

**Clinical trial results:****A Phase 1/2 Study of the Highly-selective RET Inhibitor, BLU-667, in Patients with Thyroid Cancer, Non-Small Cell Lung Cancer (NSCLC) and Other Advanced Solid Tumors****Summary**

EudraCT number	2016-004390-41
Trial protocol	GB DE NL BE
Global end of trial date	21 March 2024

Results information

Result version number	v1 (current)
This version publication date	04 April 2025
First version publication date	04 April 2025

Trial information**Trial identification**

Sponsor protocol code	BO42863
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03037385
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse, 124, Basel, Switzerland, CH-4058
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 March 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the study is to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and preliminary antineoplastic activity of pralsetinib (BLU-667) administered orally in participants with medullary thyroid cancer (MTC), rearranged during transfection (RET)-altered NSCLC and other RET-altered solid tumors.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	China: 111
Country: Number of subjects enrolled	Germany: 39
Country: Number of subjects enrolled	Spain: 37
Country: Number of subjects enrolled	France: 45
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	Italy: 40
Country: Number of subjects enrolled	Korea, Republic of: 59
Country: Number of subjects enrolled	Netherlands: 15
Country: Number of subjects enrolled	Singapore: 12
Country: Number of subjects enrolled	Taiwan: 10
Country: Number of subjects enrolled	United States: 207
Worldwide total number of subjects	590
EEA total number of subjects	178

Notes:

Subjects enrolled per age group

In utero	0
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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)	405
From 65 to 84 years	180
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

A total of 590 participants with rearranged during transfection (RET) fusion-positive NSCLC, RET mutation-positive MTC (also known as RET-mutant MTC), RET fusion-positive thyroid cancer (TC) and other advanced solid tumors took part in the study at 74 investigative sites across 13 countries from 17 March 2017 to 21 March 2024.

Pre-assignment

Screening details:

The study was divided into two phases. In Phase 1 (Dose Escalation), participants received pralsetinib at varying doses. In Phase 2 (Dose Expansion), participants received fixed dose of pralsetinib.

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
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Arm title	Phase I: Pralsetinib 30 mg
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Arm description:

Participants received pralsetinib 30 milligrams (mg), orally, once a day (QD) until discontinuation due to toxicity, disease progression, or other reasons.

Arm type	Experimental
Investigational medicinal product name	Pralsetinib
Investigational medicinal product code	RO7499790
Other name	BLU-667
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pralsetinib, 30 mg, orally was administered to participants, QD.

Arm title	Phase I: Pralsetinib 60 mg
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Arm description:

Participants received pralsetinib 60 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.

Arm type	Experimental
Investigational medicinal product name	Pralsetinib
Investigational medicinal product code	RO7499790
Other name	BLU-667
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pralsetinib, 60 mg, orally was administered to participants, QD.

Arm title	Phase I: Pralsetinib 100 mg
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Arm description:

Participants received pralsetinib 100 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.

Arm type	Experimental
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Investigational medicinal product name	Pralsetinib
Investigational medicinal product code	RO7499790
Other name	BLU-667
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pralsetinib, 100 mg, orally was administered to participants, QD.

Arm title	Phase I: Pralsetinib 200 mg
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Arm description:

Participants received pralsetinib 200 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.

Arm type	Experimental
Investigational medicinal product name	Pralsetinib
Investigational medicinal product code	RO7499790
Other name	BLU-667
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pralsetinib, 200 mg, orally was administered to participants, QD.

Arm title	Phase I: Pralsetinib 300 mg
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Arm description:

Participants received pralsetinib 300 mg, orally, QD until discontinuation due to toxicity, disease progression, or other reasons.

Arm type	Experimental
Investigational medicinal product name	Pralsetinib
Investigational medicinal product code	RO7499790
Other name	BLU-667
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pralsetinib, 300 mg, orally was administered to participants, QD.

Arm title	Phase I: Pralsetinib 400 mg
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Arm description:

Participants received pralsetinib 400 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.

Arm type	Experimental
Investigational medicinal product name	Pralsetinib
Investigational medicinal product code	RO7499790
Other name	BLU-667
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pralsetinib, 400 mg, orally was administered to participants, QD.

Arm title	Phase I: Pralsetinib 600 mg
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Arm description:

Participants received pralsetinib 600 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.

Arm type	Experimental
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Investigational medicinal product name	Pralsetinib
Investigational medicinal product code	RO7499790
Other name	BLU-667
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pralsetinib, 600 mg, orally was administered to participants, QD.

Arm title	Phase I: Pralsetinib 100/100 mg
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Arm description:

Participants received pralsetinib 100 mg, orally, twice a day (BID) until discontinuation due to toxicity, disease progression, or other reasons.

Arm type	Experimental
Investigational medicinal product name	Pralsetinib
Investigational medicinal product code	RO7499790
Other name	BLU-667
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pralsetinib, 100 mg, orally was administered to participants, BID.

Arm title	Phase I: Pralsetinib 200/100 mg
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Arm description:

Participants received pralsetinib 200 mg in the morning and then 100 mg in the evening orally until discontinuation due to toxicity, disease progression, or other reasons.

Arm type	Experimental
Investigational medicinal product name	Pralsetinib
Investigational medicinal product code	RO7499790
Other name	BLU-667
Pharmaceutical forms	Tablet, Tablet
Routes of administration	Oral use, Oral use

Dosage and administration details:

Pralsetinib, 200 mg in the morning and then 100 mg in the evening was administered to participants, orally.

Arm title	Phase II: Pralsetinib 400 mg
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Arm description:

Participants with advanced NSCLC, advanced non-resectable TC and other advanced non-resectable solid tumors with various RET-alterations were enrolled in this arm to receive pralsetinib, 400 mg, QD until discontinuation due to toxicity, disease progression, or other reasons.

Arm type	Experimental
Investigational medicinal product name	Pralsetinib
Investigational medicinal product code	RO7499790
Other name	BLU-667
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pralsetinib, 400 mg, orally was administered to participants, QD.

Number of subjects in period 1	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg
Started	2	6	5
Completed	0	0	0
Not completed	2	6	5
Initiation Of Another Therapy	1	-	-
Consent withdrawn by subject	-	-	1
Physician decision	-	-	-
Adverse Event	-	-	1
Death	1	4	2
Reason Not Specified	-	1	-
Progressive Disease	-	1	1
Lost to follow-up	-	-	-

Number of subjects in period 1	Phase I: Pralsetinib 200 mg	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg
Started	13	11	12
Completed	0	0	0
Not completed	13	11	12
Initiation Of Another Therapy	-	-	-
Consent withdrawn by subject	2	1	3
Physician decision	-	-	-
Adverse Event	-	-	-
Death	2	5	2
Reason Not Specified	4	3	6
Progressive Disease	5	2	-
Lost to follow-up	-	-	1

Number of subjects in period 1	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg	Phase I: Pralsetinib 200/100 mg
Started	4	6	3
Completed	0	0	0
Not completed	4	6	3
Initiation Of Another Therapy	-	1	-
Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Adverse Event	-	-	-
Death	1	5	2
Reason Not Specified	2	-	1
Progressive Disease	1	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Phase II: Pralsetinib 400 mg
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Started	528
Completed	0
Not completed	528
Initiation Of Another Therapy	2
Consent withdrawn by subject	52
Physician decision	1
Adverse Event	6
Death	240
Reason Not Specified	181
Progressive Disease	30
Lost to follow-up	16

Baseline characteristics

Reporting groups

Reporting group title	Phase I: Pralsetinib 30 mg
Reporting group description: Participants received pralsetinib 30 milligrams (mg), orally, once a day (QD) until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 60 mg
Reporting group description: Participants received pralsetinib 60 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 100 mg
Reporting group description: Participants received pralsetinib 100 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 200 mg
Reporting group description: Participants received pralsetinib 200 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 300 mg
Reporting group description: Participants received pralsetinib 300 mg, orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 400 mg
Reporting group description: Participants received pralsetinib 400 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 600 mg
Reporting group description: Participants received pralsetinib 600 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 100/100 mg
Reporting group description: Participants received pralsetinib 100 mg, orally, twice a day (BID) until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 200/100 mg
Reporting group description: Participants received pralsetinib 200 mg in the morning and then 100 mg in the evening orally until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase II: Pralsetinib 400 mg
Reporting group description: Participants with advanced NSCLC, advanced non-resectable TC and other advanced non-resectable solid tumors with various RET-alterations were enrolled in this arm to receive pralsetinib, 400 mg, QD until discontinuation due to toxicity, disease progression, or other reasons.	

Reporting group values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg
Number of subjects	2	6	5
Age categorical			
Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	54.5 ± 9.2	49.5 ± 18.0	51.2 ± 13.2
Sex: Female, Male Units: participants			
Female	1	3	4
Male	1	3	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	2	1
Not Hispanic or Latino	0	4	4
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized Units: Subjects			
Asian	0	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	3	2
Other	0	0	0
Unknown or Not Reported	2	2	1

Reporting group values	Phase I: Pralsetinib 200 mg	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg
Number of subjects	13	11	12
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	53.8 ± 13.6	60.6 ± 11.0	49.2 ± 17.8
Sex: Female, Male Units: participants			
Female	5	4	3
Male	8	7	9
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	3
Not Hispanic or Latino	12	11	9
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized Units: Subjects			
Asian	0	0	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	1
White	11	11	9
Other	0	0	0
Unknown or Not Reported	1	0	0

Reporting group values	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg	Phase I: Pralsetinib 200/100 mg
Number of subjects	4	6	3
Age categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	59.5	63.7	60.0
standard deviation	± 9.1	± 10.7	± 21.9
Sex: Female, Male Units: participants			
Female	3	2	1
Male	1	4	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	4	4	3
Unknown or Not Reported	0	2	0
Race/Ethnicity, Customized Units: Subjects			
Asian	0	1	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	4	4	3
Other	0	0	0
Unknown or Not Reported	0	1	0

Reporting group values	Phase II: Pralsetinib 400 mg	Total	
Number of subjects	528	590	
Age categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	57.7	-	
standard deviation	± 12.6		
Sex: Female, Male Units: participants			
Female	257	283	
Male	271	307	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	19	28	
Not Hispanic or Latino	465	516	
Unknown or Not Reported	44	46	
Race/Ethnicity, Customized Units: Subjects			
Asian	203	209	

Native Hawaiian or Other Pacific Islander	2	2	
Black or African American	4	6	
White	284	331	
Other	3	3	
Unknown or Not Reported	32	39	

End points

End points reporting groups

Reporting group title	Phase I: Pralsetinib 30 mg
Reporting group description: Participants received pralsetinib 30 milligrams (mg), orally, once a day (QD) until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 60 mg
Reporting group description: Participants received pralsetinib 60 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 100 mg
Reporting group description: Participants received pralsetinib 100 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 200 mg
Reporting group description: Participants received pralsetinib 200 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 300 mg
Reporting group description: Participants received pralsetinib 300 mg, orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 400 mg
Reporting group description: Participants received pralsetinib 400 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 600 mg
Reporting group description: Participants received pralsetinib 600 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 100/100 mg
Reporting group description: Participants received pralsetinib 100 mg, orally, twice a day (BID) until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase I: Pralsetinib 200/100 mg
Reporting group description: Participants received pralsetinib 200 mg in the morning and then 100 mg in the evening orally until discontinuation due to toxicity, disease progression, or other reasons.	
Reporting group title	Phase II: Pralsetinib 400 mg
Reporting group description: Participants with advanced NSCLC, advanced non-resectable TC and other advanced non-resectable solid tumors with various RET-alterations were enrolled in this arm to receive pralsetinib, 400 mg, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	Phase 1: All Participants QD
Subject analysis set type	Per protocol
Subject analysis set description: Participants received pralsetinib at varying doses at a QD schedule until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	Pralsetinib \leq 300 mg QD
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received pralsetinib, 300 mg or less, orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	Pralsetinib 400 mg QD

Subject analysis set type	Safety analysis
Subject analysis set description: Participants received pralsetinib, 400 mg, orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	Pralsetinib BID Dosing Schedule
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received pralsetinib, 100 mg, orally, BID or 200 mg in the morning and then 100 mg in the evening, orally, until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	RET- fusion Positive NSCLC With Prior Platinum Treatment
Subject analysis set type	Per protocol
Subject analysis set description: Participants who had RET-fusion positive NSCLC previously treated with platinum-based chemotherapies received pralsetinib, 400 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment
Subject analysis set type	Per protocol
Subject analysis set description: Participants who had RET-fusion positive NSCLC previously treated with non-platinum or systemic therapies received pralsetinib, 400 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment
Subject analysis set type	Per protocol
Subject analysis set description: Participants who had RET-fusion positive NSCLC not previously treated with systemic or platinum-based chemotherapies received pralsetinib, 400 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	RET-mutation MTC With Cabozantinib and/or Vandetanib Treatment
Subject analysis set type	Per protocol
Subject analysis set description: Participants who had RET- mutation positive MTC previously treated with either cabozantinib and/or vandetanib therapies received pralsetinib, 400 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	RET-mutation MTC With No Cabozantinib/Vandetanib Treatment
Subject analysis set type	Per protocol
Subject analysis set description: Participants who had RET- mutation positive MTC not previously treated with cabozantinib or vandetanib therapies received pralsetinib, 400 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	RET-fusion Positive TC
Subject analysis set type	Per protocol
Subject analysis set description: Participants who had RET-fusion positive TC received pralsetinib, 400 mg, orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	RET-fusion Positive Solid Tumors Other Than NSCLC and TC
Subject analysis set type	Per protocol
Subject analysis set description: Participants who had other RET-positive solid tumors other than NSCLC and TC received pralsetinib, 400 mg, orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	RET-altered Solid Tumors Previously Treated With RET Inhibitor
Subject analysis set type	Per protocol
Subject analysis set description: Participants who had RET-altered (fusion or mutation) solid tumors previously treated with a selective RET tyrosine kinase inhibitor (TKI) received pralsetinib, 400 mg, orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	

Subject analysis set title	RET-mutation Positive Tumors Other Than MTC
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants who had RET-mutation positive solid tumors received pralsetinib, 400 mg, orally, QD until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	RET- fusion Positive NSCLC Participants
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants who had RET-fusion positive NSCLC received pralsetinib, 400 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons. This arm was specifically planned for reporting PK data.	
Subject analysis set title	Tumor-agnostic Participants
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants who had RET-fusion positive NSCLC or TC, or RET-mutation positive MTC, each with different genetic mutations received pralsetinib, 400 mg orally, QD until discontinuation due to toxicity, disease progression, or other reasons. This arm was specifically planned for reporting PK data.	
Subject analysis set title	RET-altered Solid Tumors Participants
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants who had RET-altered (fusion or mutation) solid tumors previously treated with a selective RET TKI received pralsetinib, 400 mg, orally, QD until discontinuation due to toxicity, disease progression, or other reasons. This arm was specifically planned for reporting PK data.	
Subject analysis set title	RET-mutation Positive Tumors other than MTC Participants
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants who had RET-mutation positive solid tumors received Pralsetinib 400 mg, orally, QD until discontinuation due to toxicity, disease progression, or other reasons. This arm was specifically planned for reporting PK data.	
Subject analysis set title	Phase I: Pralsetinib 200/100 mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received pralsetinib 200 mg in the morning and then 100 mg in the evening orally until discontinuation due to toxicity, disease progression, or other reasons.	
Subject analysis set title	Pralsetinib All Doses
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received pralsetinib at varying doses at the QD and BID schedule until discontinuation due to toxicity, disease progression, or other reasons.	

Primary: Phase 1 : Maximum Tolerated Dose (MTD) and Recommended Phase 2 Dose (RP2D) of Pralsetinib

End point title	Phase 1 : Maximum Tolerated Dose (MTD) and Recommended Phase 2 Dose (RP2D) of Pralsetinib ^[1]
End point description:	
MTD was defined as the highest tolerated dose of pralsetinib without causing dose limiting toxicities (DLTs). DLT was defined as any Grade ≥ 3 adverse event (AE) occurring during Cycle 1 during Phase 1 (dose escalation) that is not clearly caused by something other than pralsetinib. RP2D was defined as the highest dose with acceptable toxicity as determined from dose-escalation phase. Dose-determining population included all participants in the dose-escalation part who have received $\geq 75\%$ (21 days) of the study drug and completed safety evaluations through Cycle 1 Day 28 or experienced a DLT.	
End point type	Primary
End point timeframe:	
Up to approximately 30.8 months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistics was planned for this endpoint.

End point values	Phase 1: All Participants QD			
Subject group type	Subject analysis set			
Number of subjects analysed	51			
Units: mg				
MTD	400			
RP2D	400			

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1 and Phase 2: Number of Participants With AEs and Serious AEs (SAEs)

End point title	Phase 1 and Phase 2: Number of Participants With AEs and Serious AEs (SAEs) ^[2]
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End point description:

AE=any untoward medical occurrence associated with use of drug in humans, whether or not considered drug related. AE can be any unfavorable & unintended sign, symptom/disease temporally associated with use of drug, without any judgment about causality. SAE=any significant hazard, contraindication, side effect that is fatal/life-threatening, requires hospitalization/prolongation of existing hospitalization, results in persistent/significant disability, is congenital anomaly/birth defect, is medically significant/requires intervention to prevent the outcomes listed above. Safety Population included all participants who have received at least 1 dose of the study drug regardless of starting dose levels. As pre-specified in the SAP, safety data was to be analyzed and reported as per the pre-planned grouped dose level II (SAP section 3.6.5.2). Hence, per dose safety data is not presented for this study.

End point type	Primary
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End point timeframe:

From Cycle 1 Day 1 up to 30 days after the final dose of study drug (up to approximately 6.7 years)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistics was planned for this endpoint.

End point values	Pralsetinib ≤ 300 mg QD	Pralsetinib 400 mg QD	Pralsetinib BID Dosing Schedule	Pralsetinib All Doses
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	37	540	9	590
Units: percentage of participants				
number (not applicable)				
AEs	37	540	9	590
SAEs	26	381	7	416

Statistical analyses

Primary: Phase 2: Overall Response Rate (ORR)

End point title	Phase 2: Overall Response Rate (ORR) ^[3]
End point description:	ORR=percentage of participants with a confirmed complete response (CR)/partial response (PR) for at least 2 assessments with at least 28 days apart & no disease progression (PD) in between. Per Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1), CR=disappearance of all target lesions/any pathological lymph nodes (whether target/non-target) having a reduction in short axis to <10 millimeters(mm). PR=at least 30% decrease in sum of diameters (SOD) of all target lesions, taking as reference baseline SOD, in absence of CR. PD=at least a 20% increase in SOD of target lesions, taking as reference smallest SOD on study (including baseline). RET-altered measurable disease population=participants in efficacy population who had measurable (target) disease per RECIST v1.1 at baseline according to blinded central review (BICR) & sufficient evidence of RET alteration. As prespecified in SAP, Phase 1 participants treated at 400 mg QD were included in Phase 2 efficacy analysis.
End point type	Primary
End point timeframe:	Up to approximately 79.8 months

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 formal statistics was planned for this endpoint.

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment	RET-mutation MTC With Cabozantinib and/or Vandetanib Treatment
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130	23	106	60
Units: percentage of participants				
number (confidence interval 95%)	63.1 (54.2 to 71.4)	73.9 (51.6 to 89.8)	78.3 (69.2 to 85.7)	56.7 (43.2 to 69.4)

End point values	RET-mutation MTC With No Cabozantinib/Vandetanib Treatment	RET-fusion Positive TC	RET-fusion Positive Solid Tumors Other Than NSCLC and TC	RET-altered Solid Tumors Previously Treated With RET Inhibitor
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	72	27	28	21
Units: percentage of participants				
number (confidence interval 95%)	77.8 (66.4 to 86.7)	85.2 (66.3 to 95.8)	46.4 (27.5 to 66.1)	19.0 (5.4 to 41.9)

End point values	RET-mutation Positive Tumors Other Than MTC			
Subject group type	Subject analysis set			
Number of subjects analysed	13			

Units: percentage of participants				
number (confidence interval 95%)	7.7 (0.99 to 36.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: ORR

End point title	Phase 1: ORR ^[4]
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End point description:

ORR was defined as percentage of participants with a confirmed CR or PR for at least two assessments with at least 28 days apart and no PD in between. Per RECIST v1.1, CR was defined as the disappearance of all target lesions or any pathological lymph nodes (whether target or non-target) having a reduction in the short axis to <10 mm. PR was defined as at least a 30% decrease in the SOD of all target lesions, taking as reference the baseline SOD, in the absence of CR. PD was defined as at least a 20% increase in SOD of target lesions, taking as reference the smallest SOD on study (including baseline). ORR and its two-sided 95% CI, based on the exact binomial distribution (Clopper-Pearson), was presented. Efficacy population included all participants who have been exposed to at least one dose of the study on/prior to 11 July 2019. -0.9999&9999=The lower and upper limit of 95% confidence interval (CI) was not estimable due to insufficient number of participants with events.

End point type	Secondary
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End point timeframe:

Up to approximately 28 months

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was planned to report data for Phase I of the study only. Hence, Phase II arm is not included.

End point values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg	Phase I: Pralsetinib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	5	13
Units: percentage of participants				
number (confidence interval 95%)	0 (-0.9999 to 9999)	50.0 (11.8 to 88.2)	40.0 (5.3 to 85.3)	38.5 (13.9 to 68.4)

End point values	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	4	5
Units: percentage of participants				
number (confidence interval 95%)	45.5 (16.7 to 76.6)	41.7 (15.2 to 72.3)	25.0 (0.99 to 80.6)	80.0 (28.4 to 99.5)

End point values	Phase I:			

	Pralsetinib 200/100 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: percentage of participants				
number (confidence interval 95%)	75.0 (19.4 to 99.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and Phase 2: ORR in RET-fusion Positive NSCLC Participants with Specific RET Gene Status

End point title	Phase 1 and Phase 2: ORR in RET-fusion Positive NSCLC Participants with Specific RET Gene Status
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End point description:

Oncogenic RET rearrangements have been identified in 1–2% of NSCLC. These rearrangements typically produce chimeric transcripts encoding fusion protein consisting of RET kinase domain coupled to a protein with dimerization domain (eg Kinesin family member 5B(KIF5B), coiled-coil domain containing 6(CCDC6), nuclear receptor coactivator 4(NCOA4). RET genotypes determined by local testing/central analysis of circulating tumor deoxyribonucleic acid(ctDNA). ORR=% of participants with confirmed CR/PR for at least 2 assessments 28 days apart & no PD in between. CR/PR/PD: defined per RECIST as outlined in description for ORR endpoint (EP). RET-altered measurable disease (RAMD) population. As prespecified in SAP, Phase 1 participants treated at 400 mg are pooled with Phase 2 participants for efficacy analysis. n=number of participants with specified mutation. 9999=95% CI was not estimable due to insufficient number of participants with events. 99999=no participants had the specified mutation.

End point type	Secondary
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End point timeframe:

Up to approximately 79.8 months

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	130	23	106	
Units: percentage of participants				
number (confidence interval 95%)				
KIF5B(n=91,17,76)	63.7 (53.0 to 73.6)	82.4 (56.6 to 96.2)	78.9 (68.1 to 87.5)	
CCDC6(n=25,4,19)	68.0 (46.5 to 85.1)	75.0 (19.4 to 99.4)	84.2 (60.4 to 96.6)	
NCOA4(n=1,0,0)	100 (2.5 to 100)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Other(n=13,2,11)	46.2 (19.2 to 74.9)	0 (-9999 to 9999)	63.6 (30.8 to 89.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and Phase 2: ORR in RET-mutation MTC Participants With Specific RET Gene Status

End point title	Phase 1 and Phase 2: ORR in RET-mutation MTC Participants With Specific RET Gene Status
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End point description:

Oncogenic RET activation has been implicated as a driver in MTC. These rearrangements typically produce chimeric transcripts that encode a fusion protein consisting of the RET kinase domain coupled to a protein with a dimerization domain (e.g., M918T, cysteine rich domain, V804X). RET genotypes were determined by local testing and/or central analysis of ctDNA. ORR was assessed in participants having specific RET rearrangements. ORR was defined as the percentage of participants with a confirmed CR or PR for at least 2 assessments with at least 28 days apart and no PD in between. CR, PR, and PD were defined per RECIST as outlined in the description for ORR EP. RAMD population. As prespecified in the SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. n=number of participants with the specified mutation. -0.9999&9999=Since only 1 participant was analyzed upper and lower limit of 95% CI was not evaluable..

End point type	Secondary
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End point timeframe:

Up to approximately 79.8 months

End point values	RET-mutation MTC With Cabozantinib and/or Vandetanib Treatment	RET-mutation MTC With No Cabozantinib/Vandetanib Treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	72		
Units: percentage of participants				
number (confidence interval 95%)				
M918T (n=41,43)	53.7 (37.4 to 69.3)	74.4 (58.8 to 86.5)		
Cysteine Rich Domain(n=13,25)	46.2 (19.2 to 74.9)	88.0 (68.8 to 97.5)		
V804X(n=2,1)	100 (15.8 to 100)	0 (-0.9999 to 9999)		
Other(n=4,3)	100 (39.8 to 100)	66.7 (9.4 to 99.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and Phase 2: ORR in RET-fusion Positive TC Participants With Specific RET Gene Status

End point title	Phase 1 and Phase 2: ORR in RET-fusion Positive TC Participants With Specific RET Gene Status
End point description:	
<p>Oncogenic RET activation has been implicated as a driver in both MTC and differentiated TC (DTC). These rearrangements typically produce chimeric transcripts that encode a fusion protein consisting of the RET kinase domain coupled to a protein with a dimerization domain (e.g., KIF5B, CCDC6, NCOA4). RET genotypes were determined by local testing and/or central analysis of ctDNA. ORR was assessed in participants having specific RET rearrangements. ORR was defined as the percentage of participants with a confirmed CR or PR for at least 2 assessments with at least 28 days apart and no PD in between. CR, PR, and PD were defined per RECIST as outlined in the description for ORR EP. RAMD population. As prespecified in the SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. n=number of participants with the specified mutation. 9999=no participants exhibited the specified mutation.</p>	
End point type	Secondary
End point timeframe:	
Up to approximately 79.8 months	

End point values	RET-fusion Positive TC			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: percentage of participants				
number (confidence interval 95%)				
KIF5B(n=0)	9999 (9999 to 9999)			
CCDC6(n=17)	82.4 (56.6 to 96.2)			
NCOA4(n=6)	100 (54.1 to 100)			
Other(n=4)	75.0 (19.4 to 99.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and Phase 2: Clinical Benefit Rate (CBR) in RET-fusion Positive NSCLC Participants With Specific RET Gene Status

End point title	Phase 1 and Phase 2: Clinical Benefit Rate (CBR) in RET-fusion Positive NSCLC Participants With Specific RET Gene Status
End point description:	
<p>Oncogenic RET rearrangements have been identified in 1%–2% of NSCLC. These rearrangements typically produce chimeric transcripts that encode fusion protein consisting of RET kinase domain coupled to a protein with a dimerization domain. RET genotypes were determined by local testing/central analysis of ctDNA. CBR was defined as percentage of participants with confirmed CR, PR or stable disease (SD) which has been lasting at least 16 weeks from 1st dose date. CR, PR & PD were defined per RECIST as outlined in description for ORR EP. SD=neither sufficient shrinkage to qualify for CR/PR nor sufficient increase to qualify for PD. RAMD population. As prespecified in SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. n=number of participants with specified mutation. 9999=95% CI was not estimable due to insufficient number of participants with events. 99999=no participants exhibited the specified mutation.</p>	
End point type	Secondary

End point timeframe:
Up to approximately 79.8 months

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	130	23	106	
Units: percentage of participants				
number (confidence interval 95%)				
KIF5B(n=91,17,76)	76.9 (66.9 to 85.1)	88.2 (63.6 to 98.5)	81.6 (71.0 to 89.5)	
CCDC6(n=25,4,19)	76.0 (54.9 to 90.6)	75.0 (19.4 to 99.4)	84.2 (60.4 to 96.6)	
NCOA4(n=1,0,0)	100 (2.5 to 100)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Other(13,2,11)	53.8 (25.1 to 80.8)	0 (-9999 to 9999)	63.6 (30.8 to 89.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and Phase 2: CBR in RET-mutation MTC Participants With Specific RET Gene Status

End point title	Phase 1 and Phase 2: CBR in RET-mutation MTC Participants With Specific RET Gene Status
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End point description:

Oncogenic RET activation has been implicated as a driver in MTC. These rearrangements typically produce chimeric transcripts that encode fusion protein consisting of RET kinase domain coupled to a protein with a dimerization domain(e.g. M918T, cysteine rich domain, V804X). RET genotypes were determined by local testing/central analysis of ctDNA. CBR was defined as percentage of participants with confirmed CR, PR or SD which has been lasting at least 16 weeks from first dose date. CR and PR were defined per RECIST as outlined in description for EP 3. SD was defined as neither sufficient shrinkage to qualify for CR/PR nor sufficient increase to qualify for PD. PD was defined as at least a 20% increase in SOD of target lesions, taking as reference smallest SOD on study (including baseline). RAMD population. As prespecified in SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. n=number of participants with specified mutation.

End point type	Secondary
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End point timeframe:

Up to approximately 79.8 months

End point values	RET-mutation MTC With Cabozantinib and/or Vandetanib Treatment	RET-mutation MTC With No Cabozantinib/Vandetanib Treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	72		
Units: percentage of participants				
number (confidence interval 95%)				
M918T(n=41,43)	78.0 (62.4 to 89.4)	86.0 (72.1 to 94.7)		
Cysteine Rich Domain(n=13,25)	76.9 (46.2 to 95.0)	96.0 (79.6 to 99.9)		
V804X(n=2,1)	100 (15.8 to 100)	100 (2.5 to 100)		
Other(n=4,3)	100 (39.8 to 100)	100 (29.2 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and Phase 2: CBR in RET-fusion Positive TC Participants With Specific RET Gene Status

End point title	Phase 1 and Phase 2: CBR in RET-fusion Positive TC Participants With Specific RET Gene Status
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End point description:

Oncogenic RET activation has been implicated as a driver in both MTC & DTC. These rearrangements typically produce chimeric transcripts that encode fusion protein consisting of RET kinase domain coupled to protein with a dimerization domain(e.g., KIF5B, CCDC6, NCOA4). RET genotypes were determined by local testing/central analysis of ctDNA. CBR=percentage of participants with a confirmed CR/PR/SD which has been lasting at least 16 weeks from first dose date. CR & PR were defined per RECIST as outlined in description for ORR EP. SD=neither sufficient shrinkage to qualify for CR/PR nor sufficient increase to qualify for PD. PD=at least a 20% increase in SOD of target lesions, taking as reference the smallest SOD on study (including baseline). RAMD population. As prespecified in SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. n=number of participants with specified mutation. 9999=no participants exhibited the specified mutation.

End point type	Secondary
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End point timeframe:

Up to approximately 79.8 months

End point values	RET-fusion Positive TC			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: percentage of participants				
number (confidence interval 95%)				
KIF5B(n=0)	9999 (9999 to 9999)			
CCDC6(n=17)	82.4 (56.6 to 96.2)			

NCOA4(n=6)	100 (54.1 to 100)			
Other(n=4)	75.0 (19.4 to 99.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and Phase 2: Disease Control Rate (DCR) in RET-fusion Positive NSCLC Participants With Specific RET Gene Status

End point title	Phase 1 and Phase 2: Disease Control Rate (DCR) in RET-fusion Positive NSCLC Participants With Specific RET Gene Status
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End point description:

Oncogenic RET rearrangements have been identified in 1-2% of NSCLC. These rearrangements typically produce chimeric transcripts that encode a fusion protein consisting of the RET kinase domain coupled to a protein with a dimerization domain (e.g., KIF5B, CCDC6, NCOA4). RET genotypes were determined by local testing/central analysis of ctDNA. DCR was assessed in participants having specific RET rearrangements. DCR=percentage of participants with confirmed CR/PR/SD. CR & PR were defined per RECIST as outlined in the description for ORR EP. SD=neither sufficient shrinkage to qualify for CR/PR nor sufficient increase to qualify for PD. PD=at least a 20% increase in SOD of target lesions, taking as reference the smallest SOD on study (including baseline). RAMD population. As per SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. n=number of participants with specified mutation. 9999=no participants exhibited the specified mutation.

End point type	Secondary
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End point timeframe:

Up to approximately 79.8 months

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	130	23	106	
Units: percentage of participants				
number (confidence interval 95%)				
KIF5B(n=91,17,76)	93.4 (86.2 to 97.5)	94.1 (71.3 to 99.9)	88.2 (78.7 to 94.4)	
CCDC6(n=25,4,19)	88.0 (68.8 to 97.5)	100 (39.8 to 100)	89.5 (66.9 to 98.7)	
NCOA4(n=1,0,0)	100 (2.5 to 100)	9999 (9999 to 9999)	9999 (9999 to 9999)	
Other(n=13,2,11)	84.6 (54.6 to 98.1)	50.0 (1.3 to 98.7)	100 (71.5 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and Phase 2: DCR in RET-mutation MTC Participants With Specific RET Gene Status

End point title	Phase 1 and Phase 2: DCR in RET-mutation MTC Participants With Specific RET Gene Status
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End point description:

Oncogenic RET activation has been implicated as a driver in MTC. These rearrangements typically produce chimeric transcripts that encode a fusion protein consisting of the RET kinase domain coupled to a protein with a dimerization domain (e.g., M918T, cysteine rich domain, V804X). RET genotypes were determined by local testing/central analysis of ctDNA. DCR was assessed in participants having specific RET rearrangements. DCR=percentage of participants with a confirmed CR/PR/SD. CR & PR were defined per RECIST as outlined in the description for ORR EP. SD=neither sufficient shrinkage to qualify for CR or PR nor sufficient increase to qualify for PD. PD=at least a 20% increase in SOD of target lesions, taking as reference the smallest SOD on study (including baseline). RAMD population. As prespecified in SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. n=number of participants with specified mutation.

End point type	Secondary
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End point timeframe:

Up to approximately 79.8 months

End point values	RET-mutation MTC With Cabozantinib and/or Vandetanib Treatment	RET-mutation MTC With No Cabozantinib/Vandetanib Treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	72		
Units: percentage of participants				
number (confidence interval 95%)				
M918T(n=41,43)	95.1 (83.5 to 99.4)	90.7 (77.9 to 97.4)		
Cysteine Rich Domain(n=13,25)	92.3 (64.0 to 99.8)	96.0 (79.6 to 99.9)		
V804X(n=2,1)	100 (15.8 to 100)	100 (2.5 to 100)		
Other(n=4,3)	100 (39.8 to 100)	100 (29.2 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and Phase 2: DCR in RET-fusion Positive TC Participants With Specific RET Gene Status

End point title	Phase 1 and Phase 2: DCR in RET-fusion Positive TC Participants With Specific RET Gene Status
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End point description:

Oncogenic RET activation has been implicated as a driver in both MTC & DTC. These rearrangements typically produce chimeric transcripts that encode a fusion protein consisting of RET kinase domain coupled to protein with a dimerization domain(e.g., KIF5B, CCDC6, NCOA4). RET genotypes were determined by local testing/central analysis of ctDNA. DCR was assessed in participants having specific

RET rearrangements. DCR=percentage of participants with confirmed CR/PR/SD. CR & PR were defined per RECIST as outlined in the description for ORR EP. SD=neither sufficient shrinkage to qualify for CR/PR nor sufficient increase to qualify for PD. PD=at least a 20% increase in SOD of target lesions, taking as reference the smallest SOD on study (including baseline). RAMD population. As per SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. n=number of participants with specified mutation. 9999=no participants exhibited the specified mutation.

End point type	Secondary
End point timeframe:	
Up to approximately 79.8 months	

End point values	RET-fusion Positive TC			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: percentage of participants				
number (confidence interval 95%)				
KIF5B(n=0)	9999 (9999 to 9999)			
CCDC6(n=17)	94.1 (71.3 to 99.9)			
NCOA4(n=6)	100 (54.1 to 100)			
Other(n=4)	100 (39.8 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and Phase 2: Duration of Response (DOR) in RET-mutation MTC Participants With Specific RET Gene Status

End point title	Phase 1 and Phase 2: Duration of Response (DOR) in RET-mutation MTC Participants With Specific RET Gene Status
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End point description:

Oncogenic RET activation has been implicated as a driver in MTC. RET genotypes were determined by local testing/central analysis of ctDNA. DOR=time from first documented CR/PR to date of first documented PD/death due to any cause, whichever occurs first. CR, PR and PD were defined per RECIST as outlined in description for ORR EP. DOR was analyzed using the Kaplan-Meier (KM) method. RAMD population. As prespecified in SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. Participants with a response of CR/PR were analyzed. n=number of participants with specified mutation. 9999=upper limit of 95% CI was not estimable due to insufficient number of participants with events. 99999=median & upper limit of 95% CI was not estimable due to insufficient number of participants with events. 999999=median & 95% CI was not estimable due to insufficient number of participants with events. 9999999=no participants exhibited the specified mutation.

End point type	Secondary
End point timeframe:	
Up to approximately 79.8 months	

End point values	RET-mutation MTC With Cabozantinib and/or Vandetanib Treatment	RET-mutation MTC With No Cabozantinib/Vandetanib Treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	56		
Units: months				
median (confidence interval 95%)				
M918T(n=22,32)	18.4 (15.1 to 25.8)	51.8 (40.0 to 9999)		
Cysteine Rich Domain(n=6,22)	29.5 (8.9 to 9999)	36.8 (23.1 to 9999)		
V804X(n=2,0)	21.8 (14.2 to 29.4)	9999999 (9999999 to 9999999)		
Other(n=4,2)	99999 (14.5 to 99999)	999999 (999999 to 999999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and Phase 2: DOR in RET-mutation NSCLC Participants With Specific RET Gene Status

End point title	Phase 1 and Phase 2: DOR in RET-mutation NSCLC Participants With Specific RET Gene Status
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End point description:

Oncogenic RET rearrangements have been identified in 1%–2% of NSCLC. RET genotypes were determined by local testing and/or central analysis of ctDNA. DOR=time from first documented CR/PR to date of first documented PD/death due to any cause, whichever occurs first. CR, PR and PD were defined per RECIST as outlined in description for ORR EP. DOR was analyzed using the KM method. RAMD population. As prespecified in SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. Participants with a response of CR/PR were analyzed. n=number of participants with specified mutation. 9999=upper limit of 95% CI was not estimable due to insufficient number of participants with events. 0.999=lower limit of 95% CI was not estimable due to insufficient number of participants with events. 99999=no participants exhibited the specified mutation.

End point type	Secondary
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End point timeframe:

Up to approximately 79.8 months

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	82	17	83	
Units: months				
median (confidence interval 95%)				

KIF5B (n=58,14,60)	15.1 (8.8 to 34.2)	21.5 (9.3 to 9999)	9.2 (7.4 to 13.4)	
CCDC6 (n=17,34,16)	46.7 (33.7 to 9999)	29.6 (11.3 to 47.9)	0.999 (-9999 to 9999)	
NCOA4 (n=1,0,0)	0.999 (-9999 to 9999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Other (n=6,0,7)	35.2 (10.6 to 9999)	99999 (99999 to 99999)	41.2 (27.9 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and Phase 2: DOR in RET-fusion Positive TC Participants With Specific RET Gene Status

End point title	Phase 1 and Phase 2: DOR in RET-fusion Positive TC Participants With Specific RET Gene Status
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End point description:

Oncogenic RET activation has been implicated as a driver in MTC. RET genotypes were determined by local testing/central analysis of ctDNA. DOR=time from first documented CR or PR to date of first documented PD or death due to any cause, whichever occurs first. CR and PR were defined per RECIST v1.1 as outlined in description for ORR EP. PD was defined as at least a 20% increase in SOD of target lesions, taking as reference smallest SOD on study (including baseline). DOR was analyzed using the KM method. RAMD population. As prespecified in SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. Participants who had a response of CR/PR were analyzed in this outcome measure. n=number of participants with specified mutation. 9999=upper limit of 95% CI was not estimable due to insufficient number of participants with events. 99999=median and upper limit of 95% CI was not estimable due to insufficient number of participants with events.

End point type	Secondary
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End point timeframe:

Up to approximately 79.8 months

End point values	RET-fusion Positive TC			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: months				
median (confidence interval 95%)				
CCDC6(n=14)	99999 (11.2 to 99999)			
NCOA4(n=6)	15.2 (6.9 to 9999)			
Other(n=3)	99999 (23.6 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: DOR

End point title	Phase 2: DOR
End point description:	
DOR was defined as time from first documented response (CR/PR) to the date of first documented PD or death due to any cause, whichever occurs first. CR and PR were defined as per RECIST v1.1 as outlined in description for ORR endpoint. PD was defined as at least a 20% increase in SOD of target lesions, taking as reference smallest SOD on study (including baseline). DOR was analyzed using KM methods. RAMD population. As prespecified in SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. Participants who had a response of CR/PR were analyzed in this endpoint. 9999=upper limit of 95% CI was not estimable due to insufficient number of participants with events. 999 =median & upper limit of 95% CI was not estimable due to insufficient number of participants with events. 0.999 and 999999=95% CI was not estimable due to insufficient number of participants with events.	
End point type	Secondary
End point timeframe:	
Up to approximately 79.8 months	

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment	RET-mutation MTC With Cabozantinib and/or Vandetanib Treatment
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	82	17	83	34
Units: months				
median (confidence interval 95%)	31.8 (15.1 to 40.4)	22.6 (11.1 to 47.9)	13.4 (9.4 to 21.7)	21.7 (15.1 to 34.8)

End point values	RET-mutation MTC With No Cabozantinib/Vandetanib Treatment	RET-fusion Positive TC	RET-fusion Positive Solid Tumors Other Than NSCLC and TC	RET-altered Solid Tumors Previously Treated With RET Inhibitor
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	23	13	4
Units: months				
median (confidence interval 95%)	51.8 (36.8 to 9999)	999 (12.9 to 999)	11.1 (5.5 to 25.1)	99999 (6.0 to 99999)

End point values	RET-mutation Positive Tumors Other Than MTC			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: months				
median (confidence interval 95%)	5.5 (0.999 to 999999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: CBR

End point title

Phase 2: CBR

End point description:

CBR was defined as the percentage of participants with CR or PR, or SD which has been lasting at least 16 weeks (i.e. 4 cycles if 28 days are in one cycle) from the first dose date. CR was defined as the disappearance of all target lesions or any pathological lymph nodes (whether target or non-target) having a reduction in the short axis to <10 mm. PR was defined as at least a 30% decrease in the SOD of all target lesions, taking as reference the baseline SOD, in the absence of CR. SD was defined as neither sufficient shrinkage to qualify for CR or PR nor sufficient increase to qualify for PD. PD was defined as at least a 20% increase in SOD of target lesions, taking as reference the smallest SOD on study (including baseline). CBR and its two-sided 95% CI, which is based on the exact binomial distribution (Clopper-Pearson), were presented. RAMD population. As prespecified in SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis.

End point type

Secondary

End point timeframe:

Up to approximately 79.8 months

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment	RET-mutation MTC With Cabozantinib and/or Vandetanib Treatment
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130	23	106	60
Units: percentage of participants				
number (confidence interval 95%)	74.6 (66.2 to 81.8)	78.3 (56.3 to 92.5)	80.2 (71.3 to 87.3)	80.0 (67.7 to 89.2)

End point values	RET-mutation MTC With No Cabozantinib/Vandetanib Treatment	RET-fusion Positive TC	RET-fusion Positive Solid Tumors Other Than NSCLC and TC	RET-altered Solid Tumors Previously Treated With RET Inhibitor
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	72	27	28	21
Units: percentage of participants				
number (confidence interval 95%)	90.3 (81.0 to 96.0)	85.2 (66.3 to 95.8)	60.7 (40.6 to 78.5)	28.6 (11.3 to 52.2)

End point values	RET-mutation Positive Tumors Other Than MTC			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: percentage of participants				
number (confidence interval 95%)	23.1 (5.0 to 53.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: DCR

End point title	Phase 2: DCR
End point description:	
<p>DCR was defined as the percentage of participants with a confirmed CR/PR, or SD, per RECIST v1.1. CR was defined as the disappearance of all target lesions or any pathological lymph nodes (whether target or non-target) having a reduction in the short axis to <10 mm. PR was defined as at least a 30% decrease in the SOD of all target lesions, taking as reference the baseline SOD, in the absence of CR. SD was defined as neither sufficient shrinkage to qualify for CR or PR nor sufficient increase to qualify for PD. PD was defined as at least a 20% increase in SOD of target lesions, taking as reference the smallest SOD on study (including baseline). DCR and its two-sided 95% CI, which is based on the exact binomial distribution (Clopper-Pearson), were presented. RAMD population. As prespecified in SAP, Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis.</p>	
End point type	Secondary
End point timeframe:	
Up to approximately 79.8 months	

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment	RET-mutation MTC With Cabozantinib and/or Vandetanib Treatment
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130	23	106	60
Units: percentage of participants				
number (confidence interval 95%)	91.5 (85.4 to 95.7)	91.3 (72.0 to 98.9)	89.6 (82.2 to 94.7)	95.0 (86.1 to 99.0)

End point values	RET-mutation MTC With No Cabozantinib/Vandetanib	RET-fusion Positive TC	RET-fusion Positive Solid Tumors Other Than NSCLC	RET-altered Solid Tumors Previously Treated With
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	Treatment		and TC	RET Inhibitor
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	72	27	28	21
Units: percentage of participants				
number (confidence interval 95%)	93.1 (84.5 to 97.7)	96.3 (81.0 to 99.9)	75.0 (55.1 to 89.3)	42.9 (21.8 to 66.0)

End point values	RET-mutation Positive Tumors Other Than MTC			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: percentage of participants				
number (confidence interval 95%)	69.2 (38.6 to 90.9)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Phase 2: Progression-free Survival (PFS)
End point description:	
<p>PFS was defined as the time from the first dose of pralsetinib to the date of first documented PD or death due to any cause, whichever occurred first. PD was defined as at least a 20% increase in SOD of target lesions, taking as reference the smallest SOD on study (including baseline). PFS was analyzed using KM methods. Efficacy population included all participants who have been exposed to at least one dose of the study drug at the RP2D. As pre-specified in the SAP, PFS was to be assessed in participants with RET-fusion positive NSCLC, RET-mutation MTC, RET-fusion TC, and RET-fusion solid tumors other than NSCLC and TC. Hence, only the data for these arms is presented here. Number analyzed is the number of participants with data available for analysis. 9999=upper limit of 95% CI was not estimable due to insufficient number of participants with events. 99999=median & upper limit of 95% CI was not estimable due to insufficient number of participants with events.</p>	
End point type	Secondary
End point timeframe:	
Up to approximately 7 years	

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment	RET-mutation MTC With Cabozantinib and/or Vandetanib Treatment
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	141	24	116	67
Units: months				
median (confidence interval 95%)	16.4 (11.4 to 23.5)	13.0 (9.3 to 35.1)	12.1 (9.2 to 16.6)	24.9 (19.9 to 35.0)

End point values	RET-mutation MTC With No Cabozantinib/Vandetanib Treatment	RET-fusion Positive TC	RET-fusion Positive Solid Tumors Other Than NSCLC and TC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	78	31	28	
Units: months				
median (confidence interval 95%)	55.3 (37.2 to 9999)	99999 (14.7 to 99999)	7.0 (3.9 to 12.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Overall Survival (OS)

End point title	Phase 2: Overall Survival (OS)
End point description:	
<p>OS was defined as the time from the first dose of pralsetinib to the date of death due to any causes. Efficacy population included all participants who have been exposed to at least one dose of the study drug at the RP2D. As pre-specified in the SAP, OS was to be assessed in participants with RET-fusion positive NSCLC, RET-mutation MTC, RET-fusion TC, and RET-fusion solid tumors other than NSCLC and TC. Hence, only the data for these arms is presented here. 9999=upper limit of 95% CI was not estimable due to insufficient number of participants with events. 99999=median and 95% CI was not estimable due to insufficient number of participants with events. 999999=median and upper limit of 95% CI was not estimable due to insufficient number of participants with events.</p>	
End point type	Secondary
End point timeframe:	
Up to approximately 7 years	

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment	RET-mutation MTC With Cabozantinib and/or Vandetanib Treatment
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	141	24	116	67
Units: months				
median (confidence interval 95%)	39.7 (27.8 to 53.2)	46.0 (19.1 to 62.4)	50.1 (28.3 to 9999)	42.2 (31.2 to 9999)

End point values	RET-mutation MTC With No Cabozantinib/Vandetanib	RET-fusion Positive TC	RET-fusion Positive Solid Tumors Other Than NSCLC	

	Treatment		and TC
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	78	31	29
Units: months			
median (confidence interval 95%)	99999 (99999 to 99999)	999999 (19.4 to 999999)	10.3 (6.8 to 25.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Intracranial ORR in RET-fusion Positive NSCLC Central Nervous System (CNS) Metastases Participants

End point title	Phase 2: Intracranial ORR in RET-fusion Positive NSCLC Central Nervous System (CNS) Metastases Participants
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End point description:

ORR=percentage of participants with CR/PR for at least 2 assessments, ≥ 28 days apart, with no PD in between. CR=disappearance of all target CNS/brain lesions (including brainstem/cerebellum) and non-target lesions identified at baseline, with no new CNS/brain lesions. PR=at least 30% decrease in the SOD of any CNS/brain lesion identified as RECIST 1.1 target lesions, with no progression of non-target CNS/brain lesions or new lesions. PD= $\geq 20\%$ increase in the SOD of target CNS/brain lesions, with a reference to the smallest sum on study, or unequivocal progression of non-target lesions or new lesions. RAMD population. As specified in the SAP, ORR was to be assessed in RET-fusion CNS metastases sub-population (participants with CNS metastases) only. Hence only NSCLC arms are presented here. Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. -0.9999 & 9999=95% CI was not estimable due to insufficient number of participants with events.

End point type	Secondary
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End point timeframe:

Up to approximately 79.8 months

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	1	1
Units: percentage of participants			
number (confidence interval 95%)	53.8 (25.1 to 80.8)	100 (2.5 to 100)	0 (-0.9999 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Intracranial CBR in RET-fusion Positive NSCLC CNS Metastases Participants

End point title	Phase 2: Intracranial CBR in RET-fusion Positive NSCLC CNS
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End point description:

CBR=percentage of participants with CR/PR/SD lasting ≥ 16 weeks from 1st dose date.

CR=disappearance of all target CNS/brain lesions (including brainstem/cerebellum) & non-target lesions identified at baseline, with no new CNS/brain lesions. PR=at least 30% decrease in SOD of any CNS/brain lesion identified as RECIST 1.1 target lesions, with no progression of non-target CNS/brain lesions/new lesions. SD=neither sufficient shrinkage for PR or increase for PD for target/non-target CNS/brain lesion, with reference to smallest SOD on study. PD= $\geq 20\%$ increase in SOD of target CNS/brain lesions, with a reference to smallest sum on study/unequivocal progression of non-target lesions/new lesions. As specified in SAP, CBR was in RET-fusion CNS metastases sub-population only. Hence only NSCLC arms are presented here. Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants. -0.9999 and 9999=95% CI was not estimable due to insufficient number of participants with events.

End point type Secondary

End point timeframe:

Up to approximately 79.8 months

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	13	1	1	
Units: percentage of participants				
number (confidence interval 95%)	61.5 (31.6 to 86.1)	100 (2.5 to 100)	0 (-0.9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Intracranial DCR in RET-fusion Positive NSCLC CNS Metastases Participants

End point title Phase 2: Intracranial DCR in RET-fusion Positive NSCLC CNS Metastases Participants

End point description:

DCR=percentage of participants with a confirmed CR/PR, or SD. CR=disappearance of all target CNS/brain lesions (including brainstem/cerebellum) & non-target lesions identified at baseline, with no new CNS/brain lesions. PR=at least 30% decrease in SOD of any CNS/brain lesion identified as RECIST 1.1 target lesions, with no progression of non-target CNS/brain lesions/new lesions. SD=neither sufficient shrinkage for PR or increase for PD for target/non-target CNS/brain lesion, with reference to smallest SOD on study. PD= $\geq 20\%$ increase in SOD of target CNS/brain lesions, reference to smallest sum on study/unequivocal progression of non-target lesions/new lesions. As specified in SAP, DCR was assessed in RET-fusion CNS metastases sub-population (participants with CNS metastases) only. Hence only NSCLC arms are presented. Phase 1 participants treated at 400 mg are pooled with Phase 2 participants. -0.9999&9999=95% CI was not estimable due to insufficient number of participants with events.

End point type Secondary

End point timeframe:

Up to approximately 79.8 months

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	13	1	1	
Units: percentage of participants				
number (confidence interval 95%)	76.9 (46.2 to 95.0)	100 (2.5 to 100)	0 (-0.9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Intracranial DOR in RET-fusion Positive NSCLC CNS Metastases Participants

End point title	Phase 2: Intracranial DOR in RET-fusion Positive NSCLC CNS Metastases Participants
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End point description:

DOR=time from first documented CR/PR to the date of first documented PD/death due to any cause, whichever occurs first. CR and PR were defined per RECIST as outlined in the description for endpoint 23. PD=either at least 20% increase in SOD of target CNS/brain lesion, taking as reference smallest sum on study. Unequivocal progression of any CNS/brain lesion nontarget lesions at baseline, or identification of new CNS/brain lesion. DOR was analyzed using the KM methods. RAMD population. As specified in SAP, DOR was to be assessed in RET-fusion CNS metastases sub-population only. Hence only NSCLC arms are presented here. Participants with a CR/PR were assessed for this OM. Phase 1 participants treated at 400 mg QD are pooled with Phase 2 participants for efficacy analysis. 9999=upper limit of 95% CI was not estimable due to insufficient number of participants with events. -0.9999=lower limit of 95% CI was not estimable due to insufficient number of participants with events.

End point type	Secondary
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End point timeframe:

Up to approximately 79.8 months

End point values	RET- fusion Positive NSCLC With Prior Platinum Treatment	RET-fusion Positive NSCLC With Non-platinum Systemic Treatment	RET-fusion NSCLC With No Prior Systemic/Platinum Treatment	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	7	1	0 ^[5]	
Units: months				
median (confidence interval 95%)	28.3 (10.5 to 9999)	11.3 (-0.9999 to 9999)	(to)	

Notes:

[5] - No participants in this arm exhibited a CR/PR.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Maximum Plasma Concentration (Cmax)

End point title Phase 1: Maximum Plasma Concentration (Cmax)^[6]

End point description:

Pharmacokinetic (PK)-evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. n=number of participants with data available for analysis at the specified timepoint. 9999=Values were LTR for 1 participant. Since data was evaluable only for 1 participant geometric co-efficient of variation was not evaluable. 99999=Since data was available only for 1 participant geometric co-efficient of variation was not evaluable.

End point type Secondary

End point timeframe:

Predose on 0.5, 1, 2, 4, 6, 8 and 24 hours postdose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was planned to report PK data for Phase I of the study.

End point values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg	Phase I: Pralsetinib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	5	13
Units: nanograms per milliliters (ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1(n=2,6,5,13,11,12,4,6,3)	346 (± 9999)	335 (± 52.8)	198 (± 99.8)	459 (± 52.3)
Cycle 1 Day 15(n=1,6,3,12,9,10,2,5,2)	130 (± 99999)	420 (± 56.9)	586 (± 47.8)	525 (± 72.5)

End point values	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	4	6
Units: nanograms per milliliters (ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1(n=2,6,5,13,11,12,4,6,3)	688 (± 53.3)	1210 (± 85.3)	1820 (± 63.8)	569 (± 42.0)
Cycle 1 Day 15(n=1,6,3,12,9,10,2,5,2)	1390 (± 35.3)	1930 (± 66.7)	4330 (± 9999)	1080 (± 43.8)

End point values	Phase I: Pralsetinib 200/100 mg			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: nanograms per milliliters (ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1(n=2,6,5,13,11,12,4,6,3)	715 (± 64.1)			
Cycle 1 Day 15(n=1,6,3,12,9,10,2,5,2)	1780 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Time to Maximum Plasma Concentration (Tmax)

End point title	Phase 1: Time to Maximum Plasma Concentration (Tmax) ^[7]
End point description:	PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. n=number of participants with data available for analysis at the specified timepoint.
End point type	Secondary
End point timeframe:	Predose on 0.5, 1, 2, 4, 6, 8 and 24 hours postdose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was planned to report PK data for Phase I of the study.

End point values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg	Phase I: Pralsetinib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	5	13
Units: hour				
median (full range (min-max))				
Cycle 1 Day 1(n=2,6,5,13,11,12,4,6,3)	3.04 (2.08 to 4.00)	2.04 (1.98 to 4.00)	2.03 (2.00 to 6.03)	2.07 (0.983 to 7.98)
Cycle 1 Day 15(n=1,6,3,12,9,10,2,5,2)	1.87 (1.87 to 1.87)	2.00 (1.97 to 4.13)	3.97 (3.90 to 4.00)	2.97 (1.05 to 4.08)

End point values	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	4	6
Units: hour				
median (full range (min-max))				
Cycle 1 Day 1(n=2,6,5,13,11,12,4,6,3)	2.02 (1.72 to 7.90)	3.00 (2.00 to 6.03)	2.00 (2.00 to 2.00)	12.5 (12.2 to 14.8)

Cycle 1 Day 15(n=1,6,3,12,9,10,2,5,2)	2.23 (0.983 to 24.0)	3.03 (2.00 to 7.85)	6.00 (4.00 to 8.00)	2.00 (0.500 to 3.95)
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End point values	Phase I: Pralsetinib 200/100 mg			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: hour				
median (full range (min-max))				
Cycle 1 Day 1(n=2,6,5,13,11,12,4,6,3)	12.0 (2.07 to 12.3)			
Cycle 1 Day 15(n=1,6,3,12,9,10,2,5,2)	4.03 (1.98 to 6.08)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Time of Last Quantifiable Plasma Drug Concentration (Tlast)

End point title	Phase 1: Time of Last Quantifiable Plasma Drug Concentration (Tlast) ^[8]
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End point description:

PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. n=number of participants with data available for analysis at the specified timepoint.

End point type	Secondary
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End point timeframe:

Predose on 0.5, 1, 2, 4, 6, 8 and 24 hours postdose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was planned to report PK data for Phase I of the study.

End point values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg	Phase I: Pralsetinib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	5	13
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1(n=2,6,5,13,11,12,4,6,3)	24.0 (24.0 to 24.0)	24.0 (23.1 to 24.4)	24.0 (7.88 to 24.1)	24.0 (21.9 to 25.7)
Cycle 1 Day 15(n=1,6,3,12,9,10,2,5,2)	23.8 (23.8 to 23.8)	24.1 (23.9 to 24.4)	24.3 (23.6 to 27.8)	24.0 (8.00 to 26.6)

End point values	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg
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Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	4	6
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1(n=2,6,5,13,11,12,4,6,3)	23.8 (7.88 to 24.0)	23.8 (22.6 to 24.6)	23.9 (23.4 to 24.0)	12.5 (12.2 to 14.8)
Cycle 1 Day 15(n=1,6,3,12,9,10,2,5,2)	24.0 (22.2 to 24.8)	24.0 (7.38 to 25.4)	24.1 (24.0 to 24.2)	12.2 (7.88 to 15.7)

End point values	Phase I: Pralsetinib 200/100 mg			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1(n=2,6,5,13,11,12,4,6,3)	12.3 (12.0 to 14.4)			
Cycle 1 Day 15(n=1,6,3,12,9,10,2,5,2)	12.5 (10.1 to 14.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Area Under the Plasma Concentration Versus Time Curve From Time 0 to 24 Hours Postdose (AUC0-24)

End point title	Phase 1: Area Under the Plasma Concentration Versus Time Curve From Time 0 to 24 Hours Postdose (AUC0-24) ^[9]
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End point description:

PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analysed is the number of participants with data available for analysis. 9999=Values were LTR for 1 participant. Since data was evaluable only for 1 participant geometric co-efficient of variation was not evaluable.

End point type	Secondary
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End point timeframe:

24 hours postdose on Day 1 (1 cycle = 28 days)

Notes:

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

Justification: This endpoint was planned to report PK data for Phase I of the study.

End point values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg	Phase I: Pralsetinib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	3	11
Units: hours-nanograms/milliliters(hr-ng/mL)				
geometric mean (geometric coefficient of variation)	4450 (± 9999)	3620 (± 50.8)	3010 (± 84.8)	5260 (± 46.2)

End point values	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	8	3	0 ^[10]
Units: hours-nanograms/milliliters(hr- ng/mL)				
geometric mean (geometric coefficient of variation)	8470 (± 54.5)	14700 (± 60.3)	27700 (± 94.1)	()

Notes:

[10] - No participants in this arm were available for PK analysis.

End point values	Phase I: Pralsetinib 200/100 mg			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[11]			
Units: hours-nanograms/milliliters(hr- ng/mL)				
geometric mean (geometric coefficient of variation)	()			

Notes:

[11] - No participants in this arm were available for PK analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Plasma Drug Concentration at 24 Hours Postdose (C24hr)

End point title	Phase 1: Plasma Drug Concentration at 24 Hours Postdose (C24hr) ^[12]
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End point description:

PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analysed is the number of participants with data available for analysis. n=number of participants with data available for analysis at the specified timepoint. 9999=Values were LTR for 1 participant. Since data was evaluable only for 1 participant geometric co-efficient of variation was not evaluable. 99999=since data was available only for 1 participant geometric co-efficient of variation was not evaluable.

End point type	Secondary
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End point timeframe:

24 hours postdose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)

Notes:

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

Justification: This endpoint was planned to report PK data for Phase I of the study.

End point values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg	Phase I: Pralsetinib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	3	11
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 (n=2,6,3,11,6,8,3,0,0)	110 (± 9999)	69.2 (± 81.0)	65.8 (± 59.6)	104 (± 76.6)
Cycle 1 Day 15 (n=1,6,3,10,9,8,2,0,0)	55.9 (± 99999)	94.2 (± 123)	175 (± 31.3)	137 (± 132)

End point values	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	8	3	0 ^[13]
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 (n=2,6,3,11,6,8,3,0,0)	221 (± 64.2)	376 (± 74.1)	715 (± 75.9)	()
Cycle 1 Day 15 (n=1,6,3,10,9,8,2,0,0)	713 (± 42.2)	977 (± 107)	1950 (± 9999)	()

Notes:

[13] - No participants in this arm were available for PK analysis.

End point values	Phase I: Pralsetinib 200/100 mg			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[14]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 (n=2,6,3,11,6,8,3,0,0)	()			
Cycle 1 Day 15 (n=1,6,3,10,9,8,2,0,0)	()			

Notes:

[14] - No participants in this arm were available for PK analysis.

Statistical analyses

No statistical analyses for this end point

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

End point title	Phase 1: Apparent Volume of Distribution (V _z /F) ^[15]
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End point description:

PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analysed is the number of participants with data available for analysis. n=number of participants with data available for analysis at the specified timepoint. 9999=Values were LTR for 1 participant. Since data was evaluable only for 1 participant geometric co-efficient of variation was not evaluable. 99999=since data was available only for 1 participant geometric co-efficient of variation was not evaluable.

End point type	Secondary
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End point timeframe:

Predose on 0.5, 1, 2, 4, 6, 8 and 24 hours postdose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)

Notes:

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

Justification: This endpoint was planned to report PK data for Phase I of the study.

End point values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg	Phase I: Pralsetinib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	5	3	10
Units: liters				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1(n=2,5,3,10,5,7,3,0,0)	96.1 (± 9999)	230 (± 37.1)	458 (± 125)	499 (± 50.8)
Cycle 1 Day 15(1,4,3,9,5,5,1,0,0)	355 (± 99999)	171 (± 176)	232 (± 43.7)	622 (± 67.3)

End point values	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	3	0 ^[16]
Units: liters				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1(n=2,5,3,10,5,7,3,0,0)	543 (± 82.6)	430 (± 62.6)	350 (± 115)	()
Cycle 1 Day 15(1,4,3,9,5,5,1,0,0)	367 (± 86.6)	418 (± 19.9)	181 (± 99999)	()

Notes:

[16] - No participants in this arm were available for PK analysis.

End point values	Phase I: Pralsetinib 200/100 mg			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[17]			
Units: liters				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1(n=2,5,3,10,5,7,3,0,0)	()			
Cycle 1 Day 15(1,4,3,9,5,5,1,0,0)	()			

Notes:

[17] - No participants in this arm were available for PK analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Terminal Elimination Halflife (t_{1/2})

End point title Phase 1: Terminal Elimination Halflife (t_{1/2})^[18]

End point description:

PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analysed is the number of participants with data available for analysis. n=number of participants with data available for analysis at the specified timepoint. 9999=No participants with data available at the specified timepoint.

End point type	Secondary
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End point timeframe:

Predose on 0.5, 1, 2, 4, 6, 8 and 24 hours postdose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)

Notes:

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

Justification: This endpoint was planned to report PK data for Phase I of the study.

End point values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg	Phase I: Pralsetinib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	5	3	10
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1 (n=2,5,3,10,5,7,3,0,1)	16.3 (11.8 to 20.8)	9.87 (8.98 to 18.3)	14.3 (8.12 to 31.5)	12.6 (6.69 to 34.9)
Cycle 1 Day 15(n=1,4,3,9,5,5,1,0,0)	17.6 (17.6 to 17.6)	8.10 (5.25 to 39.6)	13.4 (12.5 to 14.4)	13.2 (10.1 to 21.8)

End point values	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	3	0 ^[19]
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1 (n=2,5,3,10,5,7,3,0,1)	12.2 (9.53 to 34.5)	16.5 (10.2 to 48.7)	19.7 (12.8 to 36.1)	(to)
Cycle 1 Day 15(n=1,4,3,9,5,5,1,0,0)	20.4 (9.91 to 27.3)	20.9 (9.21 to 33.6)	13.0 (13.0 to 13.0)	(to)

Notes:

[19] - No participants in this arm were available for PK analysis.

End point values	Phase I: Pralsetinib 200/100 mg			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1 (n=2,5,3,10,5,7,3,0,1)	10.7 (10.7 to 10.7)			
Cycle 1 Day 15(n=1,4,3,9,5,5,1,0,0)	9999 (9999 to 9999)			

Statistical analyses

No statistical analyses for this end point

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

End point title Phase 1: Apparent Oral Clearance (CL/F)^[20]

End point description:

PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analysed is the number of participants with data available for analysis. n=number of participants with data available for analysis at the specified timepoint. 9999=Values were LTR for 1 participant. Since data was evaluable only for 1 participant geometric co-efficient of variation was not evaluable. 99999=Since data was available only for 1 participant geometric co-efficient of variation was not evaluable.

End point type Secondary

End point timeframe:

Predose on 0.5, 1, 2, 4, 6, 8 and 24 hours postdose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)

Notes:

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

Justification: This endpoint was planned to report PK data for Phase I of the study.

End point values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg	Phase I: Pralsetinib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	3	10
Units: liters per hour (L/hr)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1(n=2,5,3,10,5,7,3,0,0)	4.26 (± 9999)	14.7 (± 42.3)	20.6 (± 48.1)	27.3 (± 60.3)
Cycle 1 Day 15(n=1,6,3,10,9,8,2,0,0)	14.0 (± 99999)	11.3 (± 51.2)	12.0 (± 38.9)	31.4 (± 97.8)

End point values	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	8	3	0 ^[21]
Units: liters per hour (L/hr)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1(n=2,5,3,10,5,7,3,0,0)	23.3 (± 40.2)	15.2 (± 88.1)	11.6 (± 81.3)	()
Cycle 1 Day 15(n=1,6,3,10,9,8,2,0,0)	13.2 (± 33.0)	11.1 (± 72.2)	8.57 (± 9999)	()

Notes:

[21] - No participants in this arm were available for PK analysis.

End point values	Phase I: Pralsetinib 200/100 mg			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[22]			
Units: liters per hour (L/hr)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1(n=2,5,3,10,5,7,3,0,0)	()			
Cycle 1 Day 15(n=1,6,3,10,9,8,2,0,0)	()			

Notes:

[22] - No participants in this arm were available for PK analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Accumulation Ratio for Cmax (RCmax)

End point title	Phase 1: Accumulation Ratio for Cmax (RCmax) ^[23]
End point description:	PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analyzed is the number of participants with data available for analysis. 9999=Since data was available only for 1 participant geometric co-efficient of variation was not evaluable. 99999=Values were LTR for 1 participant. Since data was evaluable only for 1 participant geometric co-efficient of variation was not evaluable.
End point type	Secondary
End point timeframe:	24 hours postdose on Day 15 of Cycle 1 (1 cycle = 28 days)

Notes:

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

Justification: This endpoint was planned to report PK data for Phase I of the study.

End point values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg	Phase I: Pralsetinib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	6	3	12
Units: ratio				
geometric mean (geometric coefficient of variation)	1.04 (± 9999)	1.25 (± 27.6)	3.20 (± 114)	1.17 (± 110)

End point values	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	2	4
Units: ratio				
geometric mean (geometric coefficient of variation)	1.87 (± 40.5)	1.62 (± 102)	2.97 (± 99999)	1.91 (± 40.7)

End point values	Phase I: Pralsetinib 200/100 mg			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: ratio				
geometric mean (geometric coefficient of variation)	1.41 (\pm 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Accumulation Ratio for AUC (RAUC)

End point title	Phase 1: Accumulation Ratio for AUC (RAUC) ^[24]
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End point description:

PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analysed is the number of participants with data available for analysis. 9999=since data was available only for 1 participant geometric co-efficient of variation was not evaluable. 99999=Values were LTR for 1 participant. Since data was evaluable only for 1 participant geometric co-efficient of variation was not evaluable.

End point type	Secondary
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End point timeframe:

24 hours postdose on Day 15 of Cycle 1 (1 cycle = 28 days)

Notes:

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

Justification: This endpoint was planned to report PK data for Phase I of the study.

End point values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg	Phase I: Pralsetinib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	6	1	8
Units: ratio				
geometric mean (geometric coefficient of variation)	1.43 (\pm 9999)	1.47 (\pm 11.1)	3.22 (\pm 9999)	1.31 (\pm 147)

End point values	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	1	2
Units: ratio				
geometric mean (geometric coefficient of variation)	2.33 (\pm 11.4)	2.75 (\pm 70.9)	2.48 (\pm 9999)	4.28 (\pm 99999)

End point values	Phase I: Pralsetinib 200/100 mg			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: ratio				
geometric mean (geometric coefficient of variation)	1.21 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Cmax

End point title	Phase 2: Cmax
End point description:	PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analysed is the number of participants with data available for analysis. n=number of participants with data available for analysis at the specified timepoint.
End point type	Secondary
End point timeframe:	Pre-dose on 0.5, 1, 2, 4, 6, 8 and 24 hours post-dose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)

End point values	RET- fusion Positive NSCLC Participants	Tumor-agnostic Participants	RET-altered Solid Tumors Participants	RET-mutation Positive Tumors other than MTC Participants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	98	5	3	4
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1(n=98,5,0,3,4)	1680 (± 69.4)	1380 (± 65.4)	2450 (± 164)	1770 (± 87.2)
Cycle 1 Day 15(n=87,5,0,3,4)	2840 (± 50.7)	2200 (± 36.7)	3440 (± 93.9)	2430 (± 55.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Tmax

End point title	Phase 2: Tmax
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End point description:

PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analysed is the number of participants with data available for analysis. n=number of participants with data available for analysis at the specified timepoint.

End point type Secondary

End point timeframe:

Predose on 0.5, 1, 2, 4, 6, 8 and 24 hours postdose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)

End point values	RET- fusion Positive NSCLC Participants	Tumor-agnostic Participants	RET-altered Solid Tumors Participants	RET-mutation Positive Tumors other than MTC Participants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	98	5	3	4
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1(n=98,5,0,3,4)	4.00 (1.90 to 23.7)	3.90 (2.0 to 6.0)	4.0 (4.0 to 6.0)	2.05 (2 to 8)
Cycle 1 Day 15(n=87,5,0,3,4)	4.00 (1.00 to 8.10)	5.00 (2.0 to 8.0)	4.00 (2.00 to 6.00)	3.05 (2 to 6)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Tlast

End point title Phase 2: Tlast

End point description:

PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analysed is the number of participants with data available for analysis. n=number of participants with data available for analysis at the specified timepoint.

End point type Secondary

End point timeframe:

Predose on 0.5, 1, 2, 4, 6, 8 and 24 hours postdose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)

End point values	RET- fusion Positive NSCLC Participants	Tumor-agnostic Participants	RET-altered Solid Tumors Participants	RET-mutation Positive Tumors other than MTC Participants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	98	5	3	4
Units: hours				
median (full range (min-max))				

Cycle 1 Day 1(n=98,5,0,3,4)	23.9 (2.40 to 24.8)	8.00 (7.8 to 23.5)	23.10 (8.0 to 24.0)	8.05 (8.0 to 24.0)
Cycle 1 Day 15(n=87,5,0,3,4)	23.8 (7.80 to 26.5)	23.70 (7.9 to 24.0)	24.00 (7.9 to 24.0)	24.00 (23.8 to 24.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: AUC0-24

End point title	Phase 2: AUC0-24
End point description:	
PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analysed is the number of participants with data available for analysis. n=number of participants with data available for analysis at the specified timepoint. 9999=Since data was available only for 1 participant geometric co-efficient of variation was not evaluable.	
End point type	Secondary
End point timeframe:	
24 hours postdose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)	

End point values	RET- fusion Positive NSCLC Participants	Tumor-agnostic Participants	RET-altered Solid Tumors Participants	RET-mutation Positive Tumors other than MTC Participants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	70	3	2	4
Units: hr-ng/ mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 (n=70,2,0,1,3)	20400 (± 64.2)	17400 (± 152)	103000 (± 9999)	18400 (± 69.8)
Cycle 1 Day 15(n=50,3,0,2,4)	40100 (± 59.5)	33900 (± 27.4)	91100 (± 46.8)	32000 (± 90.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: C24hr

End point title	Phase 2: C24hr
End point description:	
PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analysed is the number of participants with data available for analysis. n=number of participants with data available for analysis at the specified timepoint.	
End point type	Secondary

End point timeframe:

24 hours postdose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)

End point values	RET- fusion Positive NSCLC Participants	Tumor-agnostic Participants	RET-altered Solid Tumors Participants	RET-mutation Positive Tumors other than MTC Participants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	92	5	3	4
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1(n=92,5,0,3,3)	540 (± 75.4)	519 (± 197)	1020 (± 225)	415 (± 140)
Cycle 1 Day 15(n=82,5,0,2,4)	1150 (± 69)	797 (± 42.8)	1400 (± 207)	1050 (± 94.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: t_{1/2}

End point title	Phase 2: t _{1/2}
End point description:	PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analysed is the number of participants with data available for analysis. n=number of participants with data available for analysis at the specified timepoint. 9999=since data was available only for 1 participant geometric co-efficient of variation was not evaluable.
End point type	Secondary
End point timeframe:	Pre-dose on 0.5, 1, 2, 4, 6, 8 and 24 hours postdose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)

End point values	RET- fusion Positive NSCLC Participants	Tumor-agnostic Participants	RET-altered Solid Tumors Participants	RET-mutation Positive Tumors other than MTC Participants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	2	1	3
Units: hours				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1(n=57,2,0,1,3)	13.4 (± 44.1)	18.4 (± 98.8)	20.8 (± 9999)	11.0 (± 55.8)
Cycle 1 Day 15(n=47,2,0,1,2)	17.9 (± 58.8)	16.5 (± 44.6)	25.8 (± 9999)	63.0 (± 882)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: CL/F

End point title Phase 2: CL/F

End point description:

PK evaluable population included all participants who received at least one dose of pralsetinib and from whom at least one post dose PK sample was collected. Number analysed is the number of participants with data available for analysis. n=number of participants with data available for analysis at the specified timepoint. 9999=since data was available only for 1 participant geometric co-efficient of variation was not evaluable.

End point type Secondary

End point timeframe:

Pre-dose on 0.5, 1, 2, 4, 6, 8 and 24 hours post-dose on Days 1 and 15 of Cycle 1 (1 cycle = 28 days)

End point values	RET- fusion Positive NSCLC Participants	Tumor-agnostic Participants	RET-altered Solid Tumors Participants	RET-mutation Positive Tumors other than MTC Participants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	47	2	1	3
Units: liters per hour (L/hr)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1(n=30,2,0,1,3)	13.4 (± 56.8)	12.7 (± 347)	2.00 (± 9999)	16.1 (± 43.3)
Cycle 1 Day 15(n=47,2,0,1,2)	9.91 (± 58.9)	7.49 (± 64.4)	2.92 (± 9999)	1.39 (± 1220)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Percent Change From Baseline in Dual Specificity Phosphatase 6 (DUSP6)

End point title Phase 1: Percent Change From Baseline in Dual Specificity Phosphatase 6 (DUSP6)^[25]

End point description:

The dose dependent change in a mitogen-activated protein kinases (MAPK) pathway expression signature was analyzed for all available samples of MTC and NSCLC participants. Participants with archived sample (used as baseline) and on treatment Cycle 2 Day 1 (1 cycle = 28 days) tumor tissues with greater than 20% tumor cells are included in the analysis. The changes in tumor biomarker DUSP6 levels was explored. Safety Population included all participants who have received at least 1 dose of the study drug regardless of starting dose levels. Participants are presented per the planned treatment arm for this endpoint.

End point type Secondary

End point timeframe:

Baseline, Week 4

Notes:

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

Justification: This endpoint was planned to report data for Phase I of the study only. Hence, Phase II arm is not included.

End point values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg	Phase I: Pralsetinib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	5	13
Units: percent change				
arithmetic mean (standard deviation)	0 (± 0)	54.26 (± 88.318)	0 (± 0)	-20.27 (± 42.971)

End point values	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	4	5
Units: percent change				
arithmetic mean (standard deviation)	-74.87 (± 15.707)	-13.32 (± 82.394)	0 (± 0)	-81.57 (± 3.057)

End point values	Phase I: Pralsetinib 200/100 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: percent change				
arithmetic mean (standard deviation)	-61.96 (± 39.141)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Percent Change From Baseline in Sprout Receptor Tyrosine Kinase Signaling Antagonist 4 (SPRY4)

End point title	Phase 1: Percent Change From Baseline in Sprout Receptor Tyrosine Kinase Signaling Antagonist 4 (SPRY4) ^[26]
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End point description:

The dose dependent change in a MAPK pathway expression signature was analyzed for all available samples of MTC and NSCLC participants. Participants with archived sample (used as baseline) and on treatment Cycle 2 Day 1 (1 cycle = 28 days) tumor tissues with greater than 20% tumor cells are included in the analysis. The changes in tumor biomarker SPRY4 levels was explored. Safety Population included all participants who have received at least 1 dose of the study drug regardless of starting dose levels. Participants are presented per the planned treatment arm for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline, Week 4

Notes:

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

Justification: This endpoint was planned to report data for Phase I of the study only. Hence, Phase II arm is not included.

End point values	Phase I: Pralsetinib 30 mg	Phase I: Pralsetinib 60 mg	Phase I: Pralsetinib 100 mg	Phase I: Pralsetinib 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	5	13
Units: percent change				
arithmetic mean (standard deviation)	0 (± 0)	210.16 (± 309.468)	0 (± 0)	-34.98 (± 29.569)

End point values	Phase I: Pralsetinib 300 mg	Phase I: Pralsetinib 400 mg	Phase I: Pralsetinib 600 mg	Phase I: Pralsetinib 100/100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	4	5
Units: percent change				
arithmetic mean (standard deviation)	-69.00 (± 28.731)	-3.26 (± 99.349)	0 (± 0)	-75.65 (± 10.944)

End point values	Phase I: Pralsetinib 200/100 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: percent change				
arithmetic mean (standard deviation)	124.93 (± 311.210)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs: From Cycle 1 Day 1 up to 30 days after the final dose of study drug (up to approximately 6.7 years)

All-cause Mortality: Up to approximately 7 years

Adverse event reporting additional description:

Safety Population included all participants who have received at least 1 dose of the study drug regardless of starting dose levels.

As pre-specified in the SAP, safety data was to be analyzed and reported as per the pre-planned grouped dose level II (SAP section 3.6.5.2). Hence, per dose safety data is not presented for this study.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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Reporting groups

Reporting group title	Pralsetinib ≤ 300 mg QD
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Reporting group description:

Participants received pralsetinib, 300 mg or less, orally, QD until discontinuation due to toxicity, disease progression, or other reasons.

Reporting group title	Pralsetinib All Doses
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Reporting group description:

Participants received pralsetinib at varying doses at the QD and BID schedule until discontinuation due to toxicity, disease progression, or other reasons.

Reporting group title	Pralsetinib BID Dosing Schedule
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Reporting group description:

Participants received pralsetinib, 100 mg, orally, BID or 200 mg in the morning and then 100 mg in the evening, orally, until discontinuation due to toxicity, disease progression, or other reasons.

Reporting group title	Pralsetinib 400 mg QD
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Reporting group description:

Participants received pralsetinib, 400 mg, orally, QD until discontinuation due to toxicity, disease progression, or other reasons.

Serious adverse events	Pralsetinib ≤ 300 mg QD	Pralsetinib All Doses	Pralsetinib BID Dosing Schedule
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 37 (70.27%)	416 / 590 (70.51%)	7 / 9 (77.78%)
number of deaths (all causes)	15	268	7
number of deaths resulting from adverse events	0	10	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Gallbladder cancer			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung cancer metastatic			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 0
Anaplastic large-cell lymphoma			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Bone neoplasm			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Brain neoplasm			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Cancer pain			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Medullary thyroid cancer			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 0
Non-small cell lung cancer			

subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Neoplasm progression			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Neoplasm malignant			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Metastatic neoplasm			
subjects affected / exposed	0 / 37 (0.00%)	7 / 590 (1.19%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Metastasis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Metastases to liver			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Metastases to central nervous system			
subjects affected / exposed	0 / 37 (0.00%)	6 / 590 (1.02%)	0 / 9 (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
Lung neoplasm malignant			
subjects affected / exposed	1 / 37 (2.70%)	27 / 590 (4.58%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 31	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 22	0 / 0
Malignant neoplasm progression			

subjects affected / exposed	1 / 37 (2.70%)	5 / 590 (0.85%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 4	0 / 0
Malignant pleural effusion			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Paraneoplastic syndrome			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Tumour pain			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour necrosis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Thyroid cancer metastatic			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Thyroid cancer			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Vascular disorders			
Peripheral embolism			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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 arterial occlusive disease			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Embolism			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Haematoma			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 37 (0.00%)	8 / 590 (1.36%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	5 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Internal haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Jugular vein thrombosis			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Peripheral ischaemia			
subjects affected / exposed	1 / 37 (2.70%)	2 / 590 (0.34%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Phlebitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Superior vena cava syndrome			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Surgical and medical procedures			
Spinal decompression			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
General disorders and administration site conditions			
Calcinosis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Face oedema			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Drug withdrawal syndrome			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Malaise			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Impaired healing			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Granuloma			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
General physical health deterioration			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Fatigue			

subjects affected / exposed	1 / 37 (2.70%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Condition aggravated			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Death			
subjects affected / exposed	0 / 37 (0.00%)	6 / 590 (1.02%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	2 / 6	0 / 0
Disease progression			
subjects affected / exposed	0 / 37 (0.00%)	10 / 590 (1.69%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 10	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 5	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Pyrexia			
subjects affected / exposed	0 / 37 (0.00%)	15 / 590 (2.54%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	5 / 21	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Performance status decreased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Pain			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Reproductive system and breast disorders			
Abnormal uterine bleeding			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Heavy menstrual bleeding			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Ovarian cyst			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Prostatitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Uterine polyp			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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			
Epistaxis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Dyspnoea			
subjects affected / exposed	0 / 37 (0.00%)	10 / 590 (1.69%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 14	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Cough			
subjects affected / exposed	1 / 37 (2.70%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chylothorax			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asphyxia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Laryngeal oedema			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Haemothorax			
subjects affected / exposed	1 / 37 (2.70%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Interstitial lung disease			
subjects affected / exposed	0 / 37 (0.00%)	6 / 590 (1.02%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	9 / 12	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Acute respiratory failure			

subjects affected / exposed	0 / 37 (0.00%)	6 / 590 (1.02%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 1
Pneumothorax spontaneous			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Pneumothorax			
subjects affected / exposed	0 / 37 (0.00%)	6 / 590 (1.02%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis aspiration			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Pneumonitis			
subjects affected / exposed	2 / 37 (5.41%)	29 / 590 (4.92%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	3 / 3	32 / 35	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pleural effusion			
subjects affected / exposed	2 / 37 (5.41%)	14 / 590 (2.37%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 2	0 / 15	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung consolidation			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Pulmonary embolism			

subjects affected / exposed	4 / 37 (10.81%)	12 / 590 (2.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 12	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Respiratory failure			
subjects affected / exposed	2 / 37 (5.41%)	9 / 590 (1.53%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 2	2 / 10	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 1
Respiratory distress			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Pulmonary hypertension			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Delirium			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	1 / 37 (2.70%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			

Device dislocation			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Device issue			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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			
Hepatic enzyme increased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 37 (0.00%)	5 / 590 (0.85%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bilirubin conjugated increased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Alanine aminotransferase increased subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (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
Inflammatory marker increased subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Neutrophil count decreased subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Lymphocyte count decreased subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	15 / 15	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Chemical peritonitis subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Femur fracture subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Spinal compression fracture			
subjects affected / exposed	1 / 37 (2.70%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seroma			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Radiation pneumonitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Procedural pneumothorax			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Immunisation reaction			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Periprosthetic fracture			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Meniscus injury			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Joint dislocation			

subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Incisional hernia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis radiation			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Wrist fracture			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic haematoma			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			

subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Stress cardiomyopathy			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Pericardial effusion			
subjects affected / exposed	1 / 37 (2.70%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Myocardial injury			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Cardio-respiratory arrest			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac discomfort			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 37 (2.70%)	2 / 590 (0.34%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Bradycardia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Atrioventricular block complete			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haematoma			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			
subjects affected / exposed	1 / 37 (2.70%)	3 / 590 (0.51%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Epilepsy			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Encephalopathy			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			

subjects affected / exposed	0 / 37 (0.00%)	5 / 590 (0.85%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Headache			
subjects affected / exposed	1 / 37 (2.70%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Malignant spinal cord compression			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Lumbar radiculopathy			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Intracranial pressure increased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Hydrocephalus			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Neuralgia			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Neuropathy peripheral			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Vocal cord paralysis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Vertebral artery thrombosis			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Syncope			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (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
Seizure			
subjects affected / exposed	0 / 37 (0.00%)	7 / 590 (1.19%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 10	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Radiculopathy			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Radicular pain			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Presyncope			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Polyneuropathy chronic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Paraesthesia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Blood and lymphatic system disorders			
Anaemia of malignant disease			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Anaemia macrocytic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Anaemia			
subjects affected / exposed	1 / 37 (2.70%)	34 / 590 (5.76%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 1	33 / 52	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood loss anaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Eosinophilia			

subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 37 (0.00%)	5 / 590 (0.85%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	5 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	1 / 37 (2.70%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Thrombocytopenia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	62 / 62	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bicytopenia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Neutropenia			
subjects affected / exposed	0 / 37 (0.00%)	8 / 590 (1.36%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	11 / 11	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphopenia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			

subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Eye disorders			
Keratitis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 37 (0.00%)	8 / 590 (1.36%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 8	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal mass			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal distension			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Aphthous ulcer			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Dysphagia			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Diarrhoea			

subjects affected / exposed	2 / 37 (5.41%)	9 / 590 (1.53%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	4 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 37 (2.70%)	5 / 590 (0.85%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	3 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Ascites			
subjects affected / exposed	0 / 37 (0.00%)	6 / 590 (1.02%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Noninfective sialoadenitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	2 / 37 (5.41%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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 haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	8 / 590 (1.36%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 8	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			

subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Haematemesis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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 inflammation			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Large intestine perforation			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Gastrointestinal disorder			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (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
Upper gastrointestinal haemorrhage			

subjects affected / exposed	1 / 37 (2.70%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	3 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal perforation			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (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
Rectal haemorrhage			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumoperitoneum			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Pancreatitis acute			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Vomiting			

subjects affected / exposed	2 / 37 (5.41%)	7 / 590 (1.19%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis ulcerative			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	1 / 37 (2.70%)	8 / 590 (1.36%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Cholangitis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Bile duct stone			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Cholangitis acute			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Liver injury			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Liver disorder			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Hypertransaminasaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Hyperbilirubinaemia			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Hepatic function abnormal			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcapsular hepatic haematoma			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Skin and subcutaneous tissue disorders			
Dermatitis			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Rash maculo-papular			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Haematuria			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Hydronephrosis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Nephrolithiasis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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 kidney injury			
subjects affected / exposed	1 / 37 (2.70%)	6 / 590 (1.02%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive nephropathy			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Urinary tract obstruction			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 37 (2.70%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Ureterolithiasis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Urethral stenosis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Urinary retention			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Adrenal insufficiency			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 37 (5.41%)	6 / 590 (1.02%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 2	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 37 (0.00%)	9 / 590 (1.53%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 11	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Musculoskeletal pain			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Myositis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Neck pain			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Haematoma muscle			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Flank pain			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Chest wall haematoma			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 37 (0.00%)	8 / 590 (1.36%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Rotator cuff syndrome			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal disorder			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Arthritis infective			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Arthritis bacterial			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Appendicitis perforated			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Appendicitis			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute sinusitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Atypical mycobacterial pneumonia			

subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Atypical pneumonia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Coronavirus infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Clostridium difficile colitis			
subjects affected / exposed	1 / 37 (2.70%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis infective			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 37 (2.70%)	14 / 590 (2.37%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 19	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
COVID-19			
subjects affected / exposed	1 / 37 (2.70%)	17 / 590 (2.88%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 19	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Bronchopulmonary aspergillosis			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Bronchitis bacterial			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Bronchitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Bacteraemia			
subjects affected / exposed	1 / 37 (2.70%)	9 / 590 (1.53%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Enterobacter bacteraemia			
subjects affected / exposed	1 / 37 (2.70%)	1 / 590 (0.17%)	0 / 9 (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
Enterococcal bacteraemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Epididymitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	1 / 37 (2.70%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis intestinal perforated			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	3 / 37 (8.11%)	6 / 590 (1.02%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Escherichia sepsis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Influenza			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Kidney infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Klebsiella bacteraemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Klebsiella urinary tract infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Large intestine infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Lymph node tuberculosis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemophilus infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Hepatitis B reactivation			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Herpes zoster			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Nasopharyngitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Meningitis enterococcal			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Meningitis bacterial			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	5 / 37 (13.51%)	94 / 590 (15.93%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 5	30 / 127	0 / 1
deaths causally related to treatment / all	0 / 1	3 / 13	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Pancreatic abscess			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Peritonitis bacterial			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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 infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 37 (2.70%)	6 / 590 (1.02%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	5 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Meningitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Pneumonia legionella			

subjects affected / exposed	1 / 37 (2.70%)	2 / 590 (0.34%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia haemophilus			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Pneumonia staphylococcal			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoas abscess			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Pseudomembranous colitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Postoperative wound infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Renal tuberculosis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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 tract infection			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scrotal cellulitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	2 / 37 (5.41%)	25 / 590 (4.24%)	3 / 9 (33.33%)
occurrences causally related to treatment / all	0 / 2	4 / 30	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 5	0 / 1
Septic arthritis staphylococcal			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Streptococcal bacteraemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Spontaneous bacterial peritonitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Sinusitis bacterial			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Sinusitis aspergillus			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Septic shock			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Staphylococcal bacteraemia			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Tonsillitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 37 (5.41%)	26 / 590 (4.41%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 2	4 / 43	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Varicella			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			

subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	0 / 9 (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
Hypercalcaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Failure to thrive			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Electrolyte imbalance			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	1 / 37 (2.70%)	5 / 590 (0.85%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	3 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Tumour lysis syndrome			

subjects affected / exposed	2 / 37 (5.41%)	3 / 590 (0.51%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	1 / 2	2 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudohyperkalaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Hypoalbuminaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 37 (2.70%)	10 / 590 (1.69%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 1	2 / 16	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 37 (0.00%)	5 / 590 (0.85%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	0 / 9 (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
Hypocalcaemia			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	5 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events			
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Pralsetinib 400 mg QD			
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Total subjects affected by serious adverse events			
subjects affected / exposed	381 / 540 (70.56%)		
number of deaths (all causes)	245		
number of deaths resulting from adverse events	9		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gallbladder cancer			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung cancer metastatic			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 3		
Anaplastic large-cell lymphoma			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bone neoplasm			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain neoplasm			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cancer pain			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to bone			

subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Medullary thyroid cancer			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 3		
Non-small cell lung cancer			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Neoplasm progression			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Neoplasm malignant			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Metastatic neoplasm			
subjects affected / exposed	7 / 540 (1.30%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 2		
Metastasis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to liver			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to central nervous system			

subjects affected / exposed	6 / 540 (1.11%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			
subjects affected / exposed	26 / 540 (4.81%)		
occurrences causally related to treatment / all	0 / 30		
deaths causally related to treatment / all	0 / 21		
Malignant neoplasm progression			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 3		
Malignant pleural effusion			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paraneoplastic syndrome			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour pain			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Tumour necrosis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thyroid cancer metastatic			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Thyroid cancer			

subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Vascular disorders			
Peripheral embolism			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Embolism			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Haematoma			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	8 / 540 (1.48%)		
occurrences causally related to treatment / all	5 / 9		
deaths causally related to treatment / all	0 / 0		
Hypotension			

subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Internal haemorrhage			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jugular vein thrombosis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Peripheral ischaemia			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral vascular disorder			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Phlebitis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Superior vena cava syndrome			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Spinal decompression			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

Calcinosis				
subjects affected / exposed	0 / 540 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthenia				
subjects affected / exposed	4 / 540 (0.74%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 1			
Face oedema				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Drug withdrawal syndrome				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Malaise				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Impaired healing				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Granuloma				

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Fatigue			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Condition aggravated			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	6 / 540 (1.11%)		
occurrences causally related to treatment / all	2 / 6		
deaths causally related to treatment / all	2 / 6		
Disease progression			
subjects affected / exposed	10 / 540 (1.85%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 5		
Oedema peripheral			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	15 / 540 (2.78%)		
occurrences causally related to treatment / all	5 / 21		
deaths causally related to treatment / all	0 / 0		
Performance status decreased			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Abnormal uterine bleeding			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Heavy menstrual bleeding			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostatitis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Uterine polyp			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Dyspnoea				
subjects affected / exposed	10 / 540 (1.85%)			
occurrences causally related to treatment / all	1 / 14			
deaths causally related to treatment / all	0 / 2			
Cough				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chylothorax				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Asphyxia				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Laryngeal oedema				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute respiratory distress syndrome				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemothorax				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxia				

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Interstitial lung disease			
subjects affected / exposed	6 / 540 (1.11%)		
occurrences causally related to treatment / all	9 / 12		
deaths causally related to treatment / all	1 / 1		
Acute respiratory failure			
subjects affected / exposed	5 / 540 (0.93%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Pneumothorax spontaneous			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	5 / 540 (0.93%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Pneumonitis aspiration			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	27 / 540 (5.00%)		
occurrences causally related to treatment / all	29 / 32		
deaths causally related to treatment / all	1 / 1		
Pleural effusion			
subjects affected / exposed	11 / 540 (2.04%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 0		
Lung disorder			

subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lung consolidation			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	8 / 540 (1.48%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	6 / 540 (1.11%)		
occurrences causally related to treatment / all	2 / 7		
deaths causally related to treatment / all	0 / 2		
Respiratory distress			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Delirium			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Confusional state			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device dislocation			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device issue			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Electrocardiogram QT prolonged			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Blood creatine phosphokinase increased			
subjects affected / exposed	5 / 540 (0.93%)		
occurrences causally related to treatment / all	4 / 5		
deaths causally related to treatment / all	0 / 0		
Blood bilirubin increased			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		

Bilirubin conjugated increased subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Alanine aminotransferase increased subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Inflammatory marker increased subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphocyte count decreased subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	15 / 15		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications Chemical peritonitis subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Fall				
subjects affected / exposed	0 / 540 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	4 / 540 (0.74%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Seroma				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	0 / 540 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radiation pneumonitis				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Procedural pneumothorax				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Immunisation reaction				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Periprosthetic fracture				

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meniscus injury			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Incisional hernia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis radiation			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wrist fracture			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound dehiscence			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Traumatic haematoma			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Angina pectoris			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Stress cardiomyopathy			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Myocardial injury			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac failure congestive			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac discomfort			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac arrest			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bradycardia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block complete			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral infarction			

subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Cerebral haemorrhage			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral haematoma			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Carotid artery stenosis			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Ataxia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain oedema			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhage intracranial			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Epilepsy			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	5 / 540 (0.93%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
Cognitive disorder			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Migraine			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Malignant spinal cord compression			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lumbar radiculopathy			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intracranial pressure increased			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hydrocephalus			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuralgia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vocal cord paralysis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vertebral artery thrombosis			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	7 / 540 (1.30%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 1		
Radiculopathy			

subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Radicular pain			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Polyneuropathy chronic			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paraesthesia			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia of malignant disease			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anaemia macrocytic			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	32 / 540 (5.93%)		
occurrences causally related to treatment / all	33 / 50		
deaths causally related to treatment / all	0 / 0		
Blood loss anaemia			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Eosinophilia			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	5 / 540 (0.93%)		
occurrences causally related to treatment / all	5 / 6		
deaths causally related to treatment / all	0 / 0		
Leukocytosis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	62 / 62		
deaths causally related to treatment / all	0 / 0		
Bicytopenia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			

subjects affected / exposed	8 / 540 (1.48%)		
occurrences causally related to treatment / all	11 / 11		
deaths causally related to treatment / all	0 / 0		
Lymphopenia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Keratitis			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	7 / 540 (1.30%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Abdominal mass			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal distension			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Aphthous ulcer				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	0 / 540 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	7 / 540 (1.30%)			
occurrences causally related to treatment / all	4 / 7			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	4 / 540 (0.74%)			
occurrences causally related to treatment / all	3 / 6			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	6 / 540 (1.11%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 0			
Noninfective sialoadenitis				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Melaena				

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	7 / 540 (1.30%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Haematochezia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal inflammation			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorder			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stomatitis			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Small intestinal perforation			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumoperitoneum			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			

subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Oesophagitis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	5 / 540 (0.93%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Proctitis ulcerative			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis chronic			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	7 / 540 (1.30%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Hepatic failure			

subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholangitis			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bile duct stone			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholangitis acute			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Liver injury			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	1 / 1		
Liver disorder			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertransaminasaemia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperbilirubinaemia			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic function abnormal			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Subcapsular hepatic haematoma			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rash maculo-papular			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Renal colic			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	5 / 540 (0.93%)		
occurrences causally related to treatment / all	2 / 6		
deaths causally related to treatment / all	0 / 0		
Obstructive nephropathy			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ureterolithiasis			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urethral stenosis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary retention			

subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Adrenal insufficiency			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	9 / 540 (1.67%)		
occurrences causally related to treatment / all	0 / 11		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal pain			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myositis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Neck pain				
subjects affected / exposed	3 / 540 (0.56%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haematoma muscle				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Flank pain				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chest wall haematoma				
subjects affected / exposed	0 / 540 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone pain				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	3 / 540 (0.56%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	8 / 540 (1.48%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Rhabdomyolysis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
Rotator cuff syndrome			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal disorder			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Arthritis infective			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Arthritis bacterial			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis perforated			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Acute sinusitis			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal infection			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atypical mycobacterial pneumonia			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atypical pneumonia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronavirus infection			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Cholecystitis infective			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			

subjects affected / exposed	13 / 540 (2.41%)		
occurrences causally related to treatment / all	0 / 18		
deaths causally related to treatment / all	0 / 2		
COVID-19			
subjects affected / exposed	16 / 540 (2.96%)		
occurrences causally related to treatment / all	0 / 18		
deaths causally related to treatment / all	0 / 2		
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis bacterial			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			
subjects affected / exposed	8 / 540 (1.48%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Cystitis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enterobacter bacteraemia			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterococcal bacteraemia			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epididymitis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Escherichia bacteraemia			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile infection			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Empyema			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis intestinal perforated			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Device related infection			

subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Escherichia sepsis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Kidney infection			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Klebsiella bacteraemia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Klebsiella urinary tract infection			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestine infection			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymph node tuberculosis			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Haemophilus infection			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis B reactivation			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenic sepsis			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nasopharyngitis			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis enterococcal			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis bacterial			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	87 / 540 (16.11%)		
occurrences causally related to treatment / all	29 / 120		
deaths causally related to treatment / all	2 / 11		
Osteomyelitis			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pancreatic abscess			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peritonitis bacterial			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural infection			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumocystis jirovecii pneumonia			

subjects affected / exposed	5 / 540 (0.93%)		
occurrences causally related to treatment / all	5 / 6		
deaths causally related to treatment / all	1 / 1		
Meningitis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Pneumonia legionella			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia influenzal			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia haemophilus			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumonia bacterial			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 2		
Pneumonia staphylococcal			

subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Psoas abscess			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pseudomembranous colitis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative wound infection			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia viral			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal tuberculosis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			

subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Scrotal cellulitis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	20 / 540 (3.70%)		
occurrences causally related to treatment / all	4 / 23		
deaths causally related to treatment / all	0 / 4		
Septic arthritis staphylococcal			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Streptococcal bacteraemia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spontaneous bacterial peritonitis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin infection			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Sinusitis bacterial			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sinusitis aspergillus			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	23 / 540 (4.26%)		
occurrences causally related to treatment / all	4 / 40		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection bacterial			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			

subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Varicella			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Failure to thrive			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Electrolyte imbalance			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Decreased appetite			

subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Hyperuricaemia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour lysis syndrome			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pseudohyperkalaemia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoalbuminaemia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	8 / 540 (1.48%)		
occurrences causally related to treatment / all	2 / 14		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	5 / 540 (0.93%)		
occurrences causally related to treatment / all	3 / 8		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			

subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 0		
Hypophosphataemia			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Pralsetinib ≤ 300 mg QD	Pralsetinib All Doses	Pralsetinib BID Dosing Schedule
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 37 (97.30%)	585 / 590 (99.15%)	9 / 9 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 37 (0.00%)	6 / 590 (1.02%)	1 / 9 (11.11%)
occurrences (all)	0	9	1
Skin papilloma			
subjects affected / exposed	0 / 37 (0.00%)	5 / 590 (0.85%)	1 / 9 (11.11%)
occurrences (all)	0	8	2
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 37 (0.00%)	7 / 590 (1.19%)	1 / 9 (11.11%)
occurrences (all)	0	7	1
Vasodilatation			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Hypotension			
subjects affected / exposed	2 / 37 (5.41%)	15 / 590 (2.54%)	0 / 9 (0.00%)
occurrences (all)	2	18	0
Intermittent claudication			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Peripheral arterial occlusive disease			

subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Peripheral vascular disorder			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Thrombosis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Hypertension			
subjects affected / exposed	9 / 37 (24.32%)	206 / 590 (34.92%)	4 / 9 (44.44%)
occurrences (all)	12	530	11
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	4 / 37 (10.81%)	22 / 590 (3.73%)	1 / 9 (11.11%)
occurrences (all)	5	25	1
Oedema peripheral			
subjects affected / exposed	9 / 37 (24.32%)	117 / 590 (19.83%)	4 / 9 (44.44%)
occurrences (all)	10	154	4
Non-cardiac chest pain			
subjects affected / exposed	4 / 37 (10.81%)	27 / 590 (4.58%)	2 / 9 (22.22%)
occurrences (all)	4	28	2
Mucosal inflammation			
subjects affected / exposed	3 / 37 (8.11%)	43 / 590 (7.29%)	0 / 9 (0.00%)
occurrences (all)	4	60	0
Malaise			
subjects affected / exposed	0 / 37 (0.00%)	34 / 590 (5.76%)	0 / 9 (0.00%)
occurrences (all)	0	45	0
Localised oedema			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	1 / 9 (11.11%)
occurrences (all)	0	4	1
Fatigue			
subjects affected / exposed	12 / 37 (32.43%)	169 / 590 (28.64%)	2 / 9 (22.22%)
occurrences (all)	17	309	2
Face oedema			

subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	43 / 590 (7.29%) 58	0 / 9 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 4	32 / 590 (5.42%) 34	0 / 9 (0.00%) 0
Chest discomfort subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	18 / 590 (3.05%) 21	1 / 9 (11.11%) 1
Calcinosis subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	1 / 590 (0.17%) 2	1 / 9 (11.11%) 2
Asthenia subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	90 / 590 (15.25%) 194	0 / 9 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	7 / 37 (18.92%) 11	176 / 590 (29.83%) 286	3 / 9 (33.33%) 7
Reproductive system and breast disorders Breast calcifications subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	1 / 590 (0.17%) 1	1 / 9 (11.11%) 1
Erectile dysfunction subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	32 / 590 (5.42%) 36	0 / 9 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Dyspnoea exertional subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	24 / 590 (4.07%) 34	1 / 9 (11.11%) 1
Cough subjects affected / exposed occurrences (all)	9 / 37 (24.32%) 11	161 / 590 (27.29%) 236	2 / 9 (22.22%) 2
Dysphonia subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	49 / 590 (8.31%) 57	1 / 9 (11.11%) 1
Dyspnoea			

subjects affected / exposed	12 / 37 (32.43%)	127 / 590 (21.53%)	2 / 9 (22.22%)
occurrences (all)	15	165	3
Epistaxis			
subjects affected / exposed	2 / 37 (5.41%)	43 / 590 (7.29%)	0 / 9 (0.00%)
occurrences (all)	2	51	0
Oropharyngeal pain			
subjects affected / exposed	4 / 37 (10.81%)	45 / 590 (7.63%)	0 / 9 (0.00%)
occurrences (all)	4	58	0
Pleural effusion			
subjects affected / exposed	2 / 37 (5.41%)	18 / 590 (3.05%)	0 / 9 (0.00%)
occurrences (all)	2	38	0
Pneumonitis			
subjects affected / exposed	7 / 37 (18.92%)	59 / 590 (10.00%)	1 / 9 (11.11%)
occurrences (all)	11	109	1
Productive cough			
subjects affected / exposed	0 / 37 (0.00%)	36 / 590 (6.10%)	1 / 9 (11.11%)
occurrences (all)	0	40	1
Rhinorrhoea			
subjects affected / exposed	1 / 37 (2.70%)	7 / 590 (1.19%)	1 / 9 (11.11%)
occurrences (all)	1	7	1
Upper respiratory tract congestion			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Wheezing			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	1 / 9 (11.11%)
occurrences (all)	0	4	1
Nasal congestion			
subjects affected / exposed	4 / 37 (10.81%)	24 / 590 (4.07%)	1 / 9 (11.11%)
occurrences (all)	4	27	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 37 (10.81%)	32 / 590 (5.42%)	0 / 9 (0.00%)
occurrences (all)	4	35	0
Depression			
subjects affected / exposed	2 / 37 (5.41%)	21 / 590 (3.56%)	0 / 9 (0.00%)
occurrences (all)	2	22	0

Insomnia subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	52 / 590 (8.81%) 61	2 / 9 (22.22%) 2
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	16 / 37 (43.24%) 31	232 / 590 (39.32%) 495	3 / 9 (33.33%) 4
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	17 / 37 (45.95%) 41	295 / 590 (50.00%) 739	3 / 9 (33.33%) 3
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	8 / 37 (21.62%) 9	78 / 590 (13.22%) 125	1 / 9 (11.11%) 1
Blood bilirubin increased subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 5	61 / 590 (10.34%) 172	1 / 9 (11.11%) 1
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	97 / 590 (16.44%) 445	0 / 9 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	11 / 37 (29.73%) 17	158 / 590 (26.78%) 310	3 / 9 (33.33%) 4
Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	47 / 590 (7.97%) 72	0 / 9 (0.00%) 0
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	32 / 590 (5.42%) 40	0 / 9 (0.00%) 0
Electrocardiogram repolarisation abnormality subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	1 / 590 (0.17%) 1	1 / 9 (11.11%) 1
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	38 / 590 (6.44%) 108	0 / 9 (0.00%) 0

Hepatic enzyme increased subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 4	5 / 590 (0.85%) 9	1 / 9 (11.11%) 1
Lymphocyte count decreased subjects affected / exposed occurrences (all)	6 / 37 (16.22%) 18	98 / 590 (16.61%) 379	1 / 9 (11.11%) 3
Neutrophil count decreased subjects affected / exposed occurrences (all)	5 / 37 (13.51%) 16	153 / 590 (25.93%) 558	1 / 9 (11.11%) 1
Platelet count decreased subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 5	72 / 590 (12.20%) 173	0 / 9 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	38 / 590 (6.44%) 52	0 / 9 (0.00%) 0
Weight increased subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 4	64 / 590 (10.85%) 174	0 / 9 (0.00%) 0
White blood cell count decreased subjects affected / exposed occurrences (all)	14 / 37 (37.84%) 41	175 / 590 (29.66%) 636	2 / 9 (22.22%) 3
Injury, poisoning and procedural complications			
Abdominal injury subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	2 / 590 (0.34%) 2	1 / 9 (11.11%) 1
Fall subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 2	21 / 590 (3.56%) 26	2 / 9 (22.22%) 3
Hip fracture subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	1 / 590 (0.17%) 1	1 / 9 (11.11%) 1
Incision site haematoma subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	1 / 590 (0.17%) 1	1 / 9 (11.11%) 1
Joint injury			

subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 590 (0.34%) 3	1 / 9 (11.11%) 2
Procedural nausea subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	2 / 590 (0.34%) 2	1 / 9 (11.11%) 1
Procedural pain subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	4 / 590 (0.68%) 4	1 / 9 (11.11%) 1
Cardiac disorders			
Left ventricular hypertrophy subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	1 / 590 (0.17%) 1	1 / 9 (11.11%) 1
Left ventricular dysfunction subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 590 (0.34%) 2	1 / 9 (11.11%) 1
Nervous system disorders			
Hypoaesthesia subjects affected / exposed occurrences (all)	5 / 37 (13.51%) 5	40 / 590 (6.78%) 51	0 / 9 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	7 / 37 (18.92%) 9	94 / 590 (15.93%) 115	2 / 9 (22.22%) 2
Dysgeusia subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 4	77 / 590 (13.05%) 102	0 / 9 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	8 / 37 (21.62%) 8	110 / 590 (18.64%) 152	1 / 9 (11.11%) 1
Memory impairment subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	15 / 590 (2.54%) 20	1 / 9 (11.11%) 1
Paraesthesia subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	33 / 590 (5.59%) 35	0 / 9 (0.00%) 0
Peripheral sensory neuropathy			

subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	22 / 590 (3.73%) 27	1 / 9 (11.11%) 1
Neuropathy peripheral subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 4	32 / 590 (5.42%) 43	0 / 9 (0.00%) 0
Blood and lymphatic system disorders			
Leukopenia subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 11	61 / 590 (10.34%) 239	1 / 9 (11.11%) 1
Lymphopenia subjects affected / exposed occurrences (all)	7 / 37 (18.92%) 29	77 / 590 (13.05%) 359	2 / 9 (22.22%) 8
Neutropenia subjects affected / exposed occurrences (all)	8 / 37 (21.62%) 22	135 / 590 (22.88%) 456	2 / 9 (22.22%) 6
Thrombocytopenia subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 6	48 / 590 (8.14%) 105	1 / 9 (11.11%) 1
Anaemia subjects affected / exposed occurrences (all)	16 / 37 (43.24%) 45	310 / 590 (52.54%) 1168	6 / 9 (66.67%) 15
Ear and labyrinth disorders			
Hypoacusis subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 590 (0.34%) 2	1 / 9 (11.11%) 1
Eye disorders			
Vision blurred subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	37 / 590 (6.27%) 52	1 / 9 (11.11%) 1
Growth of eyelashes subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	5 / 590 (0.85%) 5	1 / 9 (11.11%) 1
Eye disorder subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 590 (0.34%) 2	1 / 9 (11.11%) 1
Corneal epithelial microcysts			

subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	1 / 590 (0.17%) 1	1 / 9 (11.11%) 1
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	5 / 37 (13.51%) 5	74 / 590 (12.54%) 95	0 / 9 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	49 / 590 (8.31%) 59	2 / 9 (22.22%) 2
Ascites subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	23 / 590 (3.90%) 35	2 / 9 (22.22%) 2
Chronic gastritis subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	5 / 590 (0.85%) 5	1 / 9 (11.11%) 1
Constipation subjects affected / exposed occurrences (all)	12 / 37 (32.43%) 16	255 / 590 (43.22%) 351	2 / 9 (22.22%) 2
Diarrhoea subjects affected / exposed occurrences (all)	10 / 37 (27.03%) 19	207 / 590 (35.08%) 407	4 / 9 (44.44%) 7
Dry mouth subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 3	96 / 590 (16.27%) 110	1 / 9 (11.11%) 1
Dyspepsia subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 5	32 / 590 (5.42%) 41	0 / 9 (0.00%) 0
Dysphagia subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	47 / 590 (7.97%) 53	1 / 9 (11.11%) 1
Gastritis subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	11 / 590 (1.86%) 11	1 / 9 (11.11%) 1
Gastrointestinal wall thickening subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	4 / 590 (0.68%) 4	1 / 9 (11.11%) 1

Abdominal distension			
subjects affected / exposed	2 / 37 (5.41%)	29 / 590 (4.92%)	0 / 9 (0.00%)
occurrences (all)	2	35	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 37 (0.00%)	37 / 590 (6.27%)	2 / 9 (22.22%)
occurrences (all)	0	44	2
Abdominal discomfort			
subjects affected / exposed	2 / 37 (5.41%)	11 / 590 (1.86%)	0 / 9 (0.00%)
occurrences (all)	2	13	0
Toothache			
subjects affected / exposed	0 / 37 (0.00%)	15 / 590 (2.54%)	1 / 9 (11.11%)
occurrences (all)	0	16	1
Stomatitis			
subjects affected / exposed	3 / 37 (8.11%)	37 / 590 (6.27%)	0 / 9 (0.00%)
occurrences (all)	3	57	0
Paraesthesia oral			
subjects affected / exposed	0 / 37 (0.00%)	3 / 590 (0.51%)	1 / 9 (11.11%)
occurrences (all)	0	3	1
Nausea			
subjects affected / exposed	10 / 37 (27.03%)	126 / 590 (21.36%)	1 / 9 (11.11%)
occurrences (all)	17	182	1
Mouth ulceration			
subjects affected / exposed	0 / 37 (0.00%)	15 / 590 (2.54%)	2 / 9 (22.22%)
occurrences (all)	0	19	2
Vomiting			
subjects affected / exposed	7 / 37 (18.92%)	95 / 590 (16.10%)	0 / 9 (0.00%)
occurrences (all)	10	123	0
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	2 / 37 (5.41%)	19 / 590 (3.22%)	1 / 9 (11.11%)
occurrences (all)	4	25	1
Acne			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	1 / 9 (11.11%)
occurrences (all)	0	5	1
Actinic keratosis			

subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 590 (0.34%) 2	1 / 9 (11.11%) 1
Alopecia subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	37 / 590 (6.27%) 40	0 / 9 (0.00%) 0
Dermatitis acneiform subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	22 / 590 (3.73%) 23	2 / 9 (22.22%) 2
Dry skin subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	25 / 590 (4.24%) 29	1 / 9 (11.11%) 1
Hyperhidrosis subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	11 / 590 (1.86%) 12	0 / 9 (0.00%) 0
Perioral dermatitis subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	4 / 590 (0.68%) 4	1 / 9 (11.11%) 1
Rash subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	61 / 590 (10.34%) 74	0 / 9 (0.00%) 0
Rash erythematous subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	8 / 590 (1.36%) 8	0 / 9 (0.00%) 0
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	15 / 590 (2.54%) 17	1 / 9 (11.11%) 1
Renal and urinary disorders			
Acute kidney injury subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	19 / 590 (3.22%) 23	1 / 9 (11.11%) 1
Dysuria subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	29 / 590 (4.92%) 35	0 / 9 (0.00%) 0
Renal failure subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	10 / 590 (1.69%) 12	1 / 9 (11.11%) 2

Urinary incontinence subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	3 / 590 (0.51%) 3	1 / 9 (11.11%) 1
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	7 / 37 (18.92%) 9	100 / 590 (16.95%) 130	3 / 9 (33.33%) 3
Back pain subjects affected / exposed occurrences (all)	6 / 37 (16.22%) 6	95 / 590 (16.10%) 126	1 / 9 (11.11%) 1
Muscle spasms subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	46 / 590 (7.80%) 54	0 / 9 (0.00%) 0
Muscular weakness subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	21 / 590 (3.56%) 25	0 / 9 (0.00%) 0
Myalgia subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	69 / 590 (11.69%) 123	0 / 9 (0.00%) 0
Neck pain subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	36 / 590 (6.10%) 41	0 / 9 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	6 / 37 (16.22%) 6	72 / 590 (12.20%) 111	0 / 9 (0.00%) 0
Infections and infestations			
COVID-19 subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 4	66 / 590 (11.19%) 75	0 / 9 (0.00%) 0
Cellulitis subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	12 / 590 (2.03%) 13	1 / 9 (11.11%) 1
Ear infection subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	4 / 590 (0.68%) 4	1 / 9 (11.11%) 1
Folliculitis			

subjects affected / exposed	0 / 37 (0.00%)	7 / 590 (1.19%)	1 / 9 (11.11%)
occurrences (all)	0	8	2
Wound infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 590 (0.17%)	1 / 9 (11.11%)
occurrences (all)	0	2	2
Urinary tract infection			
subjects affected / exposed	5 / 37 (13.51%)	87 / 590 (14.75%)	1 / 9 (11.11%)
occurrences (all)	10	182	4
Upper respiratory tract infection			
subjects affected / exposed	1 / 37 (2.70%)	53 / 590 (8.98%)	1 / 9 (11.11%)
occurrences (all)	1	63	1
Skin candida			
subjects affected / exposed	1 / 37 (2.70%)	3 / 590 (0.51%)	1 / 9 (11.11%)
occurrences (all)	1	3	1
Sinusitis			
subjects affected / exposed	3 / 37 (8.11%)	22 / 590 (3.73%)	1 / 9 (11.11%)
occurrences (all)	5	24	1
Pneumonia aspiration			
subjects affected / exposed	0 / 37 (0.00%)	2 / 590 (0.34%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Pneumonia			
subjects affected / exposed	4 / 37 (10.81%)	68 / 590 (11.53%)	0 / 9 (0.00%)
occurrences (all)	4	111	0
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 37 (0.00%)	4 / 590 (0.68%)	1 / 9 (11.11%)
occurrences (all)	0	4	1
Oral candidiasis			
subjects affected / exposed	2 / 37 (5.41%)	21 / 590 (3.56%)	1 / 9 (11.11%)
occurrences (all)	2	30	1
Lower respiratory tract infection			
subjects affected / exposed	2 / 37 (5.41%)	7 / 590 (1.19%)	1 / 9 (11.11%)
occurrences (all)	2	7	1
Influenza			
subjects affected / exposed	1 / 37 (2.70%)	15 / 590 (2.54%)	1 / 9 (11.11%)
occurrences (all)	1	16	1
Fungal foot infection			

subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 590 (0.34%) 2	1 / 9 (11.11%) 1
Bronchitis subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 2	25 / 590 (4.24%) 31	1 / 9 (11.11%) 1
Metabolism and nutrition disorders			
Hypoalbuminaemia subjects affected / exposed occurrences (all)	5 / 37 (13.51%) 6	89 / 590 (15.08%) 234	0 / 9 (0.00%) 0
Dehydration subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	12 / 590 (2.03%) 14	0 / 9 (0.00%) 0
Hypercalcaemia subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 3	24 / 590 (4.07%) 36	1 / 9 (11.11%) 1
Hyperglycaemia subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	39 / 590 (6.61%) 61	0 / 9 (0.00%) 0
Hyperkalaemia subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	33 / 590 (5.59%) 54	1 / 9 (11.11%) 1
Hyperphosphataemia subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 4	109 / 590 (18.47%) 186	3 / 9 (33.33%) 4
Decreased appetite subjects affected / exposed occurrences (all)	6 / 37 (16.22%) 6	124 / 590 (21.02%) 175	3 / 9 (33.33%) 3
Hypocalcaemia subjects affected / exposed occurrences (all)	7 / 37 (18.92%) 12	138 / 590 (23.39%) 336	1 / 9 (11.11%) 3
Hypomagnesaemia subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 5	58 / 590 (9.83%) 110	0 / 9 (0.00%) 0
Hyponatraemia subjects affected / exposed occurrences (all)	5 / 37 (13.51%) 5	79 / 590 (13.39%) 135	3 / 9 (33.33%) 6

Hypophosphataemia subjects affected / exposed occurrences (all)	6 / 37 (16.22%) 16	84 / 590 (14.24%) 151	3 / 9 (33.33%) 4
Hypokalaemia subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 19	103 / 590 (17.46%) 185	1 / 9 (11.11%) 3

Non-serious adverse events	Pralsetinib 400 mg QD		
Total subjects affected by non-serious adverse events subjects affected / exposed	536 / 540 (99.26%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Basal cell carcinoma subjects affected / exposed occurrences (all)	5 / 540 (0.93%) 8		
Skin papilloma subjects affected / exposed occurrences (all)	4 / 540 (0.74%) 6		
Vascular disorders Haematoma subjects affected / exposed occurrences (all)	6 / 540 (1.11%) 6		
Vasodilatation subjects affected / exposed occurrences (all)	0 / 540 (0.00%) 0		
Hypotension subjects affected / exposed occurrences (all)	13 / 540 (2.41%) 16		
Intermittent claudication subjects affected / exposed occurrences (all)	0 / 540 (0.00%) 0		
Peripheral arterial occlusive disease subjects affected / exposed occurrences (all)	1 / 540 (0.19%) 1		
Peripheral vascular disorder subjects affected / exposed occurrences (all)	1 / 540 (0.19%) 1		

Thrombosis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	189 / 540 (35.00%)		
occurrences (all)	499		
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	17 / 540 (3.15%)		
occurrences (all)	19		
Oedema peripheral			
subjects affected / exposed	104 / 540 (19.26%)		
occurrences (all)	140		
Non-cardiac chest pain			
subjects affected / exposed	21 / 540 (3.89%)		
occurrences (all)	22		
Mucosal inflammation			
subjects affected / exposed	40 / 540 (7.41%)		
occurrences (all)	56		
Malaise			
subjects affected / exposed	33 / 540 (6.11%)		
occurrences (all)	44		
Localised oedema			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	154 / 540 (28.52%)		
occurrences (all)	289		
Face oedema			
subjects affected / exposed	42 / 540 (7.78%)		
occurrences (all)	57		
Chills			
subjects affected / exposed	28 / 540 (5.19%)		
occurrences (all)	30		
Chest discomfort			

subjects affected / exposed occurrences (all)	16 / 540 (2.96%) 19		
Calcinosis subjects affected / exposed occurrences (all)	0 / 540 (0.00%) 0		
Asthenia subjects affected / exposed occurrences (all)	88 / 540 (16.30%) 192		
Pyrexia subjects affected / exposed occurrences (all)	164 / 540 (30.37%) 266		
Reproductive system and breast disorders			
Breast calcifications subjects affected / exposed occurrences (all)	0 / 540 (0.00%) 0		
Erectile dysfunction subjects affected / exposed occurrences (all)	30 / 540 (5.56%) 34		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional subjects affected / exposed occurrences (all)	22 / 540 (4.07%) 32		
Cough subjects affected / exposed occurrences (all)	149 / 540 (27.59%) 222		
Dysphonia subjects affected / exposed occurrences (all)	47 / 540 (8.70%) 55		
Dyspnoea subjects affected / exposed occurrences (all)	112 / 540 (20.74%) 146		
Epistaxis subjects affected / exposed occurrences (all)	41 / 540 (7.59%) 49		
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	41 / 540 (7.59%) 54		
Pleural effusion subjects affected / exposed occurrences (all)	16 / 540 (2.96%) 36		
Pneumonitis subjects affected / exposed occurrences (all)	51 / 540 (9.44%) 97		
Productive cough subjects affected / exposed occurrences (all)	35 / 540 (6.48%) 39		
Rhinorrhoea subjects affected / exposed occurrences (all)	5 / 540 (0.93%) 5		
Upper respiratory tract congestion subjects affected / exposed occurrences (all)	0 / 540 (0.00%) 0		
Wheezing subjects affected / exposed occurrences (all)	3 / 540 (0.56%) 3		
Nasal congestion subjects affected / exposed occurrences (all)	19 / 540 (3.52%) 22		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	28 / 540 (5.19%) 31		
Depression subjects affected / exposed occurrences (all)	19 / 540 (3.52%) 20		
Insomnia subjects affected / exposed occurrences (all)	47 / 540 (8.70%) 56		
Investigations Alanine aminotransferase increased			

subjects affected / exposed	212 / 540 (39.26%)		
occurrences (all)	459		
Aspartate aminotransferase increased			
subjects affected / exposed	273 / 540 (50.56%)		
occurrences (all)	693		
Blood alkaline phosphatase increased			
subjects affected / exposed	68 / 540 (12.59%)		
occurrences (all)	112		
Blood bilirubin increased			
subjects affected / exposed	58 / 540 (10.74%)		
occurrences (all)	166		
Blood creatine phosphokinase increased			
subjects affected / exposed	97 / 540 (17.96%)		
occurrences (all)	445		
Blood creatinine increased			
subjects affected / exposed	143 / 540 (26.48%)		
occurrences (all)	288		
Blood lactate dehydrogenase increased			
subjects affected / exposed	47 / 540 (8.70%)		
occurrences (all)	72		
Electrocardiogram QT prolonged			
subjects affected / exposed	31 / 540 (5.74%)		
occurrences (all)	39		
Electrocardiogram repolarisation abnormality			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	38 / 540 (7.04%)		
occurrences (all)	108		
Hepatic enzyme increased			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences (all)	4		
Lymphocyte count decreased			

subjects affected / exposed occurrences (all)	90 / 540 (16.67%) 345		
Neutrophil count decreased subjects affected / exposed occurrences (all)	146 / 540 (27.04%) 539		
Platelet count decreased subjects affected / exposed occurrences (all)	67 / 540 (12.41%) 166		
Weight decreased subjects affected / exposed occurrences (all)	36 / 540 (6.67%) 50		
Weight increased subjects affected / exposed occurrences (all)	62 / 540 (11.48%) 170		
White blood cell count decreased subjects affected / exposed occurrences (all)	157 / 540 (29.07%) 579		
Injury, poisoning and procedural complications			
Abdominal injury subjects affected / exposed occurrences (all)	0 / 540 (0.00%) 0		
Fall subjects affected / exposed occurrences (all)	18 / 540 (3.33%) 21		
Hip fracture subjects affected / exposed occurrences (all)	0 / 540 (0.00%) 0		
Incision site haematoma subjects affected / exposed occurrences (all)	0 / 540 (0.00%) 0		
Joint injury subjects affected / exposed occurrences (all)	1 / 540 (0.19%) 1		
Procedural nausea			

subjects affected / exposed occurrences (all)	0 / 540 (0.00%) 0		
Procedural pain subjects affected / exposed occurrences (all)	3 / 540 (0.56%) 3		
Cardiac disorders			
Left ventricular hypertrophy subjects affected / exposed occurrences (all)	0 / 540 (0.00%) 0		
Left ventricular dysfunction subjects affected / exposed occurrences (all)	1 / 540 (0.19%) 1		
Nervous system disorders			
Hypoaesthesia subjects affected / exposed occurrences (all)	35 / 540 (6.48%) 46		
Dizziness subjects affected / exposed occurrences (all)	83 / 540 (15.37%) 101		
Dysgeusia subjects affected / exposed occurrences (all)	74 / 540 (13.70%) 97		
Headache subjects affected / exposed occurrences (all)	100 / 540 (18.52%) 140		
Memory impairment subjects affected / exposed occurrences (all)	13 / 540 (2.41%) 18		
Paraesthesia subjects affected / exposed occurrences (all)	33 / 540 (6.11%) 35		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	21 / 540 (3.89%) 26		
Neuropathy peripheral			

subjects affected / exposed occurrences (all)	26 / 540 (4.81%) 36		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	55 / 540 (10.19%)		
occurrences (all)	226		
Lymphopenia			
subjects affected / exposed	67 / 540 (12.41%)		
occurrences (all)	321		
Neutropenia			
subjects affected / exposed	124 / 540 (22.96%)		
occurrences (all)	422		
Thrombocytopenia			
subjects affected / exposed	44 / 540 (8.15%)		
occurrences (all)	98		
Anaemia			
subjects affected / exposed	285 / 540 (52.78%)		
occurrences (all)	1098		
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences (all)	1		
Eye disorders			
Vision blurred			
subjects affected / exposed	34 / 540 (6.30%)		
occurrences (all)	49		
Growth of eyelashes			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences (all)	4		
Eye disorder			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences (all)	1		
Corneal epithelial microcysts			
subjects affected / exposed	0 / 540 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	68 / 540 (12.59%)		
occurrences (all)	89		
Abdominal pain upper			
subjects affected / exposed	46 / 540 (8.52%)		
occurrences (all)	56		
Ascites			
subjects affected / exposed	19 / 540 (3.52%)		
occurrences (all)	31		
Chronic gastritis			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences (all)	4		
Constipation			
subjects affected / exposed	238 / 540 (44.07%)		
occurrences (all)	329		
Diarrhoea			
subjects affected / exposed	189 / 540 (35.00%)		
occurrences (all)	373		
Dry mouth			
subjects affected / exposed	92 / 540 (17.04%)		
occurrences (all)	103		
Dyspepsia			
subjects affected / exposed	29 / 540 (5.37%)		
occurrences (all)	36		
Dysphagia			
subjects affected / exposed	44 / 540 (8.15%)		
occurrences (all)	50		
Gastritis			
subjects affected / exposed	10 / 540 (1.85%)		
occurrences (all)	10		
Gastrointestinal wall thickening			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences (all)	3		
Abdominal distension			
subjects affected / exposed	27 / 540 (5.00%)		
occurrences (all)	33		

Gastroesophageal reflux disease subjects affected / exposed occurrences (all)	34 / 540 (6.30%) 41		
Abdominal discomfort subjects affected / exposed occurrences (all)	9 / 540 (1.67%) 11		
Toothache subjects affected / exposed occurrences (all)	14 / 540 (2.59%) 15		
Stomatitis subjects affected / exposed occurrences (all)	33 / 540 (6.11%) 53		
Paraesthesia oral subjects affected / exposed occurrences (all)	2 / 540 (0.37%) 2		
Nausea subjects affected / exposed occurrences (all)	114 / 540 (21.11%) 163		
Mouth ulceration subjects affected / exposed occurrences (all)	13 / 540 (2.41%) 17		
Vomiting subjects affected / exposed occurrences (all)	88 / 540 (16.30%) 113		
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysesthesia syndrome subjects affected / exposed occurrences (all)	16 / 540 (2.96%) 20		
Acne subjects affected / exposed occurrences (all)	3 / 540 (0.56%) 4		
Actinic keratosis subjects affected / exposed occurrences (all)	1 / 540 (0.19%) 1		
Alopecia			

subjects affected / exposed	34 / 540 (6.30%)		
occurrences (all)	37		
Dermatitis acneiform			
subjects affected / exposed	17 / 540 (3.15%)		
occurrences (all)	18		
Dry skin			
subjects affected / exposed	21 / 540 (3.89%)		
occurrences (all)	25		
Hyperhidrosis			
subjects affected / exposed	9 / 540 (1.67%)		
occurrences (all)	10		
Perioral dermatitis			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences (all)	3		
Rash			
subjects affected / exposed	58 / 540 (10.74%)		
occurrences (all)	71		
Rash erythematous			
subjects affected / exposed	5 / 540 (0.93%)		
occurrences (all)	5		
Rash maculo-papular			
subjects affected / exposed	14 / 540 (2.59%)		
occurrences (all)	16		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	17 / 540 (3.15%)		
occurrences (all)	21		
Dysuria			
subjects affected / exposed	28 / 540 (5.19%)		
occurrences (all)	34		
Renal failure			
subjects affected / exposed	8 / 540 (1.48%)		
occurrences (all)	9		
Urinary incontinence			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences (all)	2		

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	90 / 540 (16.67%)		
occurrences (all)	118		
Back pain			
subjects affected / exposed	88 / 540 (16.30%)		
occurrences (all)	119		
Muscle spasms			
subjects affected / exposed	42 / 540 (7.78%)		
occurrences (all)	50		
Muscular weakness			
subjects affected / exposed	19 / 540 (3.52%)		
occurrences (all)	23		
Myalgia			
subjects affected / exposed	67 / 540 (12.41%)		
occurrences (all)	121		
Neck pain			
subjects affected / exposed	34 / 540 (6.30%)		
occurrences (all)	39		
Pain in extremity			
subjects affected / exposed	66 / 540 (12.22%)		
occurrences (all)	105		
Infections and infestations			
COVID-19			
subjects affected / exposed	64 / 540 (11.85%)		
occurrences (all)	71		
Cellulitis			
subjects affected / exposed	9 / 540 (1.67%)		
occurrences (all)	10		
Ear infection			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences (all)	2		
Folliculitis			
subjects affected / exposed	6 / 540 (1.11%)		
occurrences (all)	6		
Wound infection			

subjects affected / exposed	0 / 540 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	80 / 540 (14.81%)		
occurrences (all)	167		
Upper respiratory tract infection			
subjects affected / exposed	51 / 540 (9.44%)		
occurrences (all)	61		
Skin candida			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	18 / 540 (3.33%)		
occurrences (all)	18		
Pneumonia aspiration			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	64 / 540 (11.85%)		
occurrences (all)	107		
Oropharyngeal candidiasis			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences (all)	3		
Oral candidiasis			
subjects affected / exposed	17 / 540 (3.15%)		
occurrences (all)	26		
Lower respiratory tract infection			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences (all)	4		
Influenza			
subjects affected / exposed	13 / 540 (2.41%)		
occurrences (all)	14		
Fungal foot infection			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences (all)	1		
Bronchitis			

subjects affected / exposed occurrences (all)	23 / 540 (4.26%) 28		
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed occurrences (all)	84 / 540 (15.56%) 228		
Dehydration			
subjects affected / exposed occurrences (all)	10 / 540 (1.85%) 12		
Hypercalcaemia			
subjects affected / exposed occurrences (all)	21 / 540 (3.89%) 32		
Hyperglycaemia			
subjects affected / exposed occurrences (all)	37 / 540 (6.85%) 59		
Hyperkalaemia			
subjects affected / exposed occurrences (all)	29 / 540 (5.37%) 50		
Hyperphosphataemia			
subjects affected / exposed occurrences (all)	101 / 540 (18.70%) 177		
Decreased appetite			
subjects affected / exposed occurrences (all)	113 / 540 (20.93%) 164		
Hypocalcaemia			
subjects affected / exposed occurrences (all)	130 / 540 (24.07%) 321		
Hypomagnesaemia			
subjects affected / exposed occurrences (all)	54 / 540 (10.00%) 105		
Hyponatraemia			
subjects affected / exposed occurrences (all)	70 / 540 (12.96%) 122		
Hypophosphataemia			
subjects affected / exposed occurrences (all)	75 / 540 (13.89%) 131		

Hypokalaemia			
subjects affected / exposed	98 / 540 (18.15%)		
occurrences (all)	163		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 January 2017	<p>The following changes were made as per amendment 1: The inclusion criteria included only participants with unresectable disease;</p> <p>The exclusion criteria excluded participants with NSCLC with a targetable mutation in estimated glomerular filtration rate (EGFR), anaplastic lymphoma kinase (ALK), or ROS1;</p> <p>An enrollment stopping rule was incorporated that terminated further enrollment to the study if there was an excess of permanent treatment discontinuations due to study drug-related AEs;</p> <p>Strong inhibitors of cytochrome P450 family 1 subfamily A polypeptide 2 (CYP1A2), cytochrome P450 family 2 subfamily D member 6 (CYP2D6), and cytochrome P450 family 3 subfamily A member 4 (CYP3A4), as well as inducers of CYP3A4 and strong dual permeability glycoprotein (P-gp) and CYP3A4 inhibitors were included in the list of prohibited medications; An electrocardiogram (ECG) measurement was added at Day 1 and Day 15, 4 hours post-dose.</p>
02 February 2018	<p>The following change was made as per amendment 2: Exclusion criterion 1 was revised to exclude NSCLC participants with known BRAF mutations.</p>
25 July 2018	<p>The following changes were made as per amendment 4.1: Based on the favorable tolerability and encouraging efficacy observed in Phase 1, the sample size of Phase 2 was increased; A summary of Phase 1 was added, including determination of the MTD, overall safety, and preliminary efficacy for Phase 1; The overall enrollment for Phase 2 was increased to further evaluate the safety, efficacy, and PK of pralsetinib in RET-altered patients treated at the MTD/RP2D; Group 6 was added in Phase 2 to assess pralsetinib safety and efficacy in participants previously treated with a selective RET inhibitor; The allowed eastern cooperative oncology group (ECOG) performance status was changed to be 0 to 1; Quality of life assessments added.</p>
12 December 2018	<p>The following changes were made as per amendment 7:</p> <p>Phase 2:</p> <ul style="list-style-type: none">-Definitions of Groups 1 to 4 were adjusted to reflect previous treatment with approved standard of care agents.-Group 5 was split into new Group 5 and new Group 7 to reflect that solid tumor participants with RET fusions and RET mutations may be distinct clinical and/or regulatory populations; <p>Phase 2:</p> <ul style="list-style-type: none">- Sample size was 80 participants in Group 1, 40 participants in Group 2, 60 participants in Group 3, and 40 participants in Group 5 to test the efficacy hypotheses for each group (increasing the study's total sample size to 360 participants); <p>Phase 2:</p> <ul style="list-style-type: none">- Safety Review Committee was added; <p>Two new exclusion criteria were added to exclude participants with Grade 2 or serum phosphorus at baseline or with clinically significant interstitial lung disease or interstitial pneumonitis and exclusion criterion 7 was revised to clarify the washout period duration.</p>

03 July 2019	The following changes were made as per amendment 9: The study phase was updated from "1" to "1/2" to better describe the study design with the increased participant population and hypothesis testing; The Phase 2 Group 2 sample size was increased to 200 participants due to the encouraging initial data in treatment naïve RET fusion-positive NSCLC participants, to allow for enrollment of RET fusion-positive NSCLC participants with no prior treatment (increasing the study's total sample size to 527); Clarification was added that participants enrolled in Phase 1 and treated at the RP2D were pooled together with the appropriate Phase 2 groups for analyses; Statistics section was updated to align with the SAP.
08 July 2020	The following changes were made as per amendment 13: Group 5: To more accurately characterize the activity of pralsetinib across various RET fusion-positive solid tumor types, the sample size of Group 5 has increased from N ~ 40 to N ~ 100 participants (increasing the study's total sample size to 647 participants); Phase 2 secondary objective in NSCLC participants and exploratory objective in participants with tumor types other than NSCLC have been updated to assess brain metastases activity in participants with measurable (target by RECIST v1.1) lesions in the brain by BICR (brain metastases sub-population) and assess the time to intracranial progression in all participants; An additional analysis population, the RET-altered Measurable Disease Population, was added to provide an assessment of the activity of pralsetinib in a mechanistically relevant population. This will be the primary analysis population for ORR, DOR, CBR and DCR, while the remaining efficacy endpoints will be examined using the Efficacy Population; Pharmacodynamic parameters of pralsetinib included changes in tumor/blood including, but not limited to, changes in blood calcitonin and CEA and biochemical response rate (MTC participants only); Group 2: The primary intent of this cohort was to assess the activity of pralsetinib in the treatment-naïve participants with NSCLC; therefore, text was added to clarify that this group will include no more than 30 participants with prior systemic therapy; Updated study visit frequency after Cycle 17, all study visits after Cycle 17 will occur at every 4 cycles (16 weeks) (e.g. Cycle 21, Cycle 25...).
28 May 2022	The following changes were made as per amendment 14: End of study and duration of participant participation was added; Detail was provided regarding reporting of serious adverse events and reference safety information document.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported