Clinical trial results:
A Phase 2, Open-Label, Single-Arm, Multicenter Study to Evaluate the Efficacy and Safety of INCB054828 in Subjects With Advanced/Metastatic or Surgically Unresectable Cholangiocarcinoma Including FGFR2 Translocations Who Failed Previous Therapy

Summary

EudraCT number	2016-002422-36
Trial protocol	DE BE FR GB IT
Global end of trial date	01 February 2022

Results information

Result version number	v1 (current)
This version publication date	11 February 2023
First version publication date	11 February 2023

Trial information

Trial identification

Sponsor protocol code	INCB 54828-202

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Incyte Corporation
Sponsor organisation address	1801 Augustine Cutoff Drive, Wilmington, United States, 19803
Public contact	Study Director, Incyte Corporation, 1 18554633463, medinfo@incyte.com
Scientific contact	Study Director, Incyte Corporation, 1 18554633463, medinfo@incyte.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	01 February 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was evaluate the efficacy of pemigatinib in participants with advanced/metastatic or surgically unresectable cholangiocarcinoma with fibroblast growth factor (FGF) receptor 2 (FGFR2) translocation who have failed at least 1 previous treatment.

Protection of trial subjects:

This study was to be performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and conducted in adherence to the study Protocol, Good Clinical Practices as defined in Title 21 of the United States Code of Federal Regulations Parts 11, 50, 54, 56, and 312, as well as International Conference on Harmonisation Good Clinical Practice (ICH GCP) consolidated guidelines (E6) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 January 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Japan: 3
Country: Number of subjects enrolled	Korea, Republic of: 12
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Thailand: 4
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 89
Worldwide total number of subjects	147
EEA total number of subjects	29

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	101
From 65 to 84 years	46
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study enrolled participants at 68 study sites in the United States, South Korea, United Kingdom, France, Italy, Thailand, Germany, Belgium, Israel, Spain, Japan, and Taiwan.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A: FGFR2 rearrangements or fusions

Arm description:

Participants with fibroblast growth factor (FGF) receptor 2 (FGFR2) rearrangements or fusions self-administered oral pemigatinib at a starting dose of 13.5 milligrams (mg) once daily (QD) on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.

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

Dosage and administration details:

2.0- and 4.5-mg tablets; starting dose of 13.5 mg

Arm title	Cohort B: Other FGF/FGFR alterations

Arm description:

Participants with all other FGF/FGFR alterations self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.

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

Dosage and administration details:

2.0- and 4.5-mg tablets; starting dose of 13.5 mg

Arm title	Cohort C: negative for FGF/FGFR alterations

Arm description:

Participants with no FGF/FGFR alterations self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles (United States only). Pemigatinib was administered until documented disease progression or unacceptable toxicity.

Arm type	Experimental

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

Dosage and administration details:

2.0- and 4.5-mg tablets; starting dose of 13.5 mg

Arm title	Other

Arm description:

Participants with an FGF/FGFR status for whom the local laboratory FGF/FGFR results could not be confirmed centrally self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.

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

Dosage and administration details:

2.0- and 4.5-mg tablets; starting dose of 13.5 mg

Number of subjects in period 1	Cohort A: FGFR2 rearrangements or fusions	Cohort B: Other FGF/FGFR alterations	Cohort C: negative for FGF/FGFR alterations
Started	108	20	17
Completed	0	0	0
Not completed	108	20	17
Adverse event, serious fatal	73	18	15
Physician decision	1	-	-
Consent withdrawn by subject	7	2	1
Rolled Over to Another Study	1	-	-
Progressive Disease	4	-	1
Study Terminated by Sponsor	19	-	-
Lost to follow-up	3	-	-

Number of subjects in period 1	Other
Started	2
Completed	0
Not completed	2
Adverse event, serious fatal	2
Physician decision	-
Consent withdrawn by subject	-
Rolled Over to Another Study	-
Progressive Disease	-

Study Terminated by Sponsor	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A: FGFR2 rearrangements or fusions
Reporting group description:	
Participants with fibroblast growth factor (FGF) receptor 2 (FGFR2) rearrangements or fusions self-administered oral pemigatinib at a starting dose of 13.5 milligrams (mg) once daily (QD) on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.	
Reporting group title	Cohort B: Other FGF/FGFR alterations
Reporting group description:	
Participants with all other FGF/FGFR alterations self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.	
Reporting group title	Cohort C: negative for FGF/FGFR alterations
Reporting group description:	
Participants with no FGF/FGFR alterations self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles (United States only). Pemigatinib was administered until documented disease progression or unacceptable toxicity.	
Reporting group title	Other
Reporting group description:	
Participants with an FGF/FGFR status for whom the local laboratory FGF/FGFR results could not be confirmed centrally self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.	

Reporting group values	Cohort A: FGFR2 rearrangements or fusions	Cohort B: Other FGF/FGFR alterations	Cohort C: negative for FGF/FGFR alterations
Number of subjects	108	20	17
Age categorical Units: Subjects			
Adults (18-64 years)	83	10	6
From 65-84 years	25	10	11
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	55.2	61.9	65.6
standard deviation	± 12.00	± 10.99	± 7.12
Sex: Female, Male Units: participants			
Female	66	11	7
Male	42	9	10
Race, Customized Units: Subjects			
White	79	9	14
Black or African American	7	0	1
Asian	12	11	0
American-Indian/Alaska Native	0	0	1
Captured as "Other"	4	0	1
Missing	6	0	0
Ethnicity, Customized Units: Subjects			

Hispanic or Latino	2	0	4
Not Hispanic or Latino	88	18	13
Not Reported	15	0	0
Unknown	1	0	0
Captured as "Other"	2	2	0

Reporting group values	Other	Total	
Number of subjects	2	147	
Age categorical Units: Subjects			
Adults (18-64 years)	2	101	
From 65-84 years	0	46	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	41.0		
standard deviation	± 14.14	-	
Sex: Female, Male Units: participants			
Female	1	85	
Male	1	62	
Race, Customized Units: Subjects			
White	2	104	
Black or African American	0	8	
Asian	0	23	
American-Indian/Alaska Native	0	1	
Captured as "Other"	0	5	
Missing	0	6	
Ethnicity, Customized Units: Subjects			
Hispanic or Latino	0	6	
Not Hispanic or Latino	2	121	
Not Reported	0	15	
Unknown	0	1	
Captured as "Other"	0	4	

End points reporting groups

Reporting group title	Cohort A: FGFR2 rearrangements or fusions

Reporting group description:

Participants with fibroblast growth factor (FGF) receptor 2 (FGFR2) rearrangements or fusions self-administered oral pemigatinib at a starting dose of 13.5 milligrams (mg) once daily (QD) on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.

Reporting group title	Cohort B: Other FGF/FGFR alterations

Reporting group description:

Participants with all other FGF/FGFR alterations self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.

Reporting group title	Cohort C: negative for FGF/FGFR alterations

Reporting group description:

Participants with no FGF/FGFR alterations self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles (United States only). Pemigatinib was administered until documented disease progression or unacceptable toxicity.

Reporting group title	Other

Reporting group description:

Participants with an FGF/FGFR status for whom the local laboratory FGF/FGFR results could not be confirmed centrally self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.

Subject analysis set title	Cohort A + Cohort B
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with FGFR2 rearrangements or fusions (Cohort A) or with all other FGF/FGFR alterations (Cohort B) self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.

Subject analysis set title	All cohorts
Subject analysis set type	Full analysis

Subject analysis set description:

Participants in the Pharmacokinetic Population with FGFR2 rearrangements or fusions (Cohort A), participants with all other FGF/FGFR alterations (Cohort B), participants with no FGF/FGFR alterations (Cohort C; United States only), and participants with an FGF/FGFR status for whom the local laboratory FGF/FGFR results could not be confirmed centrally (Other) self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.

Primary: Objective response rate (ORR) in participants with FGFR2 rearrangements or fusions

End point title	Objective response rate (ORR) in participants with FGFR2 rearrangements or fusions[1]

End point description:

ORR was defined as the percentage of participants with a best overall response of complete response (CR) or partial response (PR) at any post-Baseline visit prior to first progressive disease (PD), per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 (v1.1). CR: disappearance of all target and non-target lesions and no appearance of any new lesions. Any pathological lymph nodes (whether target or non-target) must have a reduction in the short axis to <10 millimeters (mm). PR: complete disappearance or at least a 30% decrease in the sum of the diameters of target lesions, taking as a reference the baseline sum diameters, no new lesions, and no progression of non-target lesions. ORR was based on central genomics laboratory results. Response was based on review of scans by an independent centralized radiological review committee.

End point type	Primary

End point timeframe:

up to 1527 days

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not conducted for this endpoint.

End point values	Cohort A: FGFR2 rearrangements or fusions	Cohort B: Other FGF/FGFR alterations	Cohort C: negative for FGF/FGFR alterations	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	108	0[2]	0[3]	0[4]
Units: percentage of participants				
number (confidence interval 95%)	37.0 (27.94 to 46.86)	(to)	(to)	(to)

Notes:

[2] - Analysis was conducted in participants with FGFR2 rearrangements or fusions.

[3] - Analysis was conducted in participants with FGFR2 rearrangements or fusions.

[4] - Analysis was conducted in participants with FGFR2 rearrangements or fusions.

Statistical analyses

No statistical analyses for this end point

Secondary: ORR in participants FGF/FGFR alterations other than FGFR2 rearrangements or fusions

End point title	ORR in participants FGF/FGFR alterations other than FGFR2 rearrangements or fusions

End point description:

ORR was defined as the percentage of participants with a best overall response of CR or PR at any post-Baseline visit prior to first PD, per RECIST v1.1. CR: disappearance of all target and non-target lesions and no appearance of any new lesions. Any pathological lymph nodes (whether target or non-target) must have a reduction in the short axis to <10 mm. PR: complete disappearance or at least a 30% decrease in the sum of the diameters of target lesions, taking as a reference the baseline sum diameters, no new lesions, and no progression of non-target lesions. ORR was based on central genomics laboratory results. Response was based on review of scans by an independent centralized radiological review committee.

End point type	Secondary

End point timeframe:

up to 424 days

End point values	Cohort A: FGFR2 rearrangements or fusions	Cohort B: Other FGF/FGFR alterations	Cohort C: negative for FGF/FGFR alterations	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[5]	20	0[6]	0[7]
Units: percentage of participants				
number (confidence interval 95%)	(to)	0.0 (0.0 to 16.84)	(to)	(to)

Notes:

[5] - Analysis was conducted in participants with other FGF/FGFR alterations.

[6] - Analysis was conducted in participants with other FGF/FGFR alterations.

[7] - Analysis was conducted in participants with other FGF/FGFR alterations.

Statistical analyses

No statistical analyses for this end point

Secondary: ORR in all participants with FGF/FGFR alterations

End point title	ORR in all participants with FGF/FGFR alterations

End point description:

ORR was defined as the percentage of participants with a best overall response of CR or PR at any post-Baseline visit prior to first PD, per RECIST v1.1. CR: disappearance of all target and non-target lesions and no appearance of any new lesions. Any pathological lymph nodes (whether target or non-target) must have a reduction in the short axis to <10 mm. PR: complete disappearance or at least a 30% decrease in the sum of the diameters of target lesions, taking as a reference the baseline sum diameters, no new lesions, and no progression of non-target lesions. ORR was based on central genomics laboratory results. Response was based on review of scans by an independent centralized radiological review committee.

End point type	Secondary

End point timeframe:

up to 1527 days

End point values	Cohort A: FGFR2 rearrangements or fusions	Cohort B: Other FGF/FGFR alterations	Cohort C: negative for FGF/FGFR alterations	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[8]	0[9]	0[10]	0[11]
Units: percentage of participants				
number (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[8] - Analysis was conducted in all participants with FGF/FGFR alterations.

[9] - Analysis was conducted in all participants with FGF/FGFR alterations.

[10] - Analysis was conducted in all participants with FGF/FGFR alterations.

[11] - Analysis was conducted in all participants with FGF/FGFR alterations.

End point values	Cohort A + Cohort B			
Subject group type	Subject analysis set			
Number of subjects analysed	128			
Units: percentage of participants				
number (confidence interval 95%)	31.3 (23.35 to 40.04)			

Statistical analyses

No statistical analyses for this end point

Secondary: ORR in participants negative for FGF/FGFR alterations

End point title	ORR in participants negative for FGF/FGFR alterations

End point description:

ORR was defined as the percentage of participants with a best overall response of CR or PR at any post-Baseline visit prior to first PD, per RECIST v1.1. CR: disappearance of all target and non-target lesions and no appearance of any new lesions. Any pathological lymph nodes (whether target or non-target) must have a reduction in the short axis to <10 mm. PR: complete disappearance or at least a 30% decrease in the sum of the diameters of target lesions, taking as a reference the baseline sum diameters, no new lesions, and no progression of non-target lesions. ORR was based on central genomics laboratory results. Response was based on review of scans by an independent centralized radiological review committee.

End point type	Secondary

End point timeframe:

up to 143 days

End point values	Cohort A: FGFR2 rearrangements or fusions	Cohort B: Other FGF/FGFR alterations	Cohort C: negative for FGF/FGFR alterations	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[12]	0[13]	17	0[14]
Units: percentage of participants				
number (confidence interval 95%)	(to)	(to)	0.0 (0.0 to 19.51)	(to)

Notes:

[12] - Analysis was conducted in participants negative for FGF/FGFR alterations.

[13] - Analysis was conducted in participants negative for FGF/FGFR alterations.

[14] - Analysis was conducted in participants negative for FGF/FGFR alterations.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)

End point description:

PFS was defined as the length of time from the first dose of study drug (Day 1) to the earlier of death or disease progression by RECIST v1.1, as assessed by the independent centralized radiological review committee.

End point type	Secondary

End point timeframe:

up to 50.17 months

End point values	Cohort A: FGFR2 rearrangements or fusions	Cohort B: Other FGF/FGFR alterations	Cohort C: negative for FGF/FGFR alterations	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	108	20	17	0[15]
Units: months				
median (confidence interval 95%)	7.03 (6.08 to 10.48)	2.10 (1.18 to 4.86)	1.51 (1.38 to 1.84)	(to)

Notes:

[15] - Analysis was not conducted in this treatment group.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR)

End point title	Duration of response (DOR)

End point description:

DOR was defined as the time from the first overall response contributing to an objective response (CR or PR) as assessed by an independent centralized radiological review committee to the earlier of death or first overall response of PD occurring after the first overall response contributing to the objective response. CR: disappearance of all target and non-target lesions and no appearance of any new lesions. Any pathological lymph nodes (whether target or non-target) must have a reduction in the short axis to <10 millimeters (mm). PR: complete disappearance or at least a 30% decrease in the sum of the diameters of target lesions, taking as a reference the baseline sum diameters, no new lesions, and no progression of non-target lesions. PD: progression of a target or non-target lesion or presence of a new lesion.

End point type	Secondary

End point timeframe:

up to 47.11 months

End point values	Cohort A: FGFR2 rearrangements or fusions	Cohort B: Other FGF/FGFR alterations	Cohort C: negative for FGF/FGFR alterations	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	0[16]	0[17]	0[18]
Units: months				
median (confidence interval 95%)	9.13 (6.01 to 14.49)	(to)	(to)	(to)

Notes:

[16] - Analysis was conducted in those participants with a CR or PR.

[17] - Analysis was conducted in those participants with a CR or PR.

[18] - Analysis was not conducted in this treatment group.

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate (DCR)

End point title	Disease control rate (DCR)

End point description:

DCR was defined as the proportion of participants with an overall response of CR, PR, or stable disease (SD), per RECIST v1.1. CR: disappearance of all target and non-target lesions and no appearance of any new lesions. Any pathological lymph nodes (whether target or non-target) must have a reduction in the short axis to <10 mm. PR: complete disappearance or at least a 30% decrease in the sum of the diameters of target lesions, taking as a reference the baseline sum diameters, no new lesions, and no progression of non-target lesions. PD: progression of a target or non-target lesion or presence of a new lesion. SD: no change in target lesions to qualify for CR, PR, or PD.

End point type	Secondary

End point timeframe:

up to 1527 days

End point values	Cohort A: FGFR2 rearrangements or fusions	Cohort B: Other FGF/FGFR alterations	Cohort C: negative for FGF/FGFR alterations	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	108	20	17	0[19]
Units: percentage of participants				
number (confidence interval 95%)	82.4 (73.9 to 89.1)	40.0 (19.1 to 63.9)	17.6 (3.8 to 43.4)	(to)

Notes:

[19] - Analysis was not conducted in this treatment group.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

Overall survival was defined as the length of time from the first dose of study drug (Day 1) until the date of death due to any cause.

End point type	Secondary

End point timeframe:

up to 51.32 months

End point values	Cohort A: FGFR2 rearrangements or fusions	Cohort B: Other FGF/FGFR alterations	Cohort C: negative for FGF/FGFR alterations	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	108	20	17	0[20]
Units: months				
median (confidence interval 95%)	17.48 (14.36 to 22.93)	6.70 (2.10 to 10.55)	3.98 (1.97 to 4.60)	(to)

Notes:

[20] - Analysis was not conducted in this treatment group.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any treatment-emergent adverse event (TEAE)

End point title	Number of participants with any treatment-emergent adverse event (TEAE)

End point description:

An adverse event (AE) was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related, that occurred after a participant provided informed consent. Abnormal laboratory values or test results occurring after informed consent constituted AEs only if they induced clinical signs or symptoms, were considered clinically meaningful, required therapy (e.g., hematologic abnormality that required transfusion), or required changes in the study drug(s). A TEAE was defined as any adverse event either reported for the first time or the worsening of a pre-existing event after the first dose of study drug and within 30 days of the last dose of study drug.

End point type	Secondary

End point timeframe:

up to 1584 days

End point values	Cohort A: FGFR2 rearrangements or fusions	Cohort B: Other FGF/FGFR alterations	Cohort C: negative for FGF/FGFR alterations	Other
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	108	20	17	2
Units: participants	108	20	17	2

Statistical analyses

No statistical analyses for this end point

Secondary: First-order absorption rate constant (ka) of pemigatinib

End point title	First-order absorption rate constant (ka) of pemigatinib

End point description:

First-order absorption rate constant is defined as the rate at which a drug enters into the system.

End point type	Secondary

End point timeframe:

Predose; 1-2 hours post-dose; 4-12 hours post-dose

End point values	All cohorts			
Subject group type	Subject analysis set			
Number of subjects analysed	136			
Units: 1/hour				
arithmetic mean (standard deviation)	1.29 (± 0.827)			

Statistical analyses

No statistical analyses for this end point

Secondary: CL/F of pemigatinib

End point title	CL/F of pemigatinib

End point description:

CL/F is defined as apparent oral clearance.

End point type	Secondary

End point timeframe:

Predose; 1-2 hours post-dose; 4-12 hours post-dose

End point values	All cohorts			
Subject group type	Subject analysis set			
Number of subjects analysed	136			
Units: Liters/hour				
arithmetic mean (standard deviation)	12.2 (± 5.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: Vc/F of pemigatinib

End point title	Vc/F of pemigatinib

End point description:

Vc/F is defined as the apparent volume of distribution for the central compartment of pemigatinib.

End point type	Secondary

End point timeframe:

Predose; 1-2 hours post-dose; 4-12 hours post-dose

End point values	All cohorts			
Subject group type	Subject analysis set			
Number of subjects analysed	136			
Units: Liters				
arithmetic mean (standard deviation)	144 (± 55.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Vp/F of pemigatinib

End point title	Vp/F of pemigatinib

End point description:

Vp/F is defined as the apparent volume of distribution for the tissue (peripheral) compartment.

End point type	Secondary

End point timeframe:

Predose; 1-2 hours post-dose; 4-12 hours post-dose

End point values	All cohorts			
Subject group type	Subject analysis set			
Number of subjects analysed	136			
Units: Liters				
arithmetic mean (standard deviation)	85.6 (± 30.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

up to 1584 days

Adverse event reporting additional description:

Treatment-emergent adverse events, defined as adverse events either reported for the first time or the worsening of pre-existing events after the first dose of study drug and within 30 days of the last dose of study drug, have been reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Cohort A: FGFR2 rearrangements or fusions

Reporting group description:

Participants with fibroblast growth factor (FGF) receptor 2 (FGFR2) rearrangements or fusions self-administered oral pemigatinib at a starting dose of 13.5 milligrams (mg) once daily (QD) on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.

Reporting group title	Cohort B: Other FGF/FGFR alterations

Reporting group description:

Participants with all other FGF/FGFR alterations self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.

Reporting group title	Cohort C: negative for FGF/FGFR alterations

Reporting group description:

Participants with no FGF/FGFR alterations self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles (United States only). Pemigatinib was administered until documented disease progression or unacceptable toxicity.

Reporting group title	Other

Reporting group description:

Participants with an FGF/FGFR status for whom the local laboratory FGF/FGFR results could not be confirmed centrally self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a 2-weeks-on therapy/1-week-off schedule in 21-day cycles. Pemigatinib was administered until documented disease progression or unacceptable toxicity.

Reporting group title	Total

Reporting group description:

Total

Serious adverse events	Cohort A: FGFR2 rearrangements or fusions	Cohort B: Other FGF/FGFR alterations	Cohort C: negative for FGF/FGFR alterations
Total subjects affected by serious adverse events			
subjects affected / exposed	46 / 108 (42.59%)	10 / 20 (50.00%)	12 / 17 (70.59%)
number of deaths (all causes)	76	18	15
number of deaths resulting from adverse events	3	2	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			

subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complication associated with device			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	5 / 108 (4.63%)	1 / 20 (5.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 7	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	2 / 108 (1.85%)	2 / 20 (10.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Product issues			
Device leakage			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic cerebral infarction			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraplegia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Optic ischaemic neuropathy			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal artery occlusion			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 108 (3.70%)	1 / 20 (5.00%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	2 / 6	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Colitis			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	0 / 17 (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
Haematemesis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	0 / 17 (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
Melaena			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction gastric			

subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varices oesophageal			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary obstruction			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Biloma			

subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	5 / 108 (4.63%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Jaundice			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant biliary obstruction			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inappropriate antidiuretic hormone			

secretion			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract infection			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis infective			
subjects affected / exposed	3 / 108 (2.78%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Clostridium difficile infection			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter bacteraemia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal bacteraemia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	2 / 108 (1.85%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Septic shock			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			

subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Typhoid fever			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
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			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (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
Dehydration			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	2 / 108 (1.85%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			

subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 108 (0.93%)	2 / 20 (10.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Other	Total	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	68 / 147 (46.26%)	
number of deaths (all causes)	2	111	
number of deaths resulting from adverse events	0	6	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chills			

subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complication associated with device			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)	7 / 147 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)	5 / 147 (3.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia aspiration			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device leakage			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic cerebral infarction			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraplegia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery occlusion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			

subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	7 / 147 (4.76%)	
occurrences causally related to treatment / all	0 / 0	2 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varices oesophageal			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary obstruction			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Biloma			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	0 / 2 (0.00%)	6 / 147 (4.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 1	
Jaundice			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant biliary obstruction			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			

subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis infective			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter bacteraemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal bacteraemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Septic shock			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Typhoid fever			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Hypercalcaemia			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperuricaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort A: FGFR2 rearrangements or fusions	Cohort B: Other FGF/FGFR alterations	Cohort C: negative for FGF/FGFR alterations
Total subjects affected by non-serious adverse events			
subjects affected / exposed	108 / 108 (100.00%)	20 / 20 (100.00%)	17 / 17 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Malignant ascites			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Malignant pleural effusion			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Tumour associated fever			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	9 / 108 (8.33%)	3 / 20 (15.00%)	0 / 17 (0.00%)
occurrences (all)	11	4	0
Hypotension			
subjects affected / exposed	5 / 108 (4.63%)	2 / 20 (10.00%)	2 / 17 (11.76%)
occurrences (all)	9	2	3
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	15 / 108 (13.89%)	4 / 20 (20.00%)	1 / 17 (5.88%)
occurrences (all)	34	9	1
Chills			
subjects affected / exposed	6 / 108 (5.56%)	0 / 20 (0.00%)	2 / 17 (11.76%)
occurrences (all)	8	0	2
Fatigue			

subjects affected / exposed	50 / 108 (46.30%)	5 / 20 (25.00%)	9 / 17 (52.94%)
occurrences (all)	60	6	9
Gait disturbance			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	6 / 108 (5.56%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	7	0	0
Malaise			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	3 / 108 (2.78%)	1 / 20 (5.00%)	1 / 17 (5.88%)
occurrences (all)	3	2	1
Oedema peripheral			
subjects affected / exposed	16 / 108 (14.81%)	4 / 20 (20.00%)	6 / 17 (35.29%)
occurrences (all)	21	4	6
Pain			
subjects affected / exposed	4 / 108 (3.70%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	4	0	1
Performance status decreased			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	11 / 108 (10.19%)	3 / 20 (15.00%)	2 / 17 (11.76%)
occurrences (all)	20	3	2
Thirst			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	3 / 108 (2.78%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	3	1	0
Gynaecomastia			

subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Penile pain			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	10 / 108 (9.26%)	0 / 20 (0.00%)	2 / 17 (11.76%)
occurrences (all)	12	0	2
Dysphonia			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
Dyspnoea			
subjects affected / exposed	10 / 108 (9.26%)	3 / 20 (15.00%)	3 / 17 (17.65%)
occurrences (all)	12	3	3
Dyspnoea exertional			
subjects affected / exposed	3 / 108 (2.78%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	1
Epistaxis			
subjects affected / exposed	19 / 108 (17.59%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	24	1	0
Laryngeal inflammation			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	8 / 108 (7.41%)	1 / 20 (5.00%)	2 / 17 (11.76%)
occurrences (all)	9	1	2
Nasal dryness			
subjects affected / exposed	13 / 108 (12.04%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	14	0	0
Oropharyngeal pain			

subjects affected / exposed	11 / 108 (10.19%)	2 / 20 (10.00%)	0 / 17 (0.00%)
occurrences (all)	13	2	0
Pulmonary embolism			
subjects affected / exposed	0 / 108 (0.00%)	2 / 20 (10.00%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Rhinitis allergic			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Sinus pain			
subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Stridor			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
Depression			
subjects affected / exposed	6 / 108 (5.56%)	2 / 20 (10.00%)	1 / 17 (5.88%)
occurrences (all)	6	2	1
Hallucination			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	13 / 108 (12.04%)	2 / 20 (10.00%)	0 / 17 (0.00%)
occurrences (all)	13	2	0
Nervousness			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	3 / 108 (2.78%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Alanine aminotransferase increased			

subjects affected / exposed	12 / 108 (11.11%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	16	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	9 / 108 (8.33%)	1 / 20 (5.00%)	2 / 17 (11.76%)
occurrences (all)	16	3	2
Bilirubin conjugated increased			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Blood 1,25-dihydroxycholecalciferol decreased			
subjects affected / exposed	2 / 108 (1.85%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	4	1	0
Blood 1,25-dihydroxycholecalciferol increased			
subjects affected / exposed	2 / 108 (1.85%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	3	1	0
Blood 25-hydroxycholecalciferol decreased			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	12 / 108 (11.11%)	1 / 20 (5.00%)	2 / 17 (11.76%)
occurrences (all)	16	1	2
Blood bilirubin increased			
subjects affected / exposed	6 / 108 (5.56%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	9	0	1
Blood chloride decreased			
subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	1	4	0
Blood creatinine increased			
subjects affected / exposed	9 / 108 (8.33%)	2 / 20 (10.00%)	4 / 17 (23.53%)
occurrences (all)	12	2	4
Blood parathyroid hormone decreased			
subjects affected / exposed	3 / 108 (2.78%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	4	2	0
Blood urea increased			

subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	2 / 108 (1.85%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	2	1	0
Lipase increased			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	4 / 108 (3.70%)	1 / 20 (5.00%)	1 / 17 (5.88%)
occurrences (all)	5	2	1
Platelet count decreased			
subjects affected / exposed	8 / 108 (7.41%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	15	1	0
Transaminases increased			
subjects affected / exposed	1 / 108 (0.93%)	3 / 20 (15.00%)	0 / 17 (0.00%)
occurrences (all)	1	5	0
Tri-iodothyronine free increased			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	20 / 108 (18.52%)	4 / 20 (20.00%)	1 / 17 (5.88%)
occurrences (all)	23	4	1
Weight increased			
subjects affected / exposed	4 / 108 (3.70%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	7	2	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Fall			

subjects affected / exposed	8 / 108 (7.41%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	13	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	4	0	1
Nervous system disorders			
Coma			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	19 / 108 (17.59%)	1 / 20 (5.00%)	1 / 17 (5.88%)
occurrences (all)	23	1	1
Dysgeusia			
subjects affected / exposed	45 / 108 (41.67%)	3 / 20 (15.00%)	3 / 17 (17.65%)
occurrences (all)	49	5	3
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	20 / 108 (18.52%)	1 / 20 (5.00%)	2 / 17 (11.76%)
occurrences (all)	32	1	2
Neuropathy peripheral			
subjects affected / exposed	7 / 108 (6.48%)	2 / 20 (10.00%)	0 / 17 (0.00%)
occurrences (all)	8	2	0
Seizure			
subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Somnolence			

subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	1 / 17 (5.88%)
occurrences (all)	1	1	1
Taste disorder			
subjects affected / exposed	7 / 108 (6.48%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	9	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	16 / 108 (14.81%)	2 / 20 (10.00%)	2 / 17 (11.76%)
occurrences (all)	27	2	2
Febrile neutropenia			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Lymphopenia			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	3 / 108 (2.78%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	3	1	0
Eye disorders			
Cataract			
subjects affected / exposed	7 / 108 (6.48%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	10	0	0
Chorioretinal scar			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	38 / 108 (35.19%)	1 / 20 (5.00%)	1 / 17 (5.88%)
occurrences (all)	45	1	1
Episcleritis			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Eye discharge			

subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Eye pain			
subjects affected / exposed	6 / 108 (5.56%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	6	0	0
Growth of eyelashes			
subjects affected / exposed	8 / 108 (7.41%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	8	0	0
Keratitis			
subjects affected / exposed	4 / 108 (3.70%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	4	0	0
Lacrimation increased			
subjects affected / exposed	7 / 108 (6.48%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	12	0	0
Ocular hyperaemia			
subjects affected / exposed	6 / 108 (5.56%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	6	0	0
Presbyopia			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Punctate keratitis			
subjects affected / exposed	8 / 108 (7.41%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	8	1	0
Subretinal fluid			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Trichiasis			
subjects affected / exposed	11 / 108 (10.19%)	2 / 20 (10.00%)	0 / 17 (0.00%)
occurrences (all)	11	2	0
Trichomegaly			
subjects affected / exposed	2 / 108 (1.85%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Vitreous floaters			
subjects affected / exposed	5 / 108 (4.63%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	6	1	0
Gastrointestinal disorders			

Abdominal distension			
subjects affected / exposed	9 / 108 (8.33%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	10	0	1
Abdominal pain			
subjects affected / exposed	22 / 108 (20.37%)	3 / 20 (15.00%)	3 / 17 (17.65%)
occurrences (all)	39	3	3
Abdominal pain upper			
subjects affected / exposed	11 / 108 (10.19%)	2 / 20 (10.00%)	1 / 17 (5.88%)
occurrences (all)	16	2	1
Ascites			
subjects affected / exposed	4 / 108 (3.70%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	4	1	0
Constipation			
subjects affected / exposed	46 / 108 (42.59%)	5 / 20 (25.00%)	2 / 17 (11.76%)
occurrences (all)	68	6	2
Diarrhoea			
subjects affected / exposed	58 / 108 (53.70%)	5 / 20 (25.00%)	6 / 17 (35.29%)
occurrences (all)	169	15	6
Dry mouth			
subjects affected / exposed	42 / 108 (38.89%)	5 / 20 (25.00%)	1 / 17 (5.88%)
occurrences (all)	49	5	1
Dyspepsia			
subjects affected / exposed	14 / 108 (12.96%)	2 / 20 (10.00%)	0 / 17 (0.00%)
occurrences (all)	17	2	0
Dysphagia			
subjects affected / exposed	5 / 108 (4.63%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	5	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	13 / 108 (12.04%)	1 / 20 (5.00%)	2 / 17 (11.76%)
occurrences (all)	14	1	2
Haemorrhoids			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	45 / 108 (41.67%)	7 / 20 (35.00%)	7 / 17 (41.18%)
occurrences (all)	71	10	7

Retching			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	46 / 108 (42.59%)	6 / 20 (30.00%)	3 / 17 (17.65%)
occurrences (all)	74	10	3
Vomiting			
subjects affected / exposed	35 / 108 (32.41%)	3 / 20 (15.00%)	4 / 17 (23.53%)
occurrences (all)	55	3	5
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	3 / 108 (2.78%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	4	1	0
Hyperbilirubinaemia			
subjects affected / exposed	9 / 108 (8.33%)	2 / 20 (10.00%)	1 / 17 (5.88%)
occurrences (all)	9	2	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	64 / 108 (59.26%)	4 / 20 (20.00%)	3 / 17 (17.65%)
occurrences (all)	66	4	3
Decubitus ulcer			
subjects affected / exposed	2 / 108 (1.85%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	2	1	0
Dry skin			
subjects affected / exposed	30 / 108 (27.78%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	33	0	0
Erythema			
subjects affected / exposed	8 / 108 (7.41%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	9	0	0
Hypertrichosis			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nail discolouration			
subjects affected / exposed	12 / 108 (11.11%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	12	1	0
Nail disorder			

subjects affected / exposed	6 / 108 (5.56%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	6	0	0
Nail dystrophy			
subjects affected / exposed	11 / 108 (10.19%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	14	1	0
Onychoclasis			
subjects affected / exposed	9 / 108 (8.33%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	10	0	0
Onycholysis			
subjects affected / exposed	10 / 108 (9.26%)	2 / 20 (10.00%)	1 / 17 (5.88%)
occurrences (all)	10	2	1
Onychomadesis			
subjects affected / exposed	13 / 108 (12.04%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	14	1	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	23 / 108 (21.30%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	34	2	0
Pruritus			
subjects affected / exposed	13 / 108 (12.04%)	1 / 20 (5.00%)	1 / 17 (5.88%)
occurrences (all)	15	1	1
Psoriasis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Rash			
subjects affected / exposed	12 / 108 (11.11%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	14	0	1
Rash maculo-papular			
subjects affected / exposed	2 / 108 (1.85%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	2	1	0
Skin disorder			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Skin exfoliation			
subjects affected / exposed	6 / 108 (5.56%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	6	1	0

Skin fissures			
subjects affected / exposed	4 / 108 (3.70%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	4	1	0
Skin mass			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Skin ulcer			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	5 / 108 (4.63%)	1 / 20 (5.00%)	2 / 17 (11.76%)
occurrences (all)	6	1	2
Chronic kidney disease			
subjects affected / exposed	2 / 108 (1.85%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	2	1	0
Dysuria			
subjects affected / exposed	2 / 108 (1.85%)	2 / 20 (10.00%)	0 / 17 (0.00%)
occurrences (all)	2	2	0
Haematuria			
subjects affected / exposed	0 / 108 (0.00%)	2 / 20 (10.00%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Micturition urgency			
subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Pollakiuria			
subjects affected / exposed	3 / 108 (2.78%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	4	1	0
Urinary tract pain			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	37 / 108 (34.26%)	5 / 20 (25.00%)	2 / 17 (11.76%)
occurrences (all)	52	8	3
Back pain			

subjects affected / exposed	27 / 108 (25.00%)	1 / 20 (5.00%)	2 / 17 (11.76%)
occurrences (all)	34	1	2
Flank pain			
subjects affected / exposed	5 / 108 (4.63%)	2 / 20 (10.00%)	0 / 17 (0.00%)
occurrences (all)	5	2	0
Muscle spasms			
subjects affected / exposed	11 / 108 (10.19%)	1 / 20 (5.00%)	1 / 17 (5.88%)
occurrences (all)	12	1	1
Muscular weakness			
subjects affected / exposed	5 / 108 (4.63%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	6	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Myalgia			
subjects affected / exposed	15 / 108 (13.89%)	1 / 20 (5.00%)	2 / 17 (11.76%)
occurrences (all)	19	1	2
Neck pain			
subjects affected / exposed	5 / 108 (4.63%)	0 / 20 (0.00%)	2 / 17 (11.76%)
occurrences (all)	5	0	2
Osteoporotic fracture			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	26 / 108 (24.07%)	3 / 20 (15.00%)	0 / 17 (0.00%)
occurrences (all)	41	4	0
Infections and infestations			
Acinetobacter bacteraemia			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Bacterial vaginosis			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0

Bronchitis			
subjects affected / exposed	3 / 108 (2.78%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	3	1	0
Candida infection			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Cellulitis			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Conjunctivitis			
subjects affected / exposed	7 / 108 (6.48%)	1 / 20 (5.00%)	1 / 17 (5.88%)
occurrences (all)	9	1	1
Cystitis			
subjects affected / exposed	5 / 108 (4.63%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	6	1	0
Device related infection			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Fungal skin infection			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Klebsiella infection			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	6 / 108 (5.56%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	8	0	0
Oral candidiasis			
subjects affected / exposed	5 / 108 (4.63%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	6	0	0
Oral herpes			
subjects affected / exposed	1 / 108 (0.93%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1

Paronychia			
subjects affected / exposed	9 / 108 (8.33%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	9	1	0
Peritonitis			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Peritonitis bacterial			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	2 / 108 (1.85%)	1 / 20 (5.00%)	1 / 17 (5.88%)
occurrences (all)	2	1	1
Pneumonia			
subjects affected / exposed	1 / 108 (0.93%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Rash pustular			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Trichomoniasis			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	7 / 108 (6.48%)	0 / 20 (0.00%)	0 / 17 (0.00%)
occurrences (all)	8	0	0
Urinary tract infection			
subjects affected / exposed	21 / 108 (19.44%)	2 / 20 (10.00%)	2 / 17 (11.76%)
occurrences (all)	33	3	2
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 108 (0.00%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	34 / 108 (31.48%)	7 / 20 (35.00%)	7 / 17 (41.18%)
occurrences (all)	39	10	8
Dehydration			

subjects affected / exposed	16 / 108 (14.81%)	1 / 20 (5.00%)	3 / 17 (17.65%)
occurrences (all)	17	2	4
Hypercalcaemia			
subjects affected / exposed	16 / 108 (14.81%)	4 / 20 (20.00%)	1 / 17 (5.88%)
occurrences (all)	18	5	2
Hypercholesterolaemia			
subjects affected / exposed	2 / 108 (1.85%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	2	1	0
Hyperglycaemia			
subjects affected / exposed	2 / 108 (1.85%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	4	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hyperphosphataemia			
subjects affected / exposed	60 / 108 (55.56%)	13 / 20 (65.00%)	12 / 17 (70.59%)
occurrences (all)	109	14	13
Hyperuricaemia			
subjects affected / exposed	4 / 108 (3.70%)	3 / 20 (15.00%)	1 / 17 (5.88%)
occurrences (all)	5	3	1
Hypoalbuminaemia			
subjects affected / exposed	2 / 108 (1.85%)	2 / 20 (10.00%)	3 / 17 (17.65%)
occurrences (all)	2	2	3
Hypocalcaemia			
subjects affected / exposed	2 / 108 (1.85%)	1 / 20 (5.00%)	1 / 17 (5.88%)
occurrences (all)	3	1	1
Hypokalaemia			
subjects affected / exposed	9 / 108 (8.33%)	0 / 20 (0.00%)	1 / 17 (5.88%)
occurrences (all)	10	0	1
Hyponatraemia			
subjects affected / exposed	6 / 108 (5.56%)	4 / 20 (20.00%)	4 / 17 (23.53%)
occurrences (all)	10	6	6
Hypophosphataemia			
subjects affected / exposed	28 / 108 (25.93%)	4 / 20 (20.00%)	2 / 17 (11.76%)
occurrences (all)	49	6	2
Hypovitaminosis			

subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Malnutrition			
subjects affected / exposed	0 / 108 (0.00%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Vitamin D deficiency			
subjects affected / exposed	10 / 108 (9.26%)	1 / 20 (5.00%)	0 / 17 (0.00%)
occurrences (all)	10	1	0

Non-serious adverse events	Other	Total	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	147 / 147 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Malignant ascites			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Malignant pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Tumour associated fever			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	0 / 2 (0.00%)	12 / 147 (8.16%)	
occurrences (all)	0	15	
Hypotension			
subjects affected / exposed	0 / 2 (0.00%)	9 / 147 (6.12%)	
occurrences (all)	0	14	
General disorders and administration			

site conditions				
Asthenia				
subjects affected / exposed	0 / 2 (0.00%)	20 / 147 (13.61%)		
occurrences (all)	0	44		
Chills				
subjects affected / exposed	0 / 2 (0.00%)	8 / 147 (5.44%)		
occurrences (all)	0	10		
Fatigue				
subjects affected / exposed	0 / 2 (0.00%)	64 / 147 (43.54%)		
occurrences (all)	0	75		
Gait disturbance				
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)		
occurrences (all)	0	1		
Influenza like illness				
subjects affected / exposed	0 / 2 (0.00%)	6 / 147 (4.08%)		
occurrences (all)	0	7		
Malaise				
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)		
occurrences (all)	0	1		
Non-cardiac chest pain				
subjects affected / exposed	0 / 2 (0.00%)	5 / 147 (3.40%)		
occurrences (all)	0	6		
Oedema peripheral				
subjects affected / exposed	0 / 2 (0.00%)	26 / 147 (17.69%)		
occurrences (all)	0	31		
Pain				
subjects affected / exposed	0 / 2 (0.00%)	5 / 147 (3.40%)		
occurrences (all)	0	5		
Performance status decreased				
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)		
occurrences (all)	0	1		
Pyrexia				
subjects affected / exposed	0 / 2 (0.00%)	16 / 147 (10.88%)		
occurrences (all)	0	25		
Thirst				

subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 2 (0.00%)	4 / 147 (2.72%)	
occurrences (all)	0	4	
Gynaecomastia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Penile pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	0 / 2 (0.00%)	12 / 147 (8.16%)	
occurrences (all)	0	14	
Dysphonia			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences (all)	0	3	
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	16 / 147 (10.88%)	
occurrences (all)	0	18	
Dyspnoea exertional			
subjects affected / exposed	0 / 2 (0.00%)	4 / 147 (2.72%)	
occurrences (all)	0	4	
Epistaxis			
subjects affected / exposed	0 / 2 (0.00%)	20 / 147 (13.61%)	
occurrences (all)	0	25	
Laryngeal inflammation			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Nasal congestion			

subjects affected / exposed	0 / 2 (0.00%)	11 / 147 (7.48%)	
occurrences (all)	0	12	
Nasal dryness			
subjects affected / exposed	0 / 2 (0.00%)	13 / 147 (8.84%)	
occurrences (all)	0	14	
Oropharyngeal pain			
subjects affected / exposed	0 / 2 (0.00%)	13 / 147 (8.84%)	
occurrences (all)	0	15	
Pulmonary embolism			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Rhinitis allergic			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Sinus pain			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Stridor			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	3	
Depression			
subjects affected / exposed	0 / 2 (0.00%)	9 / 147 (6.12%)	
occurrences (all)	0	9	
Hallucination			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	0 / 2 (0.00%)	15 / 147 (10.20%)	
occurrences (all)	0	15	
Nervousness			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	

Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 2 (50.00%)	4 / 147 (2.72%)	
occurrences (all)	1	4	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	13 / 147 (8.84%)	
occurrences (all)	0	17	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	12 / 147 (8.16%)	
occurrences (all)	0	21	
Bilirubin conjugated increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Blood 1,25-dihydroxycholecalciferol decreased			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences (all)	0	5	
Blood 1,25-dihydroxycholecalciferol increased			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences (all)	0	4	
Blood 25-hydroxycholecalciferol decreased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 2 (0.00%)	15 / 147 (10.20%)	
occurrences (all)	0	19	
Blood bilirubin increased			
subjects affected / exposed	0 / 2 (0.00%)	7 / 147 (4.76%)	
occurrences (all)	0	10	
Blood chloride decreased			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	5	
Blood creatinine increased			
subjects affected / exposed	0 / 2 (0.00%)	15 / 147 (10.20%)	
occurrences (all)	0	18	

Blood parathyroid hormone decreased			
subjects affected / exposed	0 / 2 (0.00%)	4 / 147 (2.72%)	
occurrences (all)	0	6	
Blood urea increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
C-reactive protein increased			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences (all)	0	3	
Lipase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Lymphocyte count decreased			
subjects affected / exposed	0 / 2 (0.00%)	6 / 147 (4.08%)	
occurrences (all)	0	8	
Platelet count decreased			
subjects affected / exposed	1 / 2 (50.00%)	10 / 147 (6.80%)	
occurrences (all)	1	17	
Transaminases increased			
subjects affected / exposed	0 / 2 (0.00%)	4 / 147 (2.72%)	
occurrences (all)	0	6	
Tri-iodothyronine free increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	1 / 2 (50.00%)	26 / 147 (17.69%)	
occurrences (all)	1	29	
Weight increased			
subjects affected / exposed	0 / 2 (0.00%)	5 / 147 (3.40%)	
occurrences (all)	0	9	
Injury, poisoning and procedural complications			

Accidental overdose			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	0 / 2 (0.00%)	9 / 147 (6.12%)	
occurrences (all)	0	14	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 2 (50.00%)	3 / 147 (2.04%)	
occurrences (all)	1	3	
Sinus tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences (all)	0	5	
Nervous system disorders			
Coma			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	0 / 2 (0.00%)	21 / 147 (14.29%)	
occurrences (all)	0	25	
Dysgeusia			
subjects affected / exposed	2 / 2 (100.00%)	53 / 147 (36.05%)	
occurrences (all)	2	59	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 2 (0.00%)	23 / 147 (15.65%)	
occurrences (all)	0	35	
Neuropathy peripheral			
subjects affected / exposed	0 / 2 (0.00%)	9 / 147 (6.12%)	
occurrences (all)	0	10	
Seizure			

subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Somnolence			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences (all)	0	3	
Taste disorder			
subjects affected / exposed	0 / 2 (0.00%)	7 / 147 (4.76%)	
occurrences (all)	0	9	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	20 / 147 (13.61%)	
occurrences (all)	0	31	
Febrile neutropenia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Iron deficiency anaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Lymphopenia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 2 (0.00%)	4 / 147 (2.72%)	
occurrences (all)	0	4	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 2 (0.00%)	7 / 147 (4.76%)	
occurrences (all)	0	10	
Chorioretinal scar			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Dry eye			
subjects affected / exposed	1 / 2 (50.00%)	41 / 147 (27.89%)	
occurrences (all)	1	48	
Episcleritis			

subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Eye discharge			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Eye pain			
subjects affected / exposed	0 / 2 (0.00%)	6 / 147 (4.08%)	
occurrences (all)	0	6	
Growth of eyelashes			
subjects affected / exposed	0 / 2 (0.00%)	8 / 147 (5.44%)	
occurrences (all)	0	8	
Keratitis			
subjects affected / exposed	1 / 2 (50.00%)	5 / 147 (3.40%)	
occurrences (all)	1	5	
Lacrimation increased			
subjects affected / exposed	0 / 2 (0.00%)	7 / 147 (4.76%)	
occurrences (all)	0	12	
Ocular hyperaemia			
subjects affected / exposed	0 / 2 (0.00%)	6 / 147 (4.08%)	
occurrences (all)	0	6	
Presbyopia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Punctate keratitis			
subjects affected / exposed	1 / 2 (50.00%)	10 / 147 (6.80%)	
occurrences (all)	1	10	
Subretinal fluid			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Trichiasis			
subjects affected / exposed	0 / 2 (0.00%)	13 / 147 (8.84%)	
occurrences (all)	0	13	
Trichomegaly			
subjects affected / exposed	1 / 2 (50.00%)	3 / 147 (2.04%)	
occurrences (all)	1	3	
Vitreous floaters			

subjects affected / exposed	0 / 2 (0.00%)	6 / 147 (4.08%)	
occurrences (all)	0	7	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 2 (0.00%)	10 / 147 (6.80%)	
occurrences (all)	0	11	
Abdominal pain			
subjects affected / exposed	1 / 2 (50.00%)	29 / 147 (19.73%)	
occurrences (all)	1	46	
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)	14 / 147 (9.52%)	
occurrences (all)	0	19	
Ascites			
subjects affected / exposed	0 / 2 (0.00%)	5 / 147 (3.40%)	
occurrences (all)	0	5	
Constipation			
subjects affected / exposed	1 / 2 (50.00%)	54 / 147 (36.73%)	
occurrences (all)	1	77	
Diarrhoea			
subjects affected / exposed	1 / 2 (50.00%)	70 / 147 (47.62%)	
occurrences (all)	1	191	
Dry mouth			
subjects affected / exposed	2 / 2 (100.00%)	50 / 147 (34.01%)	
occurrences (all)	2	57	
Dyspepsia			
subjects affected / exposed	0 / 2 (0.00%)	16 / 147 (10.88%)	
occurrences (all)	0	19	
Dysphagia			
subjects affected / exposed	0 / 2 (0.00%)	6 / 147 (4.08%)	
occurrences (all)	0	6	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 2 (0.00%)	16 / 147 (10.88%)	
occurrences (all)	0	17	
Haemorrhoids			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	

Nausea			
subjects affected / exposed	1 / 2 (50.00%)	60 / 147 (40.82%)	
occurrences (all)	2	90	
Retching			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	1 / 2 (50.00%)	56 / 147 (38.10%)	
occurrences (all)	1	88	
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	42 / 147 (28.57%)	
occurrences (all)	0	63	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 2 (0.00%)	4 / 147 (2.72%)	
occurrences (all)	0	5	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 2 (0.00%)	12 / 147 (8.16%)	
occurrences (all)	0	12	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 2 (100.00%)	73 / 147 (49.66%)	
occurrences (all)	2	75	
Decubitus ulcer			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences (all)	0	3	
Dry skin			
subjects affected / exposed	2 / 2 (100.00%)	32 / 147 (21.77%)	
occurrences (all)	2	35	
Erythema			
subjects affected / exposed	0 / 2 (0.00%)	8 / 147 (5.44%)	
occurrences (all)	0	9	
Hypertrichosis			
subjects affected / exposed	1 / 2 (50.00%)	1 / 147 (0.68%)	
occurrences (all)	1	1	
Nail discolouration			

subjects affected / exposed	1 / 2 (50.00%)	14 / 147 (9.52%)		
occurrences (all)	1	14		
Nail disorder				
subjects affected / exposed	0 / 2 (0.00%)	6 / 147 (4.08%)		
occurrences (all)	0	6		
Nail dystrophy				
subjects affected / exposed	0 / 2 (0.00%)	12 / 147 (8.16%)		
occurrences (all)	0	15		
Onychoclasis				
subjects affected / exposed	0 / 2 (0.00%)	9 / 147 (6.12%)		
occurrences (all)	0	10		
Onycholysis				
subjects affected / exposed	0 / 2 (0.00%)	13 / 147 (8.84%)		
occurrences (all)	0	13		
Onychomadesis				
subjects affected / exposed	0 / 2 (0.00%)	14 / 147 (9.52%)		
occurrences (all)	0	15		
Palmar-plantar erythrodysaesthesia syndrome				
subjects affected / exposed	0 / 2 (0.00%)	24 / 147 (16.33%)		
occurrences (all)	0	36		
Pruritus				
subjects affected / exposed	0 / 2 (0.00%)	15 / 147 (10.20%)		
occurrences (all)	0	17		
Psoriasis				
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)		
occurrences (all)	0	2		
Rash				
subjects affected / exposed	0 / 2 (0.00%)	13 / 147 (8.84%)		
occurrences (all)	0	15		
Rash maculo-papular				
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)		
occurrences (all)	0	3		
Skin disorder				
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)		
occurrences (all)	0	1		

Skin exfoliation			
subjects affected / exposed	0 / 2 (0.00%)	7 / 147 (4.76%)	
occurrences (all)	0	7	
Skin fissures			
subjects affected / exposed	0 / 2 (0.00%)	5 / 147 (3.40%)	
occurrences (all)	0	5	
Skin mass			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Skin ulcer			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	2	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 2 (0.00%)	8 / 147 (5.44%)	
occurrences (all)	0	9	
Chronic kidney disease			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences (all)	0	3	
Dysuria			
subjects affected / exposed	0 / 2 (0.00%)	4 / 147 (2.72%)	
occurrences (all)	0	4	
Haematuria			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Micturition urgency			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Pollakiuria			
subjects affected / exposed	0 / 2 (0.00%)	4 / 147 (2.72%)	
occurrences (all)	0	5	
Urinary tract pain			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	3	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)	44 / 147 (29.93%)	
occurrences (all)	0	63	
Back pain			
subjects affected / exposed	0 / 2 (0.00%)	30 / 147 (20.41%)	
occurrences (all)	0	37	
Flank pain			
subjects affected / exposed	0 / 2 (0.00%)	7 / 147 (4.76%)	
occurrences (all)	0	7	
Muscle spasms			
subjects affected / exposed	0 / 2 (0.00%)	13 / 147 (8.84%)	
occurrences (all)	0	14	
Muscular weakness			
subjects affected / exposed	0 / 2 (0.00%)	6 / 147 (4.08%)	
occurrences (all)	0	7	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)	18 / 147 (12.24%)	
occurrences (all)	0	22	
Neck pain			
subjects affected / exposed	0 / 2 (0.00%)	7 / 147 (4.76%)	
occurrences (all)	0	7	
Osteoporotic fracture			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 2 (0.00%)	29 / 147 (19.73%)	
occurrences (all)	0	45	
Infections and infestations			
Acinetobacter bacteraemia			

subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Bacterial vaginosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	0 / 2 (0.00%)	4 / 147 (2.72%)	
occurrences (all)	0	4	
Candida infection			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Cellulitis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Conjunctivitis			
subjects affected / exposed	0 / 2 (0.00%)	9 / 147 (6.12%)	
occurrences (all)	0	11	
Cystitis			
subjects affected / exposed	0 / 2 (0.00%)	6 / 147 (4.08%)	
occurrences (all)	0	7	
Device related infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Fungal skin infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Herpes zoster			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Klebsiella infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 2 (0.00%)	6 / 147 (4.08%)	
occurrences (all)	0	8	
Oral candidiasis			

subjects affected / exposed	1 / 2 (50.00%)	6 / 147 (4.08%)	
occurrences (all)	1	7	
Oral herpes			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Paronychia			
subjects affected / exposed	0 / 2 (0.00%)	10 / 147 (6.80%)	
occurrences (all)	0	10	
Peritonitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Peritonitis bacterial			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	0 / 2 (0.00%)	4 / 147 (2.72%)	
occurrences (all)	0	4	
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 147 (1.36%)	
occurrences (all)	0	2	
Rash pustular			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Trichomoniasis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)	7 / 147 (4.76%)	
occurrences (all)	0	8	
Urinary tract infection			
subjects affected / exposed	1 / 2 (50.00%)	26 / 147 (17.69%)	
occurrences (all)	1	39	
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	1 / 2 (50.00%)	49 / 147 (33.33%)	
occurrences (all)	2	59	
Dehydration			
subjects affected / exposed	1 / 2 (50.00%)	21 / 147 (14.29%)	
occurrences (all)	1	24	
Hypercalcaemia			
subjects affected / exposed	0 / 2 (0.00%)	21 / 147 (14.29%)	
occurrences (all)	0	25	
Hypercholesterolaemia			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences (all)	0	3	
Hyperglycaemia			
subjects affected / exposed	0 / 2 (0.00%)	3 / 147 (2.04%)	
occurrences (all)	0	5	
Hyperkalaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Hyperphosphataemia			
subjects affected / exposed	1 / 2 (50.00%)	86 / 147 (58.50%)	
occurrences (all)	1	137	
Hyperuricaemia			
subjects affected / exposed	1 / 2 (50.00%)	9 / 147 (6.12%)	
occurrences (all)	1	10	
Hypoalbuminaemia			
subjects affected / exposed	0 / 2 (0.00%)	7 / 147 (4.76%)	
occurrences (all)	0	7	
Hypocalcaemia			
subjects affected / exposed	0 / 2 (0.00%)	4 / 147 (2.72%)	
occurrences (all)	0	5	
Hypokalaemia			
subjects affected / exposed	0 / 2 (0.00%)	10 / 147 (6.80%)	
occurrences (all)	0	11	
Hyponatraemia			
subjects affected / exposed	0 / 2 (0.00%)	14 / 147 (9.52%)	
occurrences (all)	0	22	

Hypophosphataemia			
subjects affected / exposed	0 / 2 (0.00%)	34 / 147 (23.13%)	
occurrences (all)	0	57	
Hypovitaminosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Malnutrition			
subjects affected / exposed	0 / 2 (0.00%)	1 / 147 (0.68%)	
occurrences (all)	0	1	
Vitamin D deficiency			
subjects affected / exposed	1 / 2 (50.00%)	12 / 147 (8.16%)	
occurrences (all)	1	12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 September 2016	The primary purpose of this amendment was to amend the language regarding participants to whom the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)-BIL21 was to be administered.
05 December 2016	The primary purpose of this amendment was to update language based on Regulatory Agencies comments. Updates included but were not limited to clarification of inclusion and exclusion criteria, the addition of updated clinical experience data, and guidance for dose reductions.
18 January 2017	The primary purpose of this amendment was to update the text in the Protocol based on the European Union Voluntary Harmonisation Procedure (VHP) request, to clarify requirements for human immunodeficiency virus (HIV) screening and enrollment parameters for Cohort C.
21 March 2017	The primary purpose of this amendment was to provide new language to allow participants to enroll under local genomic testing results. Updated clinical experience data were added as well.
03 October 2017	The primary purpose of this amendment was to increase the total number of participants enrolled into the study.
15 February 2018	The primary purpose of this amendment was to ensure the study population was clearly identified, to provide guidelines for dose reductions, and to provide additional language for ophthalmologic testing and hyperphosphatemia grading.
02 April 2020	The primary purpose of this amendment was to incorporate previous administrative changes and include updated language for comprehensive eye examination, per Food and Drug Administration (FDA) feedback.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported