Clinical trial results:
A phase II multicenter, single arm study of oral BGJ398 in adult patients with advanced or metastatic cholangiocarcinoma with FGFR2 gene fusions or other FGFR genetic alterations who failed or are intolerant to platinum-based chemotherapy

Summary

EudraCT number	2013-005085-19
Trial protocol	ES BE IT DE GB
Global end of trial date	07 February 2022

Results information

Result version number	v1 (current)
This version publication date	24 December 2023
First version publication date	24 December 2023
Summary attachment (see zip file)	02. 2204-Abbr CSR_final published_Synopsis_30Jan2023 (02. 2204-Abbr CSR_final published_Synopsis_30Jan2023.pdf) CSR Final (2204-Abbr CSR_final published_30Jan2023.pdf)

Trial information

Trial identification

Sponsor protocol code	CBGJ398X2204

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02150967
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	QED Therapeutics, Inc.
Sponsor organisation address	1800 Owens Street, Suite C-1200, San Francisco, United States, CA 94158
Public contact	David van Veenhuyzen,, QED Therapeutics, Inc., +1 650 296 2307, clinicaltrials@QEDTx.com
Scientific contact	David van Veenhuyzen,, QED Therapeutics, Inc., +1 650 296 2307, clinicaltrials@QEDTx.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	30 January 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 March 2021
Global end of trial reached?	Yes
Global end of trial date	07 February 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of single agent BGJ398 in patients with advanced or metastatic cholangiocarcinoma with FGFR2 gene fusions/translocations or other FGFR genetic alterations assessed by investigator as per RECIST v1.1.

Protection of trial subjects:

Prior to the start of the study, the study protocol and Informed Consent Form (ICF) were reviewed and approved by the appropriate EC. All amendments to the protocol were approved by the EC. Subjects signed the pre-screening/generic ICF in the presence of a suitably trained staff member prior to the conduct of pre-screening procedures. Prior to the commencement of the study, each subject was provided with study-specific ICF giving details of the IMPs, procedures and potential risks involved.
Study Design: This multicenter, open-label, 3-cohort, Phase 2 study evaluated infigratinib antitumor activity in subjects with advanced or metastatic cholangiocarcinoma with FGFR genetic alterations. Documented evidence of FGFR gene alterations was required for enrollment. The specific genetic alterations allowed on study were determined through molecular prescreening and subdivided into FGFR2 fusions vs other FGFR genetic alterations.
This abbreviated CSR provides methods and safety results of the final analyses of the study for Cohorts 1, 2, and 3. Results of the primary efficacy analysis (Cohort 1) are reported in the primary CSR (X2204p].
The Schedule of Assessments used in the study is provided in the primary CSR [X2204p – Section 9.5]. To assess the efficacy of infigratinib, subjects were evaluated for tumor response radiographically every 8 weeks until disease progression using RECIST version 1.1 or until subjects discontinued from the study. Responses of partial response (PR) and complete response (CR) were confirmed by repeat assessment ≥4 weeks after the criterion for response was first met.
The safety evaluation was based on adverse event (AE) reporting, laboratory evaluations, vital signs, ophthalmic evaluations, electrocardiogram (ECG) and cardiac imaging assessments, Eastern Cooperative Oncology Group (ECOG) performance status (PS), and pregnancy outcome (if applicable).

Background therapy:

-

Evidence for comparator:

-

Actual start date of recruitment	23 July 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Ethical reason
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 1
Country: Number of subjects enrolled	Singapore: 4

Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Thailand: 3
Country: Number of subjects enrolled	United States: 94
Country: Number of subjects enrolled	Germany: 18
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	United Kingdom: 4
Worldwide total number of subjects	143
EEA total number of subjects	36

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)	107
From 65 to 84 years	36
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First participant enrolled: 23 July 2014
Last Patient Last Visit performed 07 February 2022

Pre-assignment

Screening details:

Potential participants were approached if they fulfil the inclusion/exclusion criteria and were asked if they would like to participate in the study.
Patients were divided into 3 cohorts. Cohort 1 , Cohort 2 and Cohort 3.

Period 1

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

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

Subjects with FGFR2 fusions/rearrangements (N=108).
These are the same 108 subjects as the main dataset presented in the interim CSR [X2204i] (“Interim Analysis Set 2 for Cohort 1”) and the primary CSR [X2204p] (“subjects with FGFR2 fusion/rearrangement in Cohort 1 FAS”); the only difference between reports was the length of follow-up (an additional 11 months).

Note: No new efficacy analysis was done for the final CSR (aCSR), since these subs had completed their primary efficacy analysis (reported into he primary CSR)

Arm type	Experimental
Investigational medicinal product name	Infigratinib
Investigational medicinal product code	BGJ398
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

125 mg milligram(s) per day Oral use

Arm title	Cohort 2

Arm description:

Cohort 2: Subjects with other FGFR alterations other than FGFR2 gene fusions or rearrangements (N=25).
This cohort includes all 11 subjects enrolled to Cohort 2 and the 14 subjects with other FGFR alterations enrolled to Cohort 1 under the original protocol.

Note: No efficacy analysis were performed since the study was terminated early.

Arm type	Experimental
Investigational medicinal product name	Infigratinib
Investigational medicinal product code	BGJ398
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

125 mg milligram(s) per day Oral use

Arm title	Cohort 3

Arm description:

Cohort 3: Subjects with FGFR2 gene fusions/rearrangements who have received a prior FGFR inhibitor other than infigratinib (N=10).
Note that Cohorts 2 and 3 were added at protocol amendment 4 to support exploratory objectives of the study and were not included in the analyses presented in the interim CSR [X2204i] or primary CSR [X2204p].

Arm type	Experimental
Investigational medicinal product name	Infigratinib
Investigational medicinal product code	BGJ398
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

125 mg milligram(s) per day Oral use

Number of subjects in period 1	Cohort 1	Cohort 2	Cohort 3
Started	108	25	10
Completed	108	25	10

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1

Reporting group description:

Subjects with FGFR2 fusions/rearrangements (N=108).
These are the same 108 subjects as the main dataset presented in the interim CSR [X2204i] ("Interim Analysis Set 2 for Cohort 1") and the primary CSR [X2204p] ("subjects with FGFR2 fusion/rearrangement in Cohort 1 FAS"); the only difference between reports was the length of follow-up (an additional 11 months).

Note: No new efficacy analysis was done for the final CSR (aCSR), since these subs had completed their primary efficacy analysis (reported into he primary CSR)

Reporting group title	Cohort 2

Reporting group description:

Cohort 2: Subjects with other FGFR alterations other than FGFR2 gene fusions or rearrangements (N=25).
This cohort includes all 11 subjects enrolled to Cohort 2 and the 14 subjects with other FGFR alterations enrolled to Cohort 1 under the original protocol.

Note: No efficacy analysis were performed since the study was terminated early.

Reporting group title	Cohort 3

Reporting group description:

Cohort 3: Subjects with FGFR2 gene fusions/rearrangements who have received a prior FGFR inhibitor other than infigratinib (N=10).
Note that Cohorts 2 and 3 were added at protocol amendment 4 to support exploratory objectives of the study and were not included in the analyses presented in the interim CSR [X2204i] or primary CSR [X2204p].

Reporting group values	Cohort 1	Cohort 2	Cohort 3
Number of subjects	108	25	10
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	82	17	8
From 65-84 years	26	8	2
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	67	12	3
Male	41	13	7
ECOG PS			
Measure Description: Functional status was assessed at baseline using the Eastern Cooperative Oncology Group Performance Scale (ECOG PS)			
Units: Subjects			
00	45	11	3
01	62	13	7

02	1	1	0
Primary site of cancer			
Primary site of cancer			
Units: Subjects			
Bile duct	105	24	10
Cholangiocarcinoma	1	1	0
Liver	2	0	0
Non-Liver MetastaticSite Units: Subjects			
No metastatic site	5	4	0
Had metastatic site	102	21	10
Missing	1	0	0
Histological Grade Units: Subjects			
Well differentiated	9	2	0
Moderately differentiated	42	14	7
Poorly differentiated	33	2	2
Undifferentiated	1	0	0
Unknown/missing	22	7	1
Not Applicable	1	0	0
Stage at Time of Study Entry			
The AJCC staging manual (7th edition) for intrahepaticcholangiocarcinoma was used for cancer staging at baseline, defined asfollows: Stage I: solitary tumor without vascular invasion. Stage II: solitary tumor withvascular invasion or multiple tumors with or without vascular invasion. Stage III: tumor perforating the visceral peritoneum or involving local hepaticstructure by direct invasion. Stage IV: tumor with periductal invasion, or any tumor with regional lymph node metastasis present, or any tumor with or without lymph node metastasis but metastasized to a distant site.			
Units: Subjects			
Stage II	1	3	0
Stage III	0	2	0
Stage IV	107	20	10
Best Overall Response (BOR) by Investigator			
BOR is defined as the best overall response a subject achieved during the study before any subsequent antineoplastic therapy. The endpoint is summarized for the rate of BOR of CR, PR, progressive disease(PD), and stable disease (SD), evaluated by CT or MRI scans every 28 days. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusion) Overall Number of Participants Analyzed 108			
Units: Subjects			
Confirmed CR	0	0	0
Confirmed PR	35	0	0
Stable Disease	56	0	0
Progressive Disease	11	0	0
Not Done	6	25	10
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on BOR - After 2nd line			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third or later line of treatment. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 Analyzed 59			
Units: Subjects			

Complete response	0	0	0
Partial response	0	0	0
Stable disease	19	0	0
Progressive disease	22	0	0
Unknown	18	0	0
Not done	49	25	10
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on BOR - 3rd or later			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third or later line of treatment. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 Analyzed: 59			
Units: Subjects			
Complete response	0	0	0
Partial response	17	0	0
Stable disease	31	0	0
Progressive disease	7	0	0
Unknown	0	0	0
Not done	53	25	10
Overall Response Rate (ORR) as Assessed by Blinded Independent Central Imaging Review (BICR)			
ORR is defined as the percentage (%) of subjects with a best overall response of Complete Response(CR) or Partial Response (PR), as per Response Evaluation Criteria in Solid Tumors (RECIST), Version1.1, evaluated by computed tomography (CT) or magnetic resonance imaging (MRI) scans every 28 days. Due to early termination of the study, no formal efficacy analyses were performed for Cohorts 2 and 3.			
Units: Percentage (%)of subjects with CR or PR			
median	23.1	0	0
full range (min-max)	15.6 to 32.2	0 to 0	0 to 0
Disease Control Rate (DCR) by BICR			
DCR is the percentage (%) of subjects with a BOR of CR, PR, or SD, evaluated by CT or MRI scans every 28 days. Results are based on both BICR and on Investigator assessment. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Percentage (%) with CR, PR, or SD			
median	84.3	0	0
full range (min-max)	76.0 to 90.6	0 to 0	0 to 0
Disease Control Rate (DCR) by Investigator			
DCR is the percentage (%) of subjects with a BOR of CR, PR, or SD, evaluated by CT or MRI scans every 28 days. Results are based on both BICR and on Investigator assessment. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Percentage (%) with CR, PR, or SD			
median	84.3	0	0
full range (min-max)	76.0 to 90.6	0 to 0	0 to 0
Overall Response Rate (ORR) as Assessed by the Investigator			
ORR is defined as the percentage (%) of subjects with a best overall response of CR or PR, evaluated by CT or MRI scans every 28 days.			

Due to early termination of the study, no formal efficacy analyses were performed for Cohorts 2 and 3. Overall Number of Participants Analyzed 108			
Units: Percentage (%)of subjects with CR or PR			
median	32.4	0	0
full range (min-max)	23.7 to 42.1	0 to 0	0 to 0
Progression-Free Survival (PFS) by BICR			
PFS was calculated as the number of months from the first dose of study drug to the first documented progression or death due to any cause, whichever occurred earlier. Subjects without an assessment of progression or death were censored at the last adequate tumor assessment. For subjects who had an event after ≥2 missed visits, the subject was censored at the last adequate tumor assessment before the missing visit. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Months			
median	7.29	0	0
full range (min-max)	5.59 to 7.56	0 to 0	0 to 0
Progression-Free Survival (PFS) by Investigator			
PFS was calculated as the number of months from the first dose of study drug to the first documented progression or death due to any cause, whichever occurred earlier. Subjects without an assessment of progression or death were censored at the last adequate tumor assessment. For subjects who had an event after ≥2 missed visits, the subject was censored at the last adequate tumor assessment before the missing visit. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: months			
median	6.74	0	0
full range (min-max)	5.55 to 7.56	0 to 0	0 to 0
Overall Survival (OS)			
OS was defined as the time (months) from the date of start of treatment to the date of death due to any cause. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Months			
median	11.86	0	0
full range (min-max)	10.68 to 14.85	0 to 0	0 to 0
Duration of Response (DOR) by investigator			
Number Analyzed: 35 DOR is defined as the time (months) from the initial response to the time of the event; defined as the first documented progression or death due to any cause, whichever was earlier. Note that results are based on a subgroup of subjects with confirmed responses (CR or PR) as assessed by BICR or by the Investigator. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions) Overall Number of Participants Analyzed 35			
Units: months			
median	7.23	0	0
full range (min-max)	5.16 to 9.00	0 to 0	0 to 0
Duration of Response (DOR) by BICR			
Number analyzed : 25 DOR is defined as the time (months) from the initial response to the time of the event; defined as the first documented progression or death due to any cause, whichever was earlier. Note that results are based on a subgroup of subjects with confirmed responses (CR or PR) as assessed by BICR or by the Investigator.			
Units: Months			
median	5.55	0	0
full range (min-max)	3.78 to 7.66	0 to 0	0 to 0
Response Onset by BICR			

Full Analysis Set (FAS), defined as all subjects in Cohort 1 who had received at least one dose of infigratinib. Conducted in a subgroup of subjects who were confirmed responders (CR or PR) as assessed by BICR (N = 25). Overall Number of Participants Analyzed 35			
Units: months			
median	3.61	0	0
full range (min-max)	1.38 to 7.36	0 to 0	0 to 0
Growth Modulation Index (GMI) by BICR			
The GMI is defined as the ratio of PFS (months) during treatment with infigratinib relative to the time(months) to progression (TTP) during treatment with last prior line of therapy. Subjects served as their own control. Results are provided for both BICR and Investigator assessment. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Ratio(PFS/TTP) in Months			
median	1.22	0	0
full range (min-max)	0.00 to 120	0 to 0	0 to 0
Growth Modulation Index (GMI) by Investigator			
The GMI is defined as the ratio of PFS (months) during treatment with infigratinib relative to the time(months) to progression (TTP) during treatment with last prior line of therapy. Subjects served as their own control. Results are provided for both BICR and Investigator assessment. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Ratio(PFS/TTP) in Months			
median	1.24	0	0
full range (min-max)	0.00 to 120	0 to 0	0 to 0
Response Onset by Investigator			
Full Analysis Set (FAS), defined as all subjects in Cohort 1 who had received at least one dose of infigratinib. Conducted in a subgroup of subjects who were confirmed responders (CR or PR) as assessed by the Investigator (N = 35).			
Units: months			
median	1.94	0	0
full range (min-max)	1.38 to 18.76	0 to 0	0 to 0
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on ORR After 2nd-Line			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third or later line of treatment. Investigator-assessed ORR was obtained from subjects' medical histories to provide a baseline evaluation of their response after historical second-line antineoplastic treatment prior to infigratinib treatment. Investigator-assessed ORR was then calculated in the same subjects after third- or later-line infigratinib therapy. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (22 June 2022).			
Units: Percentage(%) of patients with CR or PR			
median	0	0	0
full range (min-max)	0.0 to 6.1	0 to 0	0 to 0
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on ORR - Third or Later			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third or later line of treatment. Investigator-assessed ORR was obtained from subjects' medical histories to provide a baseline evaluation of their response after historical second-line antineoplastic treatment prior to infigratinib treatment. Investigator-assessed ORR was then calculated in the same subjects after third- or later-line infigratinib therapy. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (22 June 2022).			
Units: Percentage(%) of patients with CR or PR			

median	28.8	0	0
full range (min-max)	17.8 to 42.1	0 to 0	0 to 0
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on PFS after 2nd line			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third orlater line of treatment. Investigator-assessed PFS was obtained from subjects' medical histories to provide a baseline evaluationof their response after historical second-line antineoplastic treatment prior to infigratinib treatment.Investigator-assessed PFS was then calculated in the same subjects after third- or later-line infigratinibtherapy. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions) Analyzed:59			
Units: months			
median	5.36	0	0
full range (min-max)	3.25 to 8.15	0 to 0	0 to 0
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on PFS - Third or Later			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third orlater line of treatment. Investigator-assessed PFS was obtained from subjects' medical histories to provide a baseline evaluationof their response after historical second-line antineoplastic treatment prior to infigratinib treatment.Investigator-assessed PFS was then calculated in the same subjects after third- or later-line infigratinibtherapy. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions) Analyzed : 59			
Units: months			
median	6.93	0	0
full range (min-max)	4.76 to 7.59	0 to 0	0 to 0

Reporting group values	Total		
Number of subjects	143		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	107		
From 65-84 years	36		
85 years and over	0		
Gender categorical Units: Subjects			
Female	82		
Male	61		
ECOG PS			
Measure Description: Functional status was assessed at baseline using the Eastern Cooperative Oncology Group Performance Scale (ECOG PS)			
Units: Subjects			
00	59		
01	82		

02	2		
Primary site of cancer			
Primary site of cancer			
Units: Subjects			
Bile duct	139		
Cholangiocarcinoma	2		
Liver	2		
Non-Liver MetastaticSite Units: Subjects			
No metastatic site	9		
Had metastatic site	133		
Missing	1		
Histological Grade Units: Subjects			
Well differentiated	11		
Moderately differentiated	63		
Poorly differentiated	37		
Undifferentiated	1		
Unknown/missing	30		
Not Applicable	1		
Stage at Time of Study Entry			
The AJCC staging manual (7th edition) for intrahepaticcholangiocarcinoma was used for cancer staging at baseline, defined asfollows: Stage I: solitary tumor without vascular invasion. Stage II: solitary tumor withvascular invasion or multiple tumors with or without vascular invasion. Stage III: tumor perforating the visceral peritoneum or involving local hepaticstructure by direct invasion. Stage IV: tumor with periductal invasion, or any tumor with regional lymph node metastasis present, or any tumor with or without lymph node metastasis but metastasized to a distant site.			
Units: Subjects			
Stage II	4		
Stage III	2		
Stage IV	137		
Best Overall Response (BOR) by Investigator			
BOR is defined as the best overall response a subject achieved during the study before any subsequent antineoplastic therapy. The endpoint is summarized for the rate of BOR of CR, PR, progressive disease(PD), and stable disease (SD), evaluated by CT or MRI scans every 28 days. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusion) Overall Number of Participants Analyzed 108			
Units: Subjects			
Confirmed CR	0		
Confirmed PR	35		
Stable Disease	56		
Progressive Disease	11		
Not Done	41		
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on BOR - After 2nd line			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third or later line of treatment. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 Analyzed 59			
Units: Subjects			

Complete response	0		
Partial response	0		
Stable disease	19		
Progressive disease	22		
Unknown	18		
Not done	84		
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on BOR - 3rd or later			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third or later line of treatment. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 Analyzed: 59			
Units: Subjects			
Complete response	0		
Partial response	17		
Stable disease	31		
Progressive disease	7		
Unknown	0		
Not done	88		
Overall Response Rate (ORR) as Assessed by Blinded Independent Central Imaging Review (BICR)			
ORR is defined as the percentage (%) of subjects with a best overall response of Complete Response(CR) or Partial Response (PR), as per Response Evaluation Criteria in Solid Tumors (RECIST), Version1.1, evaluated by computed tomography (CT) or magnetic resonance imaging (MRI) scans every 28 days. Due to early termination of the study, no formal efficacy analyses were performed for Cohorts 2 and 3.			
Units: Percentage (%)of subjects with CR or PR			
median			
full range (min-max)	-		
Disease Control Rate (DCR) by BICR			
DCR is the percentage (%) of subjects with a BOR of CR, PR, or SD, evaluated by CT or MRI scans every 28 days. Results are based on both BICR and on Investigator assessment. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Percentage (%) with CR, PR, or SD			
median			
full range (min-max)	-		
Disease Control Rate (DCR) by Investigator			
DCR is the percentage (%) of subjects with a BOR of CR, PR, or SD, evaluated by CT or MRI scans every 28 days. Results are based on both BICR and on Investigator assessment. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Percentage (%) with CR, PR, or SD			
median			
full range (min-max)	-		
Overall Response Rate (ORR) as Assessed by the Investigator			
ORR is defined as the percentage (%) of subjects with a best overall response of CR or PR, evaluated by CT or MRI scans every 28 days.			

Due to early termination of the study, no formal efficacy analyses were performed for Cohorts 2 and 3. Overall Number of Participants Analyzed 108			
Units: Percentage (%)of subjects with CR or PR median full range (min-max)	- -		
Progression-Free Survival (PFS) by BICR			
PFS was calculated as the number of months from the first dose of study drug to the first documented progression or death due to any cause, whichever occurred earlier. Subjects without an assessment of progression or death were censored at the last adequate tumor assessment. For subjects who had an event after ≥2 missed visits, the subject was censored at the last adequate tumor assessment before the missing visit. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Months median full range (min-max)	- -		
Progression-Free Survival (PFS) by Investigator			
PFS was calculated as the number of months from the first dose of study drug to the first documented progression or death due to any cause, whichever occurred earlier. Subjects without an assessment of progression or death were censored at the last adequate tumor assessment. For subjects who had an event after ≥2 missed visits, the subject was censored at the last adequate tumor assessment before the missing visit. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: months median full range (min-max)	- -		
Overall Survival (OS)			
OS was defined as the time (months) from the date of start of treatment to the date of death due to any cause. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Months median full range (min-max)	- -		
Duration of Response (DOR) by investigator			
Number Analyzed: 35 DOR is defined as the time (months) from the initial response to the time of the event; defined as the first documented progression or death due to any cause, whichever was earlier. Note that results are based on a subgroup of subjects with confirmed responses (CR or PR) as assessed by BICR or by the Investigator. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions) Overall Number of Participants Analyzed 35			
Units: months median full range (min-max)	- -		
Duration of Response (DOR) by BICR			
Number analyzed : 25 DOR is defined as the time (months) from the initial response to the time of the event; defined as the first documented progression or death due to any cause, whichever was earlier. Note that results are based on a subgroup of subjects with confirmed responses (CR or PR) as assessed by BICR or by the Investigator.			
Units: Months median full range (min-max)	- -		
Response Onset by BICR			

Full Analysis Set (FAS), defined as all subjects in Cohort 1 who had received at least one dose of infigratinib. Conducted in a subgroup of subjects who were confirmed responders (CR or PR) as assessed by BICR (N = 25). Overall Number of Participants Analyzed 35			
Units: months median full range (min-max)	- 		
Growth Modulation Index (GMI) by BICR			
The GMI is defined as the ratio of PFS (months) during treatment with infigratinib relative to the time(months) to progression (TTP) during treatment with last prior line of therapy. Subjects served as their own control. Results are provided for both BICR and Investigator assessment. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Ratio(PFS/TTP) in Months median full range (min-max)	- 		
Growth Modulation Index (GMI) by Investigator			
The GMI is defined as the ratio of PFS (months) during treatment with infigratinib relative to the time(months) to progression (TTP) during treatment with last prior line of therapy. Subjects served as their own control. Results are provided for both BICR and Investigator assessment. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Ratio(PFS/TTP) in Months median full range (min-max)	- 		
Response Onset by Investigator			
Full Analysis Set (FAS), defined as all subjects in Cohort 1 who had received at least one dose of infigratinib. Conducted in a subgroup of subjects who were confirmed responders (CR or PR) as assessed by the Investigator (N = 35).			
Units: months median full range (min-max)	- 		
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on ORR After 2nd-Line			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third or later line of treatment. Investigator-assessed ORR was obtained from subjects' medical histories to provide a baseline evaluation of their response after historical second-line antineoplastic treatment prior to infigratinib treatment. Investigator-assessed ORR was then calculated in the same subjects after third- or later-line infigratinib therapy. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (22 June 2022).			
Units: Percentage(%) of patients with CR or PR median full range (min-max)	- 		
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on ORR - Third or Later			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third or later line of treatment. Investigator-assessed ORR was obtained from subjects' medical histories to provide a baseline evaluation of their response after historical second-line antineoplastic treatment prior to infigratinib treatment. Investigator-assessed ORR was then calculated in the same subjects after third- or later-line infigratinib therapy. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (22 June 2022).			
Units: Percentage(%) of patients with CR or PR			

median full range (min-max)	- 		
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on PFS after 2nd line			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third orlater line of treatment. Investigator-assessed PFS was obtained from subjects' medical histories to provide a baseline evaluationof their response after historical second-line antineoplastic treatment prior to infigratinib treatment.Investigator-assessed PFS was then calculated in the same subjects after third- or later-line infigratinibtherapy. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions) Analyzed:59			
Units: months median full range (min-max)	 -		
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on PFS - Third or Later			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third orlater line of treatment. Investigator-assessed PFS was obtained from subjects' medical histories to provide a baseline evaluationof their response after historical second-line antineoplastic treatment prior to infigratinib treatment.Investigator-assessed PFS was then calculated in the same subjects after third- or later-line infigratinibtherapy. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions) Analyzed : 59			
Units: months median full range (min-max)	 -		

Subject analysis sets

Subject analysis set title	Cohort 1
Subject analysis set type	Full analysis
Subject analysis set description: Cohort 1 (FGFR2 fusions): Primary analysis population (N=108).	
Subject analysis set title	Cohort 2
Subject analysis set type	Full analysis
Subject analysis set description: Cohort 2 (Other FGFR alterations):N=25.	
Subject analysis set title	Cohort 3
Subject analysis set type	Full analysis
Subject analysis set description: Cohort 3 (FGFR2 fusions and prior FGFR inhibitor): N=10.	

Reporting group values	Cohort 1	Cohort 2	Cohort 3
Number of subjects	108	25	10
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0

Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	82	17	8
From 65-84 years	26	8	2
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	67	12	3
Male	41	13	7
ECOG PS			
Measure Description: Functional status was assessed at baseline using the Eastern Cooperative Oncology Group Performance Scale (ECOG PS)			
Units: Subjects			
00	45	11	3
01	62	13	7
02	1	1	0
Primary site of cancer			
Primary site of cancer			
Units: Subjects			
Bile duct	105	24	10
Cholangiocarcinoma	1	1	0
Liver	2	0	0
Non-Liver MetastaticSite Units: Subjects			
No metastatic site	5	4	0
Had metastatic site	102	21	10
Missing	1	0	0
Histological Grade Units: Subjects			
Well differentiated	9	2	0
Moderately differentiated	42	14	7
Poorly differentiated	33	2	2
Undifferentiated	1	0	0
Unknown/missing	22	7	1
Not Applicable	1	0	0
Stage at Time of Study Entry			
The AJCC staging manual (7th edition) for intrahepaticcholangiocarcinoma was used for cancer staging at baseline, defined asfollows: Stage I: solitary tumor without vascular invasion. Stage II: solitary tumor withvascular invasion or multiple tumors with or without vascular invasion. Stage III: tumor perforating the visceral peritoneum or involving local hepaticstructure by direct invasion. Stage IV: tumor with periductal invasion, or any tumor with regional lymph node metastasis present, or any tumor with or without lymph node metastasis but metastasized to a distant site.			
Units: Subjects			
Stage II	1	3	0
Stage III	0	2	0
Stage IV	107	20	10
Best Overall Response (BOR) by Investigator			
BOR is defined as the best overall response a subject achieved during the study before any subsequent antineoplastic therapy. The endpoint is summarized for the rate of BOR of CR, PR, progressive disease(PD), and stable disease (SD), evaluated by CT or MRI scans every 28 days.			

Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusion)
Overall Number of Participants Analyzed 108

Units: Subjects			
Confirmed CR	0	0	0
Confirmed PR	35	0	0
Stable Disease	56	0	0
Progressive Disease	11	0	0
Not Done	6	25	10

Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on BOR - After 2nd line			

Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third or later line of treatment.

Note: The primary efficacy outcome measures were prespecified only for Cohort 1

Analyzed 59

Units: Subjects			
Complete response	0	0	0
Partial response	0	0	0
Stable disease	19	0	0
Progressive disease	22	0	0
Unknown	18	0	0
Not done	49	25	10

Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on BOR - 3rd or later			

Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third or later line of treatment.

Note: The primary efficacy outcome measures were prespecified only for Cohort 1

Analyzed: 59

Units: Subjects			
Complete response	0	0	0
Partial response	17	0	0
Stable disease	31	0	0
Progressive disease	7	0	0
Unknown	0	0	0
Not done	53	25	10

Overall Response Rate (ORR) as Assessed by Blinded Independent Central Imaging Review (BICR)			

ORR is defined as the percentage (%) of subjects with a best overall response of Complete Response(CR) or Partial Response (PR), as per Response Evaluation Criteria in Solid Tumors (RECIST), Version1.1, evaluated by computed tomography (CT) or magnetic resonance imaging (MRI) scans every 28 days.
Due to early termination of the study, no formal efficacy analyses were performed for Cohorts 2 and 3.

Units: Percentage (%)of subjects with CR or PR			
median	23.1	0	0
full range (min-max)	15.6 to 32.2	0 to 0	0 to 0

Disease Control Rate (DCR) by BICR			

DCR is the percentage (%) of subjects with a BOR of CR, PR, or SD, evaluated by CT or MRI scans every 28 days.
Results are based on both BICR and on Investigator assessment.

Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)

Units: Percentage (%) with CR, PR, or SD			
median	84.3	0	0
full range (min-max)	76.0 to 90.6	0 to 0	0 to 0
Disease Control Rate (DCR) by Investigator			
DCR is the percentage (%) of subjects with a BOR of CR, PR, or SD, evaluated by CT or MRI scans every 28 days. Results are based on both BICR and on Investigator assessment. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Percentage (%) with CR, PR, or SD			
median	84.3	0	0
full range (min-max)	76.0 to 90.6	0 to 0	0 to 0
Overall Response Rate (ORR) as Assessed by the Investigator			
ORR is defined as the percentage (%) of subjects with a best overall response of CR or PR, evaluated by CT or MRI scans every 28 days. Due to early termination of the study, no formal efficacy analyses were performed for Cohorts 2 and 3. Overall Number of Participants Analyzed 108			
Units: Percentage (%)of subjects with CR or PR			
median	32.4	0	0
full range (min-max)	23.7 to 42.1	0 to 0	0 to 0
Progression-Free Survival (PFS) by BICR			
PFS was calculated as the number of months from the first dose of study drug to the first documented progression or death due to any cause, whichever occurred earlier. Subjects without an assessment of progression or death were censored at the last adequate tumor assessment. For subjects who had an event after ≥2 missed visits, the subject was censored at the last adequate tumor assessment before the missing visit. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Months			
median	7.29	0	0
full range (min-max)	5.59 to 7.56	0 to 0	0 to 0
Progression-Free Survival (PFS) by Investigator			
PFS was calculated as the number of months from the first dose of study drug to the first documented progression or death due to any cause, whichever occurred earlier. Subjects without an assessment of progression or death were censored at the last adequate tumor assessment. For subjects who had an event after ≥2 missed visits, the subject was censored at the last adequate tumor assessment before the missing visit. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: months			
median	6.74	0	0
full range (min-max)	5.55 to 7.56	0 to 0	0 to 0
Overall Survival (OS)			
OS was defined as the time (months) from the date of start of treatment to the date of death due to any cause. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)			
Units: Months			
median	11.86	0	0
full range (min-max)	10.68 to 14.85	0 to 0	0 to 0
Duration of Response (DOR) by investigator			
Number Analyzed: 35 DOR is defined as the time (months) from the initial response to the time of the event; defined as the			

first documented progression or death due to any cause, whichever was earlier.
Note that results are based on a subgroup of subjects with confirmed responses (CR or PR) as assessed by BICR or by the Investigator.

Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)
Overall Number of Participants Analyzed 35

Units: months			
median	7.23	0	0
full range (min-max)	5.16 to 9.00	0 to 0	0 to 0

Duration of Response (DOR) by BICR			

Number analyzed : 25
DOR is defined as the time (months) from the initial response to the time of the event; defined as the first documented progression or death due to any cause, whichever was earlier.
Note that results are based on a subgroup of subjects with confirmed responses (CR or PR) as assessed by BICR or by the Investigator.

Units: Months			
median	5.55	0	0
full range (min-max)	3.78 to 7.66	0 to 0	0 to 0

Response Onset by BICR			

Full Analysis Set (FAS), defined as all subjects in Cohort 1 who had received at least one dose of infigratinib. Conducted in a subgroup of subjects who were confirmed responders (CR or PR) as assessed by BICR (N = 25).
Overall Number of Participants Analyzed 35

Units: months			
median	3.61	0	0
full range (min-max)	1.38 to 7.36	0 to 0	0 to 0

Growth Modulation Index (GMI) by BICR			

The GMI is defined as the ratio of PFS (months) during treatment with infigratinib relative to the time(months) to progression (TTP) during treatment with last prior line of therapy.
Subjects served as their own control.
Results are provided for both BICR and Investigator assessment.
Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)

Units: Ratio(PFS/TTP) in Months			
median	1.22	0	0
full range (min-max)	0.00 to 120	0 to 0	0 to 0

Growth Modulation Index (GMI) by Investigator			

The GMI is defined as the ratio of PFS (months) during treatment with infigratinib relative to the time(months) to progression (TTP) during treatment with last prior line of therapy.
Subjects served as their own control.
Results are provided for both BICR and Investigator assessment.
Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions)

Units: Ratio(PFS/TTP) in Months			
median	1.24	0	0
full range (min-max)	0.00 to 120	0 to 0	0 to 0

Response Onset by Investigator			

Full Analysis Set (FAS), defined as all subjects in Cohort 1 who had received at least one dose of infigratinib. Conducted in a subgroup of subjects who were confirmed responders (CR or PR) as assessed by the Investigator (N = 35).

Units: months			
median	1.94	0	0
full range (min-max)	1.38 to 18.76	0 to 0	0 to 0

Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on ORR After 2nd-Line			

Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third or later line of treatment.
Investigator-assessed ORR was obtained from subjects' medical histories to provide a baseline evaluation of their response after historical second-line antineoplastic treatment prior to infigratinib treatment. Investigator-assessed ORR was then calculated in the same subjects after third- or later-line

infigratinib therapy. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (22 June 2022).			
Units: Percentage(%) of patients with CR or PR			
median	0	0	0
full range (min-max)	0.0 to 6.1	0 to 0	0 to 0
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on ORR - Third or Later			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third or later line of treatment. Investigator-assessed ORR was obtained from subjects' medical histories to provide a baseline evaluation of their response after historical second-line antineoplastic treatment prior to infigratinib treatment. Investigator-assessed ORR was then calculated in the same subjects after third- or later-line infigratinib therapy. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (22 June 2022).			
Units: Percentage(%) of patients with CR or PR			
median	28.8	0	0
full range (min-max)	17.8 to 42.1	0 to 0	0 to 0
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on PFS after 2nd line			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third orlater line of treatment. Investigator-assessed PFS was obtained from subjects' medical histories to provide a baseline evaluationof their response after historical second-line antineoplastic treatment prior to infigratinib treatment.Investigator-assessed PFS was then calculated in the same subjects after third- or later-line infigratinibtherapy. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions) Analyzed:59			
Units: months			
median	5.36	0	0
full range (min-max)	3.25 to 8.15	0 to 0	0 to 0
Retrospective Analysis of Post-second-line Antineoplastic Treatment Outcomes on PFS - Third or Later			
Post-hoc subgroup assessment of efficacy in those subjects who were receiving infigratinib as a third orlater line of treatment. Investigator-assessed PFS was obtained from subjects' medical histories to provide a baseline evaluationof their response after historical second-line antineoplastic treatment prior to infigratinib treatment.Investigator-assessed PFS was then calculated in the same subjects after third- or later-line infigratinibtherapy. Note: The primary efficacy outcome measures were prespecified only for Cohort 1 (FGFR fusions) Analyzed : 59			
Units: months			
median	6.93	0	0
full range (min-max)	4.76 to 7.59	0 to 0	0 to 0

End points

End points reporting groups

Reporting group title	Cohort 1

Reporting group description:

Subjects with FGFR2 fusions/rearrangements (N=108).
These are the same 108 subjects as the main dataset presented in the interim CSR [X2204i] ("Interim Analysis Set 2 for Cohort 1") and the primary CSR [X2204p] ("subjects with FGFR2 fusion/rearrangement in Cohort 1 FAS"); the only difference between reports was the length of follow-up (an additional 11 months).

Note: No new efficacy analysis was done for the final CSR (aCSR), since these subs had completed their primary efficacy analysis (reported into he primary CSR)

Reporting group title	Cohort 2

Reporting group description:

Cohort 2: Subjects with other FGFR alterations other than FGFR2 gene fusions or rearrangements (N=25).
This cohort includes all 11 subjects enrolled to Cohort 2 and the 14 subjects with other FGFR alterations enrolled to Cohort 1 under the original protocol.

Note: No efficacy analysis were performed since the study was terminated early.

Reporting group title	Cohort 3

Reporting group description:

Cohort 3: Subjects with FGFR2 gene fusions/rearrangements who have received a prior FGFR inhibitor other than infigratinib (N=10).
Note that Cohorts 2 and 3 were added at protocol amendment 4 to support exploratory objectives of the study and were not included in the analyses presented in the interim CSR [X2204i] or primary CSR [X2204p].

Subject analysis set title	Cohort 1
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort 1 (FGFR2 fusions): Primary analysis population (N=108).

Subject analysis set title	Cohort 2
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort 2 (Other FGFR alterations):N=25.

Subject analysis set title	Cohort 3
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort 3 (FGFR2 fusions and prior FGFR inhibitor): N=10.

Primary: Cohort 1

End point title	Cohort 1[1]

End point description:

The primary endpoint for this study is overall response in Cohort 1 assessed according to blinded independent central review (BICR) using Response Evaluation Criteria in Solid Tumors

End point type	Primary

End point timeframe:

TBC

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: The primary endpoint for this study is overall response in Cohort 1 assessed according to blinded independent central review (BICR) using Response Evaluation Criteria in Solid Tumors

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	108	25	10	
Units: overall response	108	25	10	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From first administration of infigratinib with follow-up of at least 10 months after initial exposure.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0
Reporting groups	
Reporting group title	Cohort 1: FGFR2 Fusions
Reporting group description: -	
Reporting group title	Cohort 3: FGFR2 Fusions and Prior FGFR Inhibitor
Reporting group description: -	
Reporting group title	Cohort 2: Other FGFR Genetic Alterations
Reporting group description: -	

Serious adverse events	Cohort 1: FGFR2 Fusions	Cohort 3: FGFR2 Fusions and Prior FGFR Inhibitor	Cohort 2: Other FGFR Genetic Alterations
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 108 (32.41%)	2 / 10 (20.00%)	11 / 25 (44.00%)
number of deaths (all causes)	93	7	19
number of deaths resulting from adverse events	2	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Gait disturbance			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	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 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	4 / 108 (3.70%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device occlusion			

subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine increased			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Stress fracture			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hepatic encephalopathy			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	4 / 108 (3.70%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 108 (1.85%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	2 / 108 (1.85%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	2 / 108 (1.85%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	2 / 108 (1.85%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Noninfective sialoadenitis			

subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	2 / 108 (1.85%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	2 / 108 (1.85%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypothyroidism			

subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Clostridium difficile colitis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Biliary abscess			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 108 (1.85%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	2 / 108 (1.85%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral discitis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis bacterial			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	3 / 108 (2.78%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Calciphylaxis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	4 / 108 (3.70%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperphosphataemia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			

subjects affected / exposed	2 / 108 (1.85%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Cohort 1: FGFR2 Fusions	Cohort 3: FGFR2 Fusions and Prior FGFR Inhibitor	Cohort 2: Other FGFR Genetic Alterations
Total subjects affected by non-serious adverse events			
subjects affected / exposed	107 / 108 (99.07%)	10 / 10 (100.00%)	25 / 25 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	17 / 108 (15.74%)	1 / 10 (10.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	15 / 108 (13.89%)	1 / 10 (10.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	6 / 108 (5.56%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	44 / 108 (40.74%)	3 / 10 (30.00%)	10 / 25 (40.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	8 / 108 (7.41%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	0
Asthenia			

subjects affected / exposed	6 / 108 (5.56%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	9 / 108 (8.33%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	19 / 108 (17.59%)	6 / 10 (60.00%)	5 / 25 (20.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	10 / 108 (9.26%)	1 / 10 (10.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	14 / 108 (12.96%)	1 / 10 (10.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	14 / 108 (12.96%)	2 / 10 (20.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	18 / 108 (16.67%)	0 / 10 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	0
Amylase increased			
subjects affected / exposed	7 / 108 (6.48%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			

subjects affected / exposed	25 / 108 (23.15%)	0 / 10 (0.00%)	7 / 25 (28.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	17 / 108 (15.74%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	9 / 108 (8.33%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	27 / 108 (25.00%)	1 / 10 (10.00%)	8 / 25 (32.00%)
occurrences (all)	0	0	0
Creatinine renal clearance decreased			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 108 (0.93%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	13 / 108 (12.04%)	0 / 10 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	17 / 108 (15.74%)	0 / 10 (0.00%)	5 / 25 (20.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	0
Post-traumatic pain			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Peripheral sensory neuropathy			
subjects affected / exposed	6 / 108 (5.56%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	6 / 108 (5.56%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	19 / 108 (17.59%)	3 / 10 (30.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	34 / 108 (31.48%)	0 / 10 (0.00%)	6 / 25 (24.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	10 / 108 (9.26%)	0 / 10 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	9 / 108 (8.33%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	7 / 108 (6.48%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	20 / 108 (18.52%)	0 / 10 (0.00%)	5 / 25 (20.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	7 / 108 (6.48%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	0
Eye disorders			
Blepharitis			
subjects affected / exposed	12 / 108 (11.11%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Cataract			

subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	0
Growth of eyelashes			
subjects affected / exposed	7 / 108 (6.48%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	39 / 108 (36.11%)	4 / 10 (40.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	0
Chorioretinopathy			
subjects affected / exposed	10 / 108 (9.26%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Cataract nuclear			
subjects affected / exposed	8 / 108 (7.41%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	7 / 108 (6.48%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Keratopathy			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	13 / 108 (12.04%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	6 / 108 (5.56%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Punctate keratitis			
subjects affected / exposed	10 / 108 (9.26%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Retinal drusen			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Subretinal fluid			

subjects affected / exposed	6 / 108 (5.56%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Trichomegaly			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	23 / 108 (21.30%)	1 / 10 (10.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	0
Vitreous detachment			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Trichiasis			
subjects affected / exposed	13 / 108 (12.04%)	0 / 10 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	19 / 108 (17.59%)	1 / 10 (10.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	21 / 108 (19.44%)	3 / 10 (30.00%)	10 / 25 (40.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 108 (5.56%)	1 / 10 (10.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	0

Food poisoning			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	7 / 108 (6.48%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	20 / 108 (18.52%)	0 / 10 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	28 / 108 (25.93%)	1 / 10 (10.00%)	7 / 25 (28.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	27 / 108 (25.00%)	3 / 10 (30.00%)	8 / 25 (32.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	34 / 108 (31.48%)	3 / 10 (30.00%)	11 / 25 (44.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	16 / 108 (14.81%)	0 / 10 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	0
Oral dysaesthesia			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	59 / 108 (54.63%)	7 / 10 (70.00%)	13 / 25 (52.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	25 / 108 (23.15%)	3 / 10 (30.00%)	5 / 25 (20.00%)
occurrences (all)	0	0	0

Oral pain			
subjects affected / exposed	6 / 108 (5.56%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pain of skin			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	37 / 108 (34.26%)	5 / 10 (50.00%)	6 / 25 (24.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	43 / 108 (39.81%)	1 / 10 (10.00%)	9 / 25 (36.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	26 / 108 (24.07%)	3 / 10 (30.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Hyperkeratosis			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	0
Nail discolouration			
subjects affected / exposed	20 / 108 (18.52%)	2 / 10 (20.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	17 / 108 (15.74%)	0 / 10 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	0
Nail ridging			
subjects affected / exposed	8 / 108 (7.41%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Onychalgia			
subjects affected / exposed	14 / 108 (12.96%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	0
Onycholysis			

subjects affected / exposed	14 / 108 (12.96%)	2 / 10 (20.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	0
Onychomadesis			
subjects affected / exposed	19 / 108 (17.59%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	8 / 108 (7.41%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	7 / 108 (6.48%)	2 / 10 (20.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	6 / 108 (5.56%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	7 / 108 (6.48%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	35 / 108 (32.41%)	1 / 10 (10.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	16 / 108 (14.81%)	1 / 10 (10.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Coccydynia			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	0
Flank pain			

subjects affected / exposed	7 / 108 (6.48%)	2 / 10 (20.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	17 / 108 (15.74%)	1 / 10 (10.00%)	5 / 25 (20.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	14 / 108 (12.96%)	0 / 10 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Infections and infestations			
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	10 / 108 (9.26%)	1 / 10 (10.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	11 / 108 (10.19%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Enterocolitis infectious			
subjects affected / exposed	0 / 108 (0.00%)	1 / 10 (10.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	26 / 108 (24.07%)	3 / 10 (30.00%)	7 / 25 (28.00%)
occurrences (all)	0	0	0
Dehydration			

subjects affected / exposed	7 / 108 (6.48%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	25 / 108 (23.15%)	2 / 10 (20.00%)	5 / 25 (20.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	9 / 108 (8.33%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	8 / 108 (7.41%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 108 (0.00%)	0 / 10 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	8 / 108 (7.41%)	0 / 10 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	7 / 108 (6.48%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			
subjects affected / exposed	83 / 108 (76.85%)	7 / 10 (70.00%)	23 / 25 (92.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	9 / 108 (8.33%)	0 / 10 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	29 / 108 (26.85%)	1 / 10 (10.00%)	5 / 25 (20.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	14 / 108 (12.96%)	1 / 10 (10.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 January 2020	Protocol version 6 (protocol amendment 5) dated 15 January 2020 The primary purpose of this amendment was to revise the protocol based on updates to standards for safety and study conduct for BGJ398 and to add a second interim analysis for Cohort 1 when all the patients who received BGJ398 at the time of the first formal interim analysis have at least 10 months follow-up after their initial exposure to BGJ398.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported