List Test is a measure of verbal learning and uses a well validated list learning paradigm. Total number of correct responses remembering the word list on 3 consecutive trials at a single assessment was recorded. Higher scores indicate better performance. The analysis set included all enrolled subjects who received study treatment, had a baseline test assessment and at least 1 on-study test assessment. "99999" represents "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

3 years

Notes:

[198] - 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: All other reporting arms are not applicable to this end point.

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[199]	26[200]	50[201]	46[202]
Units: units on a score				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1|	-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|	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|	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|	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|	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|	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|	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|	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|	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|	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|	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|	-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|	-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|	-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|	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)

Notes:

[199] - Not all subjects had evaluable data at each time point.

[200] - Not all subjects had evaluable data at each time point.

[201] - Not all subjects had evaluable data at each time point.

[202] - Not all subjects had evaluable data at each time point.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38[203]	29[204]		
Units: units on a score				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1|	0.96 (-0.50 to 2.43)	0.16 (-1.51 to 1.83)		
Cycle 3 Day 1|	-0.08 (-1.59 to 1.44)	-0.56 (-2.21 to 1.09)		
Cycle 4 Day 1|	1.30 (-0.26 to 2.86)	-0.87 (-2.59 to 0.84)		
Cycle 5 Day 1|	1.23 (-0.36 to 2.82)	0.74 (-0.97 to 2.45)		
Cycle 6 Day 1|	0.82 (-0.83 to 2.46)	-0.51 (-2.31 to 1.29)		
Cycle 8 Day 1|	0.44 (-1.23 to 2.11)	1.70 (-0.11 to 3.50)		
Cycle 10 Day 1|	2.29 (0.53 to 4.05)	0.97 (-0.99 to 2.93)		
Cycle 12 Day 1|	1.74 (-0.25 to 3.72)	3.10 (1.06 to 5.14)		
Cycle 14 Day 1|	-4.43 (-7.11 to -1.75)	2.67 (0.09 to 5.25)		
Cycle 16 Day 1|	3.46 (-1.26 to 8.18)	1.97 (-0.93 to 4.87)		
Cycle 18 Day 1|	-0.35 (-6.90 to 6.21)	3.13 (0.00 to 6.27)		
Cycle 20 Day 1|	99999 (99999 to 99999)	0.56 (-2.89 to 4.01)		
Cycle 22 Day 1|	99999 (99999 to 99999)	3.99 (0.07 to 7.91)		
Cycle 24 Day 1|	99999 (99999 to 99999)	99999 (99999 to 99999)		
End of treatment|	2.37 (-0.54 to 5.27)	-0.60 (-4.09 to 2.89)		

Notes:

[203] - Not all subjects had evaluable data at each time point.

[204] - Not all subjects had evaluable data at each time point.

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)[205]

End point description:

The International Shopping List Test-Delayed Recall is a measure of memory and uses a well validated list learning paradigm. Total number of correct responses made in remembering the word list after a delay was recorded. Higher scores indicate better performance. The analysis set included all enrolled subjects who received study treatment, had a baseline test assessment and at least 1 on-study test assessment. "99999" represents "not applicable" or "non evaluable" data.

End point type	Secondary

End point timeframe:

3 years

Notes:

[205] - 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: All other reporting arms are not applicable to this end point.

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[206]	26[207]	50[208]	46[209]
Units: units on a score				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1|	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|	-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|	-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|	-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|	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|	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|	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|	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|	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|	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|	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|	-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|	-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|	-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|	-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)

Notes:

[206] - Not all subjects had evaluable data at each time point.

[207] - Not all subjects had evaluable data at each time point.

[208] - Not all subjects had evaluable data at each time point.

[209] - Not all subjects had evaluable data at each time point.

End point values	EXP-5 (Phase 2)	EXP-6 (Phase 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38[210]	29[211]		
Units: units on a score				
least squares mean (confidence interval 95%)				
Cycle 2 Day 1|	-0.22 (-0.96 to 0.53)	-0.25 (-1.11 to 0.62)		
Cycle 3 Day 1|	-0.87 (-1.64 to -0.10)	-0.30 (-1.15 to 0.56)		
Cycle 4 Day 1|	-0.02 (-0.82 to 0.78)	-1.06 (-1.95 to -0.18)		
Cycle 5 Day 1|	0.09 (-0.74 to 0.92)	0.17 (-0.72 to 1.05)		
Cycle 6 Day 1|	0.30 (-0.55 to 1.15)	-0.28 (-1.21 to 0.66)		
Cycle 8 Day 1|	-1.08 (-1.94 to -0.22)	-0.16 (-1.10 to 0.77)		
Cycle 10 Day 1|	0.25 (-0.67 to 1.16)	-0.00 (-1.02 to 1.02)		
Cycle 12 Day 1|	0.60 (-0.43 to 1.64)	0.42 (-0.64 to 1.49)		
Cycle 14 Day 1|	-1.80 (-3.31 to -0.30)	0.35 (-1.00 to 1.71)		
Cycle 16 Day 1|	0.40 (-2.09 to 2.88)	-0.22 (-1.75 to 1.30)		
Cycle 18 Day 1|	-0.39 (-3.85 to 3.07)	-0.33 (-1.97 to 1.32)		
Cycle 20 Day 1|	99999 (99999 to 99999)	-0.70 (-2.52 to 1.11)		
Cycle 22 Day 1|	99999 (99999 to 99999)	0.37 (-1.70 to 2.43)		
Cycle 24 Day 1|	99999 (99999 to 99999)	99999 (99999 to 99999)		
End of treatment|	-0.19 (-1.71 to 1.34)	0.11 (-1.72 to 1.95)		

Notes:

[210] - Not all subjects had evaluable data at each time point.

[211] - Not all subjects had evaluable data at each time point.

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

3 years

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 subject and as non-serious in another subject, or one subject may have experienced both a serious and non-serious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

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 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. 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 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	75 mg QD (Phase 1)

Reporting group description:

PF-06463922 75 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	100 mg QD (Phase 1)

Reporting group description:

PF-06463922 100 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	150 mg QD (Phase 1)

Reporting group description:

PF-06463922 150 mg was orally given 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. 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 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	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 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	EXP-1 (Phase 2)

Reporting group description:

Treatment-naïve subjects with advanced ALK-positive NSCLC with or without asymptomatic central nervous system (CNS) metastases were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for subjects 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	100 mg BID (Phase 1)

Reporting group description:

PF-06463922 100 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	EXP-2 (Phase 2)

Reporting group description:

Subjects with advanced ALK-positive NSCLC with or without asymptomatic CNS metastases relapsing after only crizotinib therapy were given PF-06463922 100 mg orally once daily (QD) on Day -7 (only for subjects 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:

Subjects 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 subjects 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 once daily (QD) on Day -7 (only for subjects 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:

subjects 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 subjects 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:

Subjects 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 subjects 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:

Subjects 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 subjects 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 twice daily (BID) 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.

Serious adverse events	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 mg QD (Phase 1)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events			
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	0 / 0	0 / 0	0 / 0

treatment / all			
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
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
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
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
Fatigue			
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
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
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
Psychiatric disorders			
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
Mental status changes			
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
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
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	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
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
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
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
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
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
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
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
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
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
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
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
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
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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	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
Hypoxia			
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
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	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
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
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
Asthma			
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
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
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
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
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
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
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
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
Nervous system disorders			
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
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
Presyncope			
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
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%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 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
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
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
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
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
Eye disorders			
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
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
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
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
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
Crohn's 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
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
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
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
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
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
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
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
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
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
Lung 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
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
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
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
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

Serious adverse events	75 mg QD (Phase 1)	100 mg QD (Phase 1)	150 mg QD (Phase 1)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 12 (33.33%)	9 / 17 (52.94%)	3 / 3 (100.00%)
number of deaths (all causes)	1	3	3
number of deaths resulting from adverse events			
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (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
Embolism venous			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (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
Aortic dissection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (8.33%)	3 / 17 (17.65%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 3	0 / 1
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (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
Asthenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (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
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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			
Confusional state			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (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
Mental status changes			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	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
Hallucination			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural			

complications			
Subdural haematoma			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	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
Fall			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	1 / 17 (5.88%)	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

Hypoxia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (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 / 1
Pleural effusion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	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
Haemoptysis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	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 pulmonary oedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)

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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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			
Haemorrhage intracranial			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (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
Headache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (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
Brain compression			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences causally related to	0 / 0	0 / 0	0 / 0

treatment / all			
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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			
Cataract			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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	1 / 12 (8.33%)	0 / 17 (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	1 / 12 (8.33%)	0 / 17 (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
Abdominal pain upper			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	1 / 17 (5.88%)	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
Jaundice			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)

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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (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
Hyperuricaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (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
Hypertriglyceridaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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	1 / 12 (8.33%)	0 / 17 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (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
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (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
Respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	1 / 17 (5.88%)	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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	1 / 17 (5.88%)	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
Diverticulitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
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)	35 mg BID (Phase 1)	75 mg BID (Phase 1)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	2 / 3 (66.67%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Vascular disorders			
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
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	0 / 0	0 / 0	0 / 0

treatment / all			
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
General disorders and administration site conditions			
Disease progression			
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 / 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
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
Fatigue			
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
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
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
Psychiatric disorders			
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
Mental status changes			
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	0 / 0	0 / 0	0 / 0

treatment / all			
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
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	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
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
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
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
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
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
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
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%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)
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
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
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
Cardiac disorders			
Cardiac arrest			
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
Pericardial effusion			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
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
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
Supraventricular tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to	0 / 0	0 / 0	0 / 0

treatment / all			
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%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
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
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 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
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
Asthma			
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
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
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
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
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
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
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
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
Nervous system disorders			
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
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
Presyncope			
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
Cerebrovascular 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
Seizure			
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
Brain 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
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
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
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
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
Eye disorders			
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
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
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
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
Gastrointestinal disorders			
Abdominal pain			
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
Crohn's 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
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
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
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
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
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
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
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
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
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
Lung 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	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
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	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
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
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

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
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
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

Serious adverse events	EXP-1 (Phase 2)	100 mg BID (Phase 1)	EXP-2 (Phase 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 30 (26.67%)	2 / 4 (50.00%)	5 / 27 (18.52%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	0 / 27 (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

Asthenia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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			
Confusional state			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			

subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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	1 / 30 (3.33%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood cholesterol increased			

subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (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
Atrial fibrillation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (3.33%)	1 / 4 (25.00%)	0 / 27 (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
Hypoxia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (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
Interstitial lung disease			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)

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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory failure			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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			
Haemorrhage intracranial			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (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
Presyncope			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences causally related to	0 / 0	0 / 0	0 / 0

treatment / all			
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (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 compression			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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			
Cataract			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (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
Blepharitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)

occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (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
Ileus			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (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
Gastritis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (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
Nausea			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (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
Hypercalcaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)

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	1 / 30 (3.33%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (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
Bronchitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
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	EXP-3 (Phase 2)	EXP-4 (Phase 2)	EXP-5 (Phase 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 60 (30.00%)	24 / 65 (36.92%)	18 / 46 (39.13%)
number of deaths (all causes)	4	8	4
number of deaths resulting from adverse events			
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 60 (0.00%)	1 / 65 (1.54%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1

deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Embolism venous			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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
Superior vena cava syndrome			
subjects affected / exposed	0 / 60 (0.00%)	2 / 65 (3.08%)	0 / 46 (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 / 60 (0.00%)	0 / 65 (0.00%)	2 / 46 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	6 / 60 (10.00%)	6 / 65 (9.23%)	5 / 46 (10.87%)
occurrences causally related to treatment / all	0 / 6	0 / 6	0 / 5

deaths causally related to treatment / all	0 / 2	0 / 4	0 / 1
Pyrexia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 65 (1.54%)	0 / 46 (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
Asthenia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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	1 / 60 (1.67%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 60 (0.00%)	1 / 65 (1.54%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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
Femoral neck fracture			
subjects affected / exposed	1 / 60 (1.67%)	1 / 65 (1.54%)	0 / 46 (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
Hip fracture			
subjects affected / exposed	0 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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

Humerus fracture			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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
Lipase increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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 cholesterol increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (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
Ejection fraction decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	1 / 65 (1.54%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 60 (0.00%)	2 / 65 (3.08%)	0 / 46 (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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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 / 60 (1.67%)	3 / 65 (4.62%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Hypoxia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 60 (1.67%)	1 / 65 (1.54%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (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

Acute respiratory failure			
subjects affected / exposed	1 / 60 (1.67%)	1 / 65 (1.54%)	0 / 46 (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
Asthma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (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
Dyspnoea exertional			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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
Pleuritic pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			

subjects affected / exposed	0 / 60 (0.00%)	2 / 65 (3.08%)	0 / 46 (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
Pulmonary congestion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 60 (0.00%)	2 / 65 (3.08%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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	1 / 60 (1.67%)	1 / 65 (1.54%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 60 (1.67%)	1 / 65 (1.54%)	0 / 46 (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
Presyncope			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)

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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 compression			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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
Partial seizures			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (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
Vagus nerve disorder			
subjects affected / exposed	0 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall haematoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glossitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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 / 60 (0.00%)	2 / 65 (3.08%)	0 / 46 (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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0

deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatomyositis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	1 / 65 (1.54%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	1 / 46 (2.17%)

occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia			
subjects affected / exposed	0 / 60 (0.00%)	3 / 65 (4.62%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
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 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences causally related to	0 / 0	0 / 0	0 / 0

treatment / all			
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung abscess			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (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
Sepsis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (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
Upper respiratory tract infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (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 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (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	EXP-6 (Phase 2)	Japan Lead-In Cohort (LIC)	
Total subjects affected by serious adverse events			

subjects affected / exposed	16 / 47 (34.04%)	0 / 3 (0.00%)	
number of deaths (all causes)	5	0	
number of deaths resulting from adverse events			
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism venous			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic dissection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	5 / 47 (10.64%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 4	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to	0 / 0	0 / 0	

treatment / all			
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	

occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood cholesterol increased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	

occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	

occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain compression			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain oedema			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ischaemic stroke			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar stroke			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vagus nerve disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blepharitis			

subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall haematoma			

subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric volvulus			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glossitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biloma			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	

occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatomyositis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperuricaemia			

subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	

occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	10 mg QD (Phase 1)	25 mg QD (Phase 1)	50 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%)
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Haematoma			
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
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Shock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
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
Immune system disorders			
Hypersensitivity			
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	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	2
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Gait disturbance			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	2	2
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Oedema peripheral			
subjects affected / exposed	3 / 3 (100.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	3	1	1
Pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)

occurrences (all)	1	0	0
Pyrexia			
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	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Catheter site extravasation			
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
Chills			
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	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Performance status decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Swelling			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Affect lability			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
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
Agitation			
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
Bradyphrenia			
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
Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hallucination			
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nightmare			
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
Sleep 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
Mood swings			
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
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
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
Incision site pain			
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
Laceration			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
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
Procedural pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Amylase increased			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
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
Blood triglycerides increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Electrocardiogram QT prolonged			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)

occurrences (all)	2	0	0
Lipase increased			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Blood creatinine increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
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
Lipids increased			
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
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
Electrocardiogram PR prolongation			
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	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pericardial effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
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	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
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	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
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
Pleuritic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive cough			
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	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 oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
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
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	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Febrile neutropenia			
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	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
Leukocytosis			
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
Thrombocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Cognitive disorder			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Disturbance in attention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Memory impairment			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Neuropathy peripheral			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Slow speech			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Ataxia			
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
Carpal tunnel syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
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
Formication			
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

Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Mental impairment			
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
Nervous system disorder			
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
Neurotoxicity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Partial seizures			
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seizure			
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
Speech disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Visual impairment			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Asthenopia			
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
Conjunctival oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Photophobia			
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
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
Eye irritation			
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	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Ear discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypoacusis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vertigo positional			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Dyspepsia			
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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
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
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Crohn's disease			
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Faeces discoloured			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Odynophagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatocellular injury			
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
Chronic kidney disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	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
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
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	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
Swelling face			
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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

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	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
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%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
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
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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	1	6	2
Hyperglycaemia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Hyperlipidaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	9	4
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Hypophosphataemia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Dehydration			
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
Hypercalcaemia			
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
Hypocholesterolaemia			
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
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
Lung infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
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	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

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
Enterococcal bacteraemia			
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
Helicobacter infection			
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
Laryngitis			
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
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

Non-serious adverse events	75 mg QD (Phase 1)	100 mg QD (Phase 1)	150 mg QD (Phase 1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	17 / 17 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 12 (16.67%)	1 / 17 (5.88%)	1 / 3 (33.33%)
occurrences (all)	3	1	1
Deep vein thrombosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)

occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhage			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Shock			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tumour pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 12 (25.00%)	3 / 17 (17.65%)	0 / 3 (0.00%)
occurrences (all)	7	3	0
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Face oedema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)

occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	4 / 12 (33.33%)	4 / 17 (23.53%)	2 / 3 (66.67%)
occurrences (all)	4	5	4
Gait disturbance			
subjects affected / exposed	1 / 12 (8.33%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Mucosal inflammation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	2 / 12 (16.67%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Oedema peripheral			
subjects affected / exposed	3 / 12 (25.00%)	9 / 17 (52.94%)	3 / 3 (100.00%)
occurrences (all)	4	16	7
Pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	2 / 12 (16.67%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	3 / 17 (17.65%)	1 / 3 (33.33%)
occurrences (all)	0	3	1
Axillary pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site extravasation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Chest discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)

occurrences (all)	1	0	0
Disease progression			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Generalised oedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Performance status decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Swelling			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Affect lability			
subjects affected / exposed	3 / 12 (25.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Anxiety			
subjects affected / exposed	2 / 12 (16.67%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Insomnia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Irritability			
subjects affected / exposed	0 / 12 (0.00%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Abnormal dreams			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Agitation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Attention deficit/hyperactivity			

disorder			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Bradyphrenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	0 / 12 (0.00%)	2 / 17 (11.76%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Depressed mood			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hallucination			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Mental status changes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nightmare			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reading disorder			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Sleep disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mood swings			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hallucination, auditory			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vaginal haemorrhage			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Incision site pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toxicity to various agents			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	2 / 12 (16.67%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	4	3	0
Amylase increased			
subjects affected / exposed	1 / 12 (8.33%)	4 / 17 (23.53%)	0 / 3 (0.00%)
occurrences (all)	3	11	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 12 (16.67%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	5	3	0
Blood cholesterol increased			
subjects affected / exposed	6 / 12 (50.00%)	3 / 17 (17.65%)	1 / 3 (33.33%)
occurrences (all)	9	8	1
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Blood triglycerides increased			
subjects affected / exposed	2 / 12 (16.67%)	3 / 17 (17.65%)	1 / 3 (33.33%)
occurrences (all)	3	8	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	2 / 12 (16.67%)	5 / 17 (29.41%)	0 / 3 (0.00%)
occurrences (all)	5	20	0
Weight increased			
subjects affected / exposed	3 / 12 (25.00%)	3 / 17 (17.65%)	1 / 3 (33.33%)
occurrences (all)	7	5	1
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 12 (8.33%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Blood creatinine increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	2 / 3 (66.67%)
occurrences (all)	3	0	2
Blood phosphorus decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)

occurrences (all)	0	0	0
Candida test positive			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Ejection fraction decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Glucose urine present			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
International normalised ratio increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Lipids increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Liver function test increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Transaminases increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Atrial fibrillation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ventricular dysfunction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 12 (8.33%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dysphonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 12 (0.00%)	3 / 17 (17.65%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Dyspnoea exertional			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Haemoptysis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)

occurrences (all)	0	0	0
Acute respiratory failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Bronchitis chronic			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Laryngeal inflammation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pleuritic pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Productive cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pulmonary embolism			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)

occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 12 (16.67%)	6 / 17 (35.29%)	3 / 3 (100.00%)
occurrences (all)	3	14	5
Thrombocytopenia			
subjects affected / exposed	1 / 12 (8.33%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Febrile neutropenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhagic diathesis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Leukocytosis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Neutropenia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Thrombocytosis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Aphasia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	2 / 12 (16.67%)	0 / 17 (0.00%)	2 / 3 (66.67%)
occurrences (all)	2	0	2
Disturbance in attention			
subjects affected / exposed	2 / 12 (16.67%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Dizziness			
subjects affected / exposed	1 / 12 (8.33%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Dysgeusia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Headache			
subjects affected / exposed	3 / 12 (25.00%)	1 / 17 (5.88%)	1 / 3 (33.33%)
occurrences (all)	3	2	1
Memory impairment			
subjects affected / exposed	1 / 12 (8.33%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Neuropathy peripheral			
subjects affected / exposed	5 / 12 (41.67%)	2 / 17 (11.76%)	1 / 3 (33.33%)
occurrences (all)	7	2	3
Paraesthesia			
subjects affected / exposed	1 / 12 (8.33%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	4	2	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 12 (8.33%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Presyncope			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Slow speech			
subjects affected / exposed	1 / 12 (8.33%)	3 / 17 (17.65%)	0 / 3 (0.00%)
occurrences (all)	1	4	0

Ataxia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dysaesthesia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dysarthria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Formication			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hemiparesis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	3 / 12 (25.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
Mental impairment			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nervous system disorder			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neuralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Neurotoxicity			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Partial seizures			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Peroneal nerve palsy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Seizure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sensory disturbance			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Speech disorder			
subjects affected / exposed	2 / 12 (16.67%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Tremor			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 12 (0.00%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Visual impairment			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	3
Asthenopia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Astigmatism			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)

occurrences (all)	0	1	0
Conjunctival oedema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Diplopia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Presbyopia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Retinal vein occlusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	1 / 12 (8.33%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Eye irritation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	3 / 12 (25.00%)	3 / 17 (17.65%)	1 / 3 (33.33%)
occurrences (all)	4	3	1
Ear discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			

subjects affected / exposed	1 / 12 (8.33%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Vertigo			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vertigo positional			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	2 / 12 (16.67%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Constipation			
subjects affected / exposed	3 / 12 (25.00%)	3 / 17 (17.65%)	0 / 3 (0.00%)
occurrences (all)	3	4	0
Diarrhoea			
subjects affected / exposed	3 / 12 (25.00%)	3 / 17 (17.65%)	1 / 3 (33.33%)
occurrences (all)	6	4	1
Dyspepsia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dysphagia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 12 (8.33%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Nausea			
subjects affected / exposed	2 / 12 (16.67%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)	3 / 17 (17.65%)	0 / 3 (0.00%)
occurrences (all)	1	4	0

Abdominal discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Crohn's disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Faeces discoloured			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Intestinal obstruction			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Swollen tongue			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 12 (0.00%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Chronic kidney disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hydronephrosis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Micturition urgency			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Urinary incontinence			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Pruritus			

subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	3 / 12 (25.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	4	1	0
Dermatitis acneiform			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dermatomyositis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Night sweats			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Rash pruritic			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rosacea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin lesion			

subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Swelling face			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 12 (16.67%)	4 / 17 (23.53%)	0 / 3 (0.00%)
occurrences (all)	3	5	0
Back pain			
subjects affected / exposed	2 / 12 (16.67%)	6 / 17 (35.29%)	0 / 3 (0.00%)
occurrences (all)	2	7	0
Bone pain			
subjects affected / exposed	1 / 12 (8.33%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Joint swelling			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 12 (0.00%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Myalgia			
subjects affected / exposed	1 / 12 (8.33%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	1	2	0

Pain in extremity			
subjects affected / exposed	1 / 12 (8.33%)	1 / 17 (5.88%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Arthritis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Bone lesion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 12 (0.00%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Limb discomfort			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	1 / 12 (8.33%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Osteoarthritis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Osteoporosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 12 (0.00%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Plantar fasciitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Torticollis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Musculoskeletal stiffness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hyperparathyroidism			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	7 / 12 (58.33%)	12 / 17 (70.59%)	2 / 3 (66.67%)
occurrences (all)	25	38	4
Hyperglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Hyperlipidaemia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Hypertriglyceridaemia			
subjects affected / exposed	4 / 12 (33.33%)	6 / 17 (35.29%)	1 / 3 (33.33%)
occurrences (all)	9	27	1
Hyperuricaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	2 / 3 (66.67%)
occurrences (all)	0	1	7
Hypomagnesaemia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	3 / 3 (100.00%)
occurrences (all)	0	0	5
Hypophosphataemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4
Dehydration			
subjects affected / exposed	1 / 12 (8.33%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Fluid retention			
subjects affected / exposed	2 / 12 (16.67%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4
Hypocholesterolaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	2 / 17 (11.76%)	1 / 3 (33.33%)
occurrences (all)	0	3	1
Influenza			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lung infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Sinusitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 12 (16.67%)	4 / 17 (23.53%)	1 / 3 (33.33%)
occurrences (all)	6	6	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Bacterial infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Candida infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Chronic sinusitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Enteritis infectious			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Enterococcal bacteraemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Helicobacter infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Herpes virus infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Periodontitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 17 (5.88%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Soft tissue infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Urinary tract infection			
subjects affected / exposed	1 / 12 (8.33%)	2 / 17 (11.76%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Viral rhinitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 12 (0.00%)	0 / 17 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	200 mg QD (Phase 1)	35 mg BID (Phase 1)	75 mg BID (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%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematoma			
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
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypotension			
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%)	1 / 3 (33.33%)	0 / 3 (0.00%)

occurrences (all)	0	1	0

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
Immune system disorders			
Hypersensitivity			
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Gait disturbance			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Oedema			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Oedema peripheral			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	3
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Axillary pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	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
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Chills			
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	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Performance status decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Swelling			

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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Abnormal dreams			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	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
Bradyphrenia			
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%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Depressed mood			
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

Mental status changes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nightmare			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Reading disorder			
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%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mood swings			
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
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
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

Incision site pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Joint dislocation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laceration			
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
Limb injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	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
Procedural pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Amylase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
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%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood triglycerides increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Weight increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	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%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	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
Lipids increased			
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
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
Electrocardiogram PR prolongation			
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	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	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%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dysphonia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	0	3	3
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Haemoptysis			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	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	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	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
Pleuritic pain			
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
Pulmonary embolism			
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 oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rales			
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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	1	1	4
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Febrile neutropenia			
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%)	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
Leukocytosis			
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
Thrombocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Aphasia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Cognitive disorder			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Disturbance in attention			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)

occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Memory impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
Paraesthesia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Peripheral sensory neuropathy			
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%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Slow speech			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ataxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Balance disorder			
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%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dysaesthesia			
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%)	0 / 3 (0.00%)	1 / 3 (33.33%)

occurrences (all)	0	0	1
Formication			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hemiparesis			
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%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Mental impairment			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorder			
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%)	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
Partial seizures			
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%)	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
Seizure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)

occurrences (all)	0	0	0
Sensory disturbance			
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	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Visual impairment			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Asthenopia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Astigmatism			
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
Diplopia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Photopsia			

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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Eye irritation			
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	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%)	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
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vertigo positional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)

occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Dyspepsia			
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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Crohn's disease			
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%)	0 / 3 (0.00%)

occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	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%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatocellular injury			
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
Chronic kidney disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Micturition urgency			
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%)	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
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Dry skin			
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
Pruritus			
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%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash erythematous			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	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
Swelling face			
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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1

Back pain			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
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%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
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	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	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%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Arthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	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%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Musculoskeletal stiffness			
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%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)

occurrences (all)	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 (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	3 / 3 (100.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	18	1	5
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperlipidaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	10	0	2
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	11	1	0
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Dehydration			
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%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypocholesterolaemia			
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
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	3
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
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	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)

occurrences (all)	2	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%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
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
Enterococcal bacteraemia			
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
Helicobacter infection			
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
Laryngitis			
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
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	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	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

Non-serious adverse events	EXP-1 (Phase 2)	100 mg BID (Phase 1)	EXP-2 (Phase 2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 30 (100.00%)	4 / 4 (100.00%)	27 / 27 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	2	0	1
Deep vein thrombosis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Haematoma			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Haemorrhage			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Shock			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			

Hypersensitivity			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	2 / 27 (7.41%)
occurrences (all)	3	0	3
Chest pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	2
Face oedema			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	8 / 30 (26.67%)	3 / 4 (75.00%)	4 / 27 (14.81%)
occurrences (all)	11	5	7
Gait disturbance			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	3	0	0
Oedema			
subjects affected / exposed	4 / 30 (13.33%)	1 / 4 (25.00%)	1 / 27 (3.70%)
occurrences (all)	6	1	6
Oedema peripheral			
subjects affected / exposed	12 / 30 (40.00%)	3 / 4 (75.00%)	12 / 27 (44.44%)
occurrences (all)	17	7	18
Pain			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Peripheral swelling			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Pyrexia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	1 / 27 (3.70%)

occurrences (all)	4	0	2
Axillary pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Catheter site extravasation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Disease progression			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Generalised oedema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Performance status decreased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Swelling			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Affect lability			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	2 / 27 (7.41%)
occurrences (all)	0	1	2
Insomnia			

subjects affected / exposed	4 / 30 (13.33%)	0 / 4 (0.00%)	3 / 27 (11.11%)
occurrences (all)	5	0	3
Irritability			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	3	0	1
Abnormal dreams			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Bradyphrenia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Mental status changes			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nightmare			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Reading disorder			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Sleep disorder			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	5
Mood swings			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	2	0	1
Hallucination, auditory			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Incision site pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			

subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Toxicity to various agents			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 30 (16.67%)	1 / 4 (25.00%)	1 / 27 (3.70%)
occurrences (all)	6	5	1
Amylase increased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 30 (23.33%)	1 / 4 (25.00%)	1 / 27 (3.70%)
occurrences (all)	9	7	1
Blood cholesterol increased			
subjects affected / exposed	13 / 30 (43.33%)	1 / 4 (25.00%)	13 / 27 (48.15%)
occurrences (all)	41	3	55
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	3	0	1
Blood triglycerides increased			
subjects affected / exposed	2 / 30 (6.67%)	1 / 4 (25.00%)	2 / 27 (7.41%)
occurrences (all)	2	6	4
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	1 / 27 (3.70%)
occurrences (all)	0	1	2
Lipase increased			
subjects affected / exposed	3 / 30 (10.00%)	1 / 4 (25.00%)	4 / 27 (14.81%)

occurrences (all)	5	2	6
Weight increased			
subjects affected / exposed	4 / 30 (13.33%)	2 / 4 (50.00%)	4 / 27 (14.81%)
occurrences (all)	11	3	6
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Candida test positive			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 30 (0.00%)	2 / 4 (50.00%)	0 / 27 (0.00%)
occurrences (all)	0	12	0
Glucose urine present			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Lipids increased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Liver function test increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			

subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Atrial fibrillation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Ventricular dysfunction			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 30 (30.00%)	2 / 4 (50.00%)	3 / 27 (11.11%)
occurrences (all)	13	2	5
Dysphonia			
subjects affected / exposed	1 / 30 (3.33%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	1	1	0
Dyspnoea			
subjects affected / exposed	7 / 30 (23.33%)	2 / 4 (50.00%)	3 / 27 (11.11%)
occurrences (all)	8	5	3
Dyspnoea exertional			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Epistaxis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	2 / 27 (7.41%)

occurrences (all)	0	0	2
Haemoptysis			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	3	0	0
Hypoxia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Acute respiratory failure			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Bronchitis chronic			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Laryngeal inflammation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Pleuritic pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)

occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Pulmonary oedema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 30 (16.67%)	2 / 4 (50.00%)	1 / 27 (3.70%)
occurrences (all)	9	2	1
Thrombocytopenia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Febrile neutropenia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Haemorrhagic diathesis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			

subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Thrombocytosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Cognitive disorder			
subjects affected / exposed	1 / 30 (3.33%)	1 / 4 (25.00%)	1 / 27 (3.70%)
occurrences (all)	1	1	3
Disturbance in attention			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	6 / 30 (20.00%)	1 / 4 (25.00%)	4 / 27 (14.81%)
occurrences (all)	12	1	12
Dysgeusia			
subjects affected / exposed	2 / 30 (6.67%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	2	1	0
Headache			
subjects affected / exposed	5 / 30 (16.67%)	2 / 4 (50.00%)	6 / 27 (22.22%)
occurrences (all)	8	3	7
Memory impairment			
subjects affected / exposed	2 / 30 (6.67%)	1 / 4 (25.00%)	3 / 27 (11.11%)
occurrences (all)	2	2	3
Neuropathy peripheral			
subjects affected / exposed	5 / 30 (16.67%)	0 / 4 (0.00%)	3 / 27 (11.11%)
occurrences (all)	6	0	4

Paraesthesia			
subjects affected / exposed	3 / 30 (10.00%)	2 / 4 (50.00%)	4 / 27 (14.81%)
occurrences (all)	5	4	7
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	3 / 27 (11.11%)
occurrences (all)	3	0	4
Presyncope			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Slow speech			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Formication			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hemiparesis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Mental impairment			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nervous system disorder			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Neurotoxicity			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Partial seizures			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Peroneal nerve palsy			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Sensory disturbance			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Speech disorder			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Eye disorders			
Vision blurred			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	2 / 27 (7.41%)
occurrences (all)	3	0	2
Visual impairment			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Asthenopia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Astigmatism			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Conjunctival oedema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Presbyopia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Retinal vein occlusion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)

occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	2 / 30 (6.67%)	1 / 4 (25.00%)	2 / 27 (7.41%)
occurrences (all)	2	1	8
Ear discomfort			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Vertigo positional			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	2	0	1
Abdominal pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	1 / 27 (3.70%)
occurrences (all)	0	3	1
Constipation			
subjects affected / exposed	8 / 30 (26.67%)	0 / 4 (0.00%)	5 / 27 (18.52%)
occurrences (all)	9	0	6
Diarrhoea			
subjects affected / exposed	7 / 30 (23.33%)	3 / 4 (75.00%)	4 / 27 (14.81%)
occurrences (all)	13	5	6
Dyspepsia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1

Dysphagia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	4 / 30 (13.33%)	2 / 4 (50.00%)	3 / 27 (11.11%)
occurrences (all)	4	4	4
Vomiting			
subjects affected / exposed	4 / 30 (13.33%)	2 / 4 (50.00%)	0 / 27 (0.00%)
occurrences (all)	7	6	0
Abdominal discomfort			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 30 (0.00%)	2 / 4 (50.00%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Ascites			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Crohn's disease			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Intestinal obstruction			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Swollen tongue			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Stomatitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	3
Toothache			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Chronic kidney disease			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)

occurrences (all)	0	1	0

Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 30 (6.67%)	1 / 4 (25.00%)	2 / 27 (7.41%)
occurrences (all)	2	1	2
Dry skin			
subjects affected / exposed	3 / 30 (10.00%)	1 / 4 (25.00%)	1 / 27 (3.70%)
occurrences (all)	3	1	1
Hyperhidrosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	5 / 30 (16.67%)	0 / 4 (0.00%)	3 / 27 (11.11%)
occurrences (all)	9	0	4
Dermatitis acneiform			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Dermatomyositis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Rash maculo-papular			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Rosacea			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 30 (16.67%)	1 / 4 (25.00%)	4 / 27 (14.81%)
occurrences (all)	9	1	4
Back pain			
subjects affected / exposed	2 / 30 (6.67%)	2 / 4 (50.00%)	5 / 27 (18.52%)
occurrences (all)	2	2	6
Bone pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Joint swelling			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	3
Muscle spasms			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)

occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	4 / 30 (13.33%)	0 / 4 (0.00%)	2 / 27 (7.41%)
occurrences (all)	5	0	3
Myalgia			
subjects affected / exposed	3 / 30 (10.00%)	1 / 4 (25.00%)	2 / 27 (7.41%)
occurrences (all)	3	1	2
Pain in extremity			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	8 / 27 (29.63%)
occurrences (all)	4	0	10
Arthritis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Bone lesion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)

occurrences (all)	0	0	0
Osteoporosis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Pain in jaw			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Torticollis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hyperparathyroidism			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 30 (13.33%)	2 / 4 (50.00%)	1 / 27 (3.70%)
occurrences (all)	4	3	1
Hypercholesterolaemia			
subjects affected / exposed	14 / 30 (46.67%)	1 / 4 (25.00%)	11 / 27 (40.74%)
occurrences (all)	61	5	39
Hyperglycaemia			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	7	0	1

Hyperlipidaemia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Hypertriglyceridaemia			
subjects affected / exposed	20 / 30 (66.67%)	1 / 4 (25.00%)	12 / 27 (44.44%)
occurrences (all)	106	3	34
Hyperuricaemia			
subjects affected / exposed	2 / 30 (6.67%)	1 / 4 (25.00%)	1 / 27 (3.70%)
occurrences (all)	2	1	1
Hypokalaemia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	4	0	0
Hypomagnesaemia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	3	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Dehydration			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hypocholesterolaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	5	0	0

Increased appetite			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 30 (3.33%)	1 / 4 (25.00%)	2 / 27 (7.41%)
occurrences (all)	1	1	2
Influenza			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	2	0	1
Lung infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Pneumonia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Rhinitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	5 / 30 (16.67%)	0 / 4 (0.00%)	2 / 27 (7.41%)
occurrences (all)	6	0	2
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	3 / 27 (11.11%)
occurrences (all)	1	0	4
Bacterial infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)

occurrences (all)	0	0	0
Chronic sinusitis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Enteritis infectious			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Enterococcal bacteraemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)

occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Soft tissue infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Viral rhinitis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	EXP-3 (Phase 2)	EXP-4 (Phase 2)	EXP-5 (Phase 2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	59 / 60 (98.33%)	65 / 65 (100.00%)	45 / 46 (97.83%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 60 (3.33%)	8 / 65 (12.31%)	4 / 46 (8.70%)
occurrences (all)	6	17	11
Deep vein thrombosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0

Haematoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Shock			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 60 (13.33%)	6 / 65 (9.23%)	5 / 46 (10.87%)
occurrences (all)	10	12	7
Chest pain			
subjects affected / exposed	2 / 60 (3.33%)	6 / 65 (9.23%)	5 / 46 (10.87%)
occurrences (all)	2	6	6
Face oedema			
subjects affected / exposed	2 / 60 (3.33%)	1 / 65 (1.54%)	1 / 46 (2.17%)
occurrences (all)	2	1	1

Fatigue			
subjects affected / exposed	3 / 60 (5.00%)	11 / 65 (16.92%)	4 / 46 (8.70%)
occurrences (all)	4	22	4
Gait disturbance			
subjects affected / exposed	0 / 60 (0.00%)	5 / 65 (7.69%)	3 / 46 (6.52%)
occurrences (all)	0	5	5
Mucosal inflammation			
subjects affected / exposed	1 / 60 (1.67%)	2 / 65 (3.08%)	1 / 46 (2.17%)
occurrences (all)	1	2	1
Oedema			
subjects affected / exposed	4 / 60 (6.67%)	6 / 65 (9.23%)	4 / 46 (8.70%)
occurrences (all)	4	7	4
Oedema peripheral			
subjects affected / exposed	29 / 60 (48.33%)	21 / 65 (32.31%)	15 / 46 (32.61%)
occurrences (all)	43	37	24
Pain			
subjects affected / exposed	1 / 60 (1.67%)	4 / 65 (6.15%)	2 / 46 (4.35%)
occurrences (all)	1	8	2
Peripheral swelling			
subjects affected / exposed	1 / 60 (1.67%)	7 / 65 (10.77%)	4 / 46 (8.70%)
occurrences (all)	1	12	5
Pyrexia			
subjects affected / exposed	5 / 60 (8.33%)	7 / 65 (10.77%)	1 / 46 (2.17%)
occurrences (all)	6	7	1
Axillary pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Catheter site extravasation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0

Disease progression			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Generalised oedema			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Performance status decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Swelling			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Affect lability			
subjects affected / exposed	2 / 60 (3.33%)	2 / 65 (3.08%)	0 / 46 (0.00%)
occurrences (all)	4	3	0
Anxiety			
subjects affected / exposed	1 / 60 (1.67%)	7 / 65 (10.77%)	1 / 46 (2.17%)
occurrences (all)	1	7	1
Insomnia			
subjects affected / exposed	5 / 60 (8.33%)	3 / 65 (4.62%)	3 / 46 (6.52%)
occurrences (all)	6	3	3
Irritability			
subjects affected / exposed	3 / 60 (5.00%)	2 / 65 (3.08%)	6 / 46 (13.04%)
occurrences (all)	4	2	6
Abnormal dreams			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)

occurrences (all)	0	0	0
Bradyphrenia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Mental status changes			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Nightmare			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Reading disorder			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	6 / 60 (10.00%)	1 / 65 (1.54%)	1 / 46 (2.17%)
occurrences (all)	7	1	1
Mood swings			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hallucination, auditory			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

Menstruation irregular			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 60 (0.00%)	5 / 65 (7.69%)	2 / 46 (4.35%)
occurrences (all)	0	11	5
Contusion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Incision site pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Toxicity to various agents			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 65 (1.54%)	0 / 46 (0.00%)
occurrences (all)	0	1	0
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	6 / 60 (10.00%)	5 / 65 (7.69%)	5 / 46 (10.87%)
occurrences (all)	12	13	7
Amylase increased			
subjects affected / exposed	4 / 60 (6.67%)	7 / 65 (10.77%)	2 / 46 (4.35%)
occurrences (all)	5	17	3
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 60 (11.67%)	7 / 65 (10.77%)	6 / 46 (13.04%)
occurrences (all)	11	9	8
Blood cholesterol increased			
subjects affected / exposed	18 / 60 (30.00%)	17 / 65 (26.15%)	16 / 46 (34.78%)
occurrences (all)	67	44	42
Blood creatine phosphokinase increased			
subjects affected / exposed	5 / 60 (8.33%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	10	0	0
Blood triglycerides increased			
subjects affected / exposed	4 / 60 (6.67%)	3 / 65 (4.62%)	3 / 46 (6.52%)
occurrences (all)	8	3	4
Electrocardiogram QT prolonged			
subjects affected / exposed	3 / 60 (5.00%)	4 / 65 (6.15%)	9 / 46 (19.57%)
occurrences (all)	7	4	10
Lipase increased			
subjects affected / exposed	1 / 60 (1.67%)	7 / 65 (10.77%)	5 / 46 (10.87%)
occurrences (all)	1	14	6
Weight increased			
subjects affected / exposed	11 / 60 (18.33%)	18 / 65 (27.69%)	10 / 46 (21.74%)
occurrences (all)	18	23	12
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)

occurrences (all)	0	0	0
Candida test positive			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Glucose urine present			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Lipids increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 60 (0.00%)	5 / 65 (7.69%)	2 / 46 (4.35%)
occurrences (all)	0	6	2

Atrial fibrillation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Ventricular dysfunction			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	3 / 46 (6.52%)
occurrences (all)	0	0	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 60 (11.67%)	11 / 65 (16.92%)	8 / 46 (17.39%)
occurrences (all)	10	14	12
Dysphonia			
subjects affected / exposed	4 / 60 (6.67%)	2 / 65 (3.08%)	2 / 46 (4.35%)
occurrences (all)	4	2	2
Dyspnoea			
subjects affected / exposed	14 / 60 (23.33%)	13 / 65 (20.00%)	9 / 46 (19.57%)
occurrences (all)	16	14	11
Dyspnoea exertional			
subjects affected / exposed	3 / 60 (5.00%)	6 / 65 (9.23%)	3 / 46 (6.52%)
occurrences (all)	6	8	5
Epistaxis			
subjects affected / exposed	3 / 60 (5.00%)	3 / 65 (4.62%)	0 / 46 (0.00%)
occurrences (all)	3	4	0
Haemoptysis			
subjects affected / exposed	2 / 60 (3.33%)	5 / 65 (7.69%)	1 / 46 (2.17%)
occurrences (all)	2	6	1
Hypoxia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 65 (1.54%)	5 / 46 (10.87%)
occurrences (all)	0	1	10
Pleural effusion			
subjects affected / exposed	0 / 60 (0.00%)	5 / 65 (7.69%)	1 / 46 (2.17%)
occurrences (all)	0	5	1
Wheezing			
subjects affected / exposed	1 / 60 (1.67%)	2 / 65 (3.08%)	3 / 46 (6.52%)

occurrences (all)	1	2	3
Acute respiratory failure			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Bronchitis chronic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Laryngeal inflammation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Pleuritic pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)

occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 60 (5.00%)	12 / 65 (18.46%)	7 / 46 (15.22%)
occurrences (all)	3	18	8
Thrombocytopenia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 65 (1.54%)	0 / 46 (0.00%)
occurrences (all)	1	1	0
Febrile neutropenia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Haemorrhagic diathesis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Thrombocytosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	6 / 60 (10.00%)	6 / 65 (9.23%)	2 / 46 (4.35%)
occurrences (all)	6	10	4

Aphasia			
subjects affected / exposed	0 / 60 (0.00%)	2 / 65 (3.08%)	2 / 46 (4.35%)
occurrences (all)	0	2	2
Cognitive disorder			
subjects affected / exposed	5 / 60 (8.33%)	6 / 65 (9.23%)	2 / 46 (4.35%)
occurrences (all)	5	7	2
Disturbance in attention			
subjects affected / exposed	1 / 60 (1.67%)	2 / 65 (3.08%)	1 / 46 (2.17%)
occurrences (all)	1	13	1
Dizziness			
subjects affected / exposed	5 / 60 (8.33%)	9 / 65 (13.85%)	7 / 46 (15.22%)
occurrences (all)	5	12	8
Dysgeusia			
subjects affected / exposed	1 / 60 (1.67%)	6 / 65 (9.23%)	2 / 46 (4.35%)
occurrences (all)	1	6	2
Headache			
subjects affected / exposed	8 / 60 (13.33%)	11 / 65 (16.92%)	10 / 46 (21.74%)
occurrences (all)	10	15	11
Memory impairment			
subjects affected / exposed	4 / 60 (6.67%)	6 / 65 (9.23%)	2 / 46 (4.35%)
occurrences (all)	5	12	2
Neuropathy peripheral			
subjects affected / exposed	6 / 60 (10.00%)	7 / 65 (10.77%)	5 / 46 (10.87%)
occurrences (all)	7	7	5
Paraesthesia			
subjects affected / exposed	11 / 60 (18.33%)	9 / 65 (13.85%)	5 / 46 (10.87%)
occurrences (all)	13	9	6
Peripheral sensory neuropathy			
subjects affected / exposed	7 / 60 (11.67%)	3 / 65 (4.62%)	4 / 46 (8.70%)
occurrences (all)	14	3	4
Presyncope			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	1	0	0
Slow speech			
subjects affected / exposed	5 / 60 (8.33%)	2 / 65 (3.08%)	0 / 46 (0.00%)
occurrences (all)	9	2	0

Ataxia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Formication			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hemiparesis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Mental impairment			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Nervous system disorder			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0

Neurotoxicity			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Partial seizures			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Peroneal nerve palsy			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Sensory disturbance			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Speech disorder			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 60 (0.00%)	3 / 65 (4.62%)	3 / 46 (6.52%)
occurrences (all)	0	3	3
Visual impairment			
subjects affected / exposed	1 / 60 (1.67%)	3 / 65 (4.62%)	3 / 46 (6.52%)
occurrences (all)	1	3	3
Asthenopia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Astigmatism			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)

occurrences (all)	0	0	0
Conjunctival oedema			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Presbyopia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Retinal vein occlusion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	3 / 60 (5.00%)	7 / 65 (10.77%)	4 / 46 (8.70%)
occurrences (all)	3	10	4
Ear discomfort			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			

subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Vertigo positional			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 60 (0.00%)	4 / 65 (6.15%)	3 / 46 (6.52%)
occurrences (all)	0	4	6
Abdominal pain			
subjects affected / exposed	2 / 60 (3.33%)	4 / 65 (6.15%)	3 / 46 (6.52%)
occurrences (all)	2	4	4
Constipation			
subjects affected / exposed	8 / 60 (13.33%)	8 / 65 (12.31%)	5 / 46 (10.87%)
occurrences (all)	10	8	5
Diarrhoea			
subjects affected / exposed	7 / 60 (11.67%)	16 / 65 (24.62%)	8 / 46 (17.39%)
occurrences (all)	14	22	9
Dyspepsia			
subjects affected / exposed	2 / 60 (3.33%)	5 / 65 (7.69%)	0 / 46 (0.00%)
occurrences (all)	2	5	0
Dysphagia			
subjects affected / exposed	3 / 60 (5.00%)	4 / 65 (6.15%)	2 / 46 (4.35%)
occurrences (all)	3	4	2
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 60 (6.67%)	1 / 65 (1.54%)	2 / 46 (4.35%)
occurrences (all)	4	1	4
Nausea			
subjects affected / exposed	4 / 60 (6.67%)	15 / 65 (23.08%)	7 / 46 (15.22%)
occurrences (all)	4	16	9
Vomiting			
subjects affected / exposed	5 / 60 (8.33%)	7 / 65 (10.77%)	3 / 46 (6.52%)
occurrences (all)	5	10	3

Abdominal discomfort			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Crohn's disease			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Intestinal obstruction			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Swollen tongue			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences (all)	1	0	1
Stomatitis			
subjects affected / exposed	2 / 60 (3.33%)	2 / 65 (3.08%)	1 / 46 (2.17%)
occurrences (all)	2	2	1
Toothache			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences (all)	1	0	1

Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 60 (1.67%)	1 / 65 (1.54%)	0 / 46 (0.00%)
occurrences (all)	1	1	0
Chronic kidney disease			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 60 (3.33%)	2 / 65 (3.08%)	3 / 46 (6.52%)
occurrences (all)	2	2	3
Dry skin			
subjects affected / exposed	2 / 60 (3.33%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	2	0	0
Hyperhidrosis			
subjects affected / exposed	2 / 60 (3.33%)	5 / 65 (7.69%)	1 / 46 (2.17%)
occurrences (all)	2	5	1
Pruritus			

subjects affected / exposed	0 / 60 (0.00%)	1 / 65 (1.54%)	4 / 46 (8.70%)
occurrences (all)	0	1	4
Rash			
subjects affected / exposed	2 / 60 (3.33%)	7 / 65 (10.77%)	2 / 46 (4.35%)
occurrences (all)	2	7	2
Dermatitis acneiform			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Dermatomyositis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Rosacea			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Skin lesion			

subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	1 / 60 (1.67%)	1 / 65 (1.54%)	0 / 46 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 60 (15.00%)	11 / 65 (16.92%)	11 / 46 (23.91%)
occurrences (all)	12	18	13
Back pain			
subjects affected / exposed	2 / 60 (3.33%)	10 / 65 (15.38%)	5 / 46 (10.87%)
occurrences (all)	2	10	5
Bone pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 65 (0.00%)	3 / 46 (6.52%)
occurrences (all)	1	0	3
Joint swelling			
subjects affected / exposed	0 / 60 (0.00%)	2 / 65 (3.08%)	0 / 46 (0.00%)
occurrences (all)	0	3	0
Muscle spasms			
subjects affected / exposed	3 / 60 (5.00%)	1 / 65 (1.54%)	3 / 46 (6.52%)
occurrences (all)	3	2	3
Muscular weakness			
subjects affected / exposed	6 / 60 (10.00%)	3 / 65 (4.62%)	1 / 46 (2.17%)
occurrences (all)	6	5	1
Musculoskeletal chest pain			
subjects affected / exposed	3 / 60 (5.00%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences (all)	3	0	1
Musculoskeletal pain			
subjects affected / exposed	3 / 60 (5.00%)	3 / 65 (4.62%)	2 / 46 (4.35%)
occurrences (all)	4	3	2
Myalgia			
subjects affected / exposed	5 / 60 (8.33%)	6 / 65 (9.23%)	5 / 46 (10.87%)
occurrences (all)	5	7	5

Pain in extremity			
subjects affected / exposed	4 / 60 (6.67%)	6 / 65 (9.23%)	4 / 46 (8.70%)
occurrences (all)	8	6	4
Arthritis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Bone lesion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Osteoporosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Torticollis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0

Musculoskeletal stiffness			
subjects affected / exposed	0 / 60 (0.00%)	3 / 65 (4.62%)	1 / 46 (2.17%)
occurrences (all)	0	3	1
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hyperparathyroidism			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 60 (0.00%)	5 / 65 (7.69%)	2 / 46 (4.35%)
occurrences (all)	0	5	2
Hypercholesterolaemia			
subjects affected / exposed	33 / 60 (55.00%)	37 / 65 (56.92%)	25 / 46 (54.35%)
occurrences (all)	126	102	62
Hyperglycaemia			
subjects affected / exposed	2 / 60 (3.33%)	3 / 65 (4.62%)	6 / 46 (13.04%)
occurrences (all)	7	9	23
Hyperlipidaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	2 / 46 (4.35%)
occurrences (all)	0	0	2
Hypertriglyceridaemia			
subjects affected / exposed	27 / 60 (45.00%)	44 / 65 (67.69%)	29 / 46 (63.04%)
occurrences (all)	99	135	100
Hyperuricaemia			
subjects affected / exposed	2 / 60 (3.33%)	1 / 65 (1.54%)	3 / 46 (6.52%)
occurrences (all)	2	1	3
Hypokalaemia			
subjects affected / exposed	4 / 60 (6.67%)	4 / 65 (6.15%)	2 / 46 (4.35%)
occurrences (all)	4	6	2
Hypomagnesaemia			

subjects affected / exposed	2 / 60 (3.33%)	1 / 65 (1.54%)	3 / 46 (6.52%)
occurrences (all)	2	1	3
Hypophosphataemia			
subjects affected / exposed	2 / 60 (3.33%)	1 / 65 (1.54%)	3 / 46 (6.52%)
occurrences (all)	2	1	4
Dehydration			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hypocholesterolaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	3 / 60 (5.00%)	4 / 65 (6.15%)	4 / 46 (8.70%)
occurrences (all)	6	5	6
Increased appetite			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 60 (1.67%)	3 / 65 (4.62%)	0 / 46 (0.00%)
occurrences (all)	1	4	0
Influenza			
subjects affected / exposed	1 / 60 (1.67%)	3 / 65 (4.62%)	0 / 46 (0.00%)
occurrences (all)	1	3	0
Lung infection			
subjects affected / exposed	3 / 60 (5.00%)	2 / 65 (3.08%)	0 / 46 (0.00%)
occurrences (all)	3	2	0

Pneumonia			
subjects affected / exposed	0 / 60 (0.00%)	8 / 65 (12.31%)	1 / 46 (2.17%)
occurrences (all)	0	8	1
Rhinitis			
subjects affected / exposed	5 / 60 (8.33%)	2 / 65 (3.08%)	0 / 46 (0.00%)
occurrences (all)	7	3	0
Sinusitis			
subjects affected / exposed	2 / 60 (3.33%)	0 / 65 (0.00%)	1 / 46 (2.17%)
occurrences (all)	3	0	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 60 (3.33%)	6 / 65 (9.23%)	1 / 46 (2.17%)
occurrences (all)	3	7	1
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 60 (3.33%)	2 / 65 (3.08%)	2 / 46 (4.35%)
occurrences (all)	4	2	3
Bacterial infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Chronic sinusitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Enteritis infectious			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Enterococcal bacteraemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0

Gastroenteritis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Soft tissue infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0

Urinary tract infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Viral rhinitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 60 (0.00%)	0 / 65 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	EXP-6 (Phase 2)	Japan Lead-In Cohort (LIC)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 47 (100.00%)	3 / 3 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	6	0	
Deep vein thrombosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Haematoma			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Haemorrhage			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hot flush			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypotension			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Shock			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	

occurrences (all)	0	0	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Tumour pain			
subjects affected / exposed	0 / 47 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 47 (4.26%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Chest pain			
subjects affected / exposed	2 / 47 (4.26%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Face oedema			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	7 / 47 (14.89%)	0 / 3 (0.00%)	
occurrences (all)	9	0	
Gait disturbance			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Mucosal inflammation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Oedema			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Oedema peripheral			

subjects affected / exposed	24 / 47 (51.06%)	1 / 3 (33.33%)	
occurrences (all)	30	1	
Pain			
subjects affected / exposed	2 / 47 (4.26%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Peripheral swelling			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Pyrexia			
subjects affected / exposed	5 / 47 (10.64%)	0 / 3 (0.00%)	
occurrences (all)	5	0	
Axillary pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Catheter site extravasation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Chest discomfort			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Disease progression			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Generalised oedema			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Performance status decreased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Swelling			

subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Affect lability			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Anxiety			
subjects affected / exposed	4 / 47 (8.51%)	0 / 3 (0.00%)	
occurrences (all)	6	0	
Insomnia			
subjects affected / exposed	4 / 47 (8.51%)	0 / 3 (0.00%)	
occurrences (all)	4	0	
Irritability			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Abnormal dreams			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Agitation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Bradyphrenia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Confusional state			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Depressed mood			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hallucination			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

Mental status changes			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nightmare			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Reading disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Sleep disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Mood swings			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hallucination, auditory			
subjects affected / exposed	0 / 47 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 47 (4.26%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Contusion			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

Incision site pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Joint dislocation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Laceration			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Ligament sprain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Limb injury			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Toxicity to various agents			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Procedural pain			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	4	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 47 (14.89%)	2 / 3 (66.67%)	
occurrences (all)	7	2	
Amylase increased			
subjects affected / exposed	7 / 47 (14.89%)	0 / 3 (0.00%)	
occurrences (all)	11	0	
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 47 (8.51%)	1 / 3 (33.33%)	
occurrences (all)	4	1	
Blood cholesterol increased			
subjects affected / exposed	18 / 47 (38.30%)	3 / 3 (100.00%)	
occurrences (all)	49	10	
Blood creatine phosphokinase increased			

subjects affected / exposed	2 / 47 (4.26%)	2 / 3 (66.67%)		
occurrences (all)	2	16		
Blood triglycerides increased				
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)		
occurrences (all)	8	0		
Electrocardiogram QT prolonged				
subjects affected / exposed	2 / 47 (4.26%)	0 / 3 (0.00%)		
occurrences (all)	2	0		
Lipase increased				
subjects affected / exposed	6 / 47 (12.77%)	1 / 3 (33.33%)		
occurrences (all)	12	4		
Weight increased				
subjects affected / exposed	10 / 47 (21.28%)	1 / 3 (33.33%)		
occurrences (all)	17	2		
Blood alkaline phosphatase increased				
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Blood creatinine increased				
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Blood phosphorus decreased				
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Candida test positive				
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Ejection fraction decreased				
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Glucose urine present				
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		

International normalised ratio increased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Lipids increased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Liver function test increased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Transaminases increased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 47 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Atrial fibrillation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Ventricular dysfunction			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pericardial effusion			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 47 (19.15%)	0 / 3 (0.00%)	
occurrences (all)	12	0	
Dysphonia			

subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	14 / 47 (29.79%)	1 / 3 (33.33%)	
occurrences (all)	20	1	
Dyspnoea exertional			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Epistaxis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Haemoptysis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypoxia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Pleural effusion			
subjects affected / exposed	4 / 47 (8.51%)	0 / 3 (0.00%)	
occurrences (all)	4	0	
Wheezing			
subjects affected / exposed	2 / 47 (4.26%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Acute respiratory failure			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Bronchitis chronic			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Laryngeal inflammation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nasal congestion			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			

subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pleuritic pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Productive cough			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pulmonary embolism			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pulmonary hypertension			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pulmonary oedema			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rales			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Respiratory tract congestion			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rhinorrhoea			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Sinus congestion			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	8	0	
Thrombocytopenia			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	8	0	

Febrile neutropenia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Haemorrhagic diathesis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Leukocytosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Thrombocytosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Amnesia			
subjects affected / exposed	2 / 47 (4.26%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Aphasia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Cognitive disorder			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	6	0	
Disturbance in attention			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Dizziness			
subjects affected / exposed	11 / 47 (23.40%)	0 / 3 (0.00%)	
occurrences (all)	20	0	
Dysgeusia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	

occurrences (all)	1	0	
Headache			
subjects affected / exposed	2 / 47 (4.26%)	1 / 3 (33.33%)	
occurrences (all)	2	1	
Memory impairment			
subjects affected / exposed	7 / 47 (14.89%)	0 / 3 (0.00%)	
occurrences (all)	16	0	
Neuropathy peripheral			
subjects affected / exposed	5 / 47 (10.64%)	0 / 3 (0.00%)	
occurrences (all)	8	0	
Paraesthesia			
subjects affected / exposed	5 / 47 (10.64%)	0 / 3 (0.00%)	
occurrences (all)	6	0	
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 47 (4.26%)	2 / 3 (66.67%)	
occurrences (all)	2	2	
Presyncope			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Slow speech			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Ataxia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Balance disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Carpal tunnel syndrome			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dysaesthesia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dysarthria			
subjects affected / exposed	0 / 47 (0.00%)	1 / 3 (33.33%)	

occurrences (all)	0	1	
Formication			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hemiparesis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypoaesthesia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Mental impairment			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Migraine			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nervous system disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Neuralgia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Neurotoxicity			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Partial seizures			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Peroneal nerve palsy			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Psychomotor hyperactivity			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Seizure			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	

occurrences (all)	0	0	
Sensory disturbance			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Speech disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Tremor			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Vision blurred			
subjects affected / exposed	2 / 47 (4.26%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Visual impairment			
subjects affected / exposed	2 / 47 (4.26%)	0 / 3 (0.00%)	
occurrences (all)	4	0	
Asthenopia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Astigmatism			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Conjunctival oedema			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Diplopia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dry eye			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Photophobia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Photopsia			

subjects affected / exposed	0 / 47 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Presbyopia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Retinal vein occlusion			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Visual acuity reduced			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Eye irritation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Ear discomfort			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypoacusis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vertigo			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vertigo positional			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	5 / 47 (10.64%)	0 / 3 (0.00%)	
occurrences (all)	5	0	
Abdominal pain			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	

occurrences (all)	1	0	
Constipation			
subjects affected / exposed	5 / 47 (10.64%)	0 / 3 (0.00%)	
occurrences (all)	5	0	
Diarrhoea			
subjects affected / exposed	7 / 47 (14.89%)	0 / 3 (0.00%)	
occurrences (all)	7	0	
Dyspepsia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Nausea			
subjects affected / exposed	6 / 47 (12.77%)	1 / 3 (33.33%)	
occurrences (all)	8	1	
Vomiting			
subjects affected / exposed	5 / 47 (10.64%)	0 / 3 (0.00%)	
occurrences (all)	5	0	
Abdominal discomfort			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Ascites			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Crohn's disease			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dry mouth			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	

occurrences (all)	0	0	
Faeces discoloured			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Intestinal obstruction			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Swollen tongue			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Odynophagia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	2 / 47 (4.26%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Toothache			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	2 / 47 (4.26%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Chronic kidney disease			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hydronephrosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

Micturition urgency			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pollakiuria			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Proteinuria			
subjects affected / exposed	0 / 47 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Urinary incontinence			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 47 (4.26%)	1 / 3 (33.33%)	
occurrences (all)	2	1	
Dry skin			
subjects affected / exposed	1 / 47 (2.13%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Hyperhidrosis			
subjects affected / exposed	4 / 47 (8.51%)	0 / 3 (0.00%)	
occurrences (all)	4	0	
Pruritus			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	4 / 47 (8.51%)	0 / 3 (0.00%)	
occurrences (all)	4	0	
Dermatitis acneiform			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dermatitis contact			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dermatomyositis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	

occurrences (all)	0	0	
Night sweats			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Photosensitivity reaction			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rash erythematous			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rash maculo-papular			
subjects affected / exposed	0 / 47 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Rash pruritic			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rosacea			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Skin lesion			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Swelling face			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	14 / 47 (29.79%)	0 / 3 (0.00%)	
occurrences (all)	17	0	

Back pain			
subjects affected / exposed	3 / 47 (6.38%)	1 / 3 (33.33%)	
occurrences (all)	3	1	
Bone pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Joint swelling			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Muscle spasms			
subjects affected / exposed	5 / 47 (10.64%)	0 / 3 (0.00%)	
occurrences (all)	5	0	
Muscular weakness			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Musculoskeletal chest pain			
subjects affected / exposed	4 / 47 (8.51%)	0 / 3 (0.00%)	
occurrences (all)	4	0	
Musculoskeletal pain			
subjects affected / exposed	2 / 47 (4.26%)	1 / 3 (33.33%)	
occurrences (all)	2	1	
Myalgia			
subjects affected / exposed	6 / 47 (12.77%)	2 / 3 (66.67%)	
occurrences (all)	7	2	
Pain in extremity			
subjects affected / exposed	8 / 47 (17.02%)	0 / 3 (0.00%)	
occurrences (all)	9	0	
Arthritis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Bone lesion			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Flank pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

Limb discomfort			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal discomfort			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Neck pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Osteoarthritis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Osteoporosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pain in jaw			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Plantar fasciitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Torticollis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal stiffness			
subjects affected / exposed	4 / 47 (8.51%)	0 / 3 (0.00%)	
occurrences (all)	4	0	
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hyperparathyroidism			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypothyroidism			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	

occurrences (all)	0	0	

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 47 (4.26%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Hypercholesterolaemia			
subjects affected / exposed	25 / 47 (53.19%)	0 / 3 (0.00%)	
occurrences (all)	60	0	
Hyperglycaemia			
subjects affected / exposed	5 / 47 (10.64%)	3 / 3 (100.00%)	
occurrences (all)	8	11	
Hyperlipidaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypertriglyceridaemia			
subjects affected / exposed	23 / 47 (48.94%)	0 / 3 (0.00%)	
occurrences (all)	78	0	
Hyperuricaemia			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Hypokalaemia			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Hypomagnesaemia			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	4	0	
Hypophosphataemia			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	5	0	
Dehydration			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Fluid retention			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

Hypercalcaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypocalcaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypocholesterolaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypoalbuminaemia			
subjects affected / exposed	2 / 47 (4.26%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Increased appetite			
subjects affected / exposed	0 / 47 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Influenza			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Lung infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rhinitis			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Sinusitis			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	

occurrences (all)	3	0	
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 47 (6.38%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Bacterial infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Candida infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Cellulitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Chronic sinusitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Enteritis infectious			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Enterococcal bacteraemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Helicobacter infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Herpes virus infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Laryngitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	

occurrences (all)	0	0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Periodontitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pharyngitis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Respiratory tract infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Soft tissue infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Tooth abscess			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Viral rhinitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Herpes zoster			
subjects affected / exposed	0 / 47 (0.00%)	1 / 3 (33.33%)	

occurrences (all)	0	1	

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.

The study is still ongoing. This report reflects data collected up to 15 Mar 2017, and will be updated after completion of the whole study.

Notes: