Clinical trial results:
A Phase 3, Double-Blind, Placebo-controlled Study of Quizartinib (AC220) Administered in Combination with Induction and Consolidation Chemotherapy, and Administered as Maintenance Therapy in Subjects 18 to 75 Years Old with Newly Diagnosed FLT3-ITD (+) Acute Myeloid Leukemia (QuANTUM First)

Summary

EudraCT number	2015-004856-24
Trial protocol	GB CZ DE HU ES RO BE PT BG HR EE IT
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	01 October 2022
First version publication date	01 October 2022

Trial information

Trial identification

Sponsor protocol code	AC220-A-U302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02668653
WHO universal trial number (UTN)	-
Other trial identifiers	JAPIC CTI: 173667

Notes:

Sponsors

Sponsor organisation name	Daiichi Sankyo, Inc.
Sponsor organisation address	211 Mount Airy Rd., Basking Ridge, United States, 07920
Public contact	Clinical Director, Daiichi Sankyo, Inc., +1 908-992-6400, CTRinfo@dsi.com
Scientific contact	Clinical Director, Daiichi Sankyo, Inc., +1 908-992-6400, CTRinfo@dsi.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	13 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 August 2021
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to compare the effect of quizartinib vs placebo (administered with standard induction and consolidation chemotherapy, then administered as maintenance therapy for up to 12 cycles) on event-free survival (EFS) in subjects with newly diagnosed FLT3-ITD (+) AML.

Protection of trial subjects:

The study protocol, amendments, the informed consent form (ICF), and information sheets were reviewed and approved by the appropriate and applicable Independent Ethics Committees (IECs) or Institutional Review Boards (IRBs). This study was conducted in compliance with the protocol, the ethical principles that have their origin in the Declaration of Helsinki, the ICH consolidated Guideline E6 for Good Clinical
Practice (GCP) (Committee for Human Medicinal Products [CHMP]/ICH/135/95), and applicable regulatory requirement(s).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 11
Country: Number of subjects enrolled	Portugal: 9
Country: Number of subjects enrolled	Romania: 17
Country: Number of subjects enrolled	Spain: 67
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Croatia: 15
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Bulgaria: 2
Country: Number of subjects enrolled	Czech Republic: 32
Country: Number of subjects enrolled	France: 25
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Serbia: 18
Country: Number of subjects enrolled	Italy: 60
Country: Number of subjects enrolled	Russian Federation: 19
Country: Number of subjects enrolled	Canada: 13
Country: Number of subjects enrolled	United States: 21
Country: Number of subjects enrolled	Ukraine: 3

Country: Number of subjects enrolled	Israel: 14
Country: Number of subjects enrolled	Brazil: 15
Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Singapore: 8
Country: Number of subjects enrolled	China: 20
Country: Number of subjects enrolled	Japan: 29
Country: Number of subjects enrolled	Korea, Republic of: 70
Country: Number of subjects enrolled	Taiwan: 29
Worldwide total number of subjects	539
EEA total number of subjects	272

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)	404
From 65 to 84 years	135
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

539 patients who met all inclusion and no exclusion criteria were randomized at 193 sites: Spain, Italy, Republic of Korea, Japan, China, US, France, Brazil, Germany, Russian Federation, Taiwan, Hungary, Czech Republic, Romania, Israel, Canada, Serbia, Poland, Australia, Belgium, Bulgaria, Croatia, Ukraine. Six patients did not receive treatment.

Pre-assignment

Screening details:

Subjects with newly diagnosed, morphologically documented AML were screened. The Screening period was the time from 7 days prior to the start of induction chemotherapy up to the day of Randomization. Subjects may have recently had some or all of the screening tests done as part of routine care and the results may be used to qualify the subject.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Quizartinib

Arm description:

Participants who were randomized to receive quizartinib treatment regimen.

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

Dosage and administration details:

Tablet was administered once daily

Arm title	Placebo

Arm description:

Participants who were randomized to receive placebo treatment regimen.

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

Dosage and administration details:

Tablet administered once daily

Number of subjects in period 1	Quizartinib	Placebo
Started	268	271
Completed	56	52
Not completed	212	219
Patient decision to stop study drug	25	23
Relapse	44	65
Refractory disease	41	70
Adverse event, non-fatal	58	23
Death	-	1
Pregnancy	-	1
Investigator decision	10	7
Failure to meet continuation criteria	5	12
Other reasons not specified	16	11
Non-protocol-specified AML therapy	12	6
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Quizartinib
Reporting group description:	
Participants who were randomized to receive quizartinib treatment regimen.	
Reporting group title	Placebo
Reporting group description:	
Participants who were randomized to receive placebo treatment regimen.	

Reporting group values	Quizartinib	Placebo	Total
Number of subjects	268	271	539
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)	198	206	404
From 65-84 years	70	65	135
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	53.6	54.3	
standard deviation	± 13.07	± 12.81	-
Gender categorical Units: Subjects			
Female	144	150	294
Male	124	121	245

End points

End points reporting groups

Reporting group title	Quizartinib
Reporting group description:	
Participants who were randomized to receive quizartinib treatment regimen.	
Reporting group title	Placebo
Reporting group description:	
Participants who were randomized to receive placebo treatment regimen.	

Primary: Overall Survival in Participants With Newly Diagnosed FLT3-ITD (+) Acute Myeloid Leukemia

End point title	Overall Survival in Participants With Newly Diagnosed FLT3-ITD (+) Acute Myeloid Leukemia
End point description:	
Overall survival is defined as the time from randomization until death from any cause.	
End point type	Primary
End point timeframe:	
Date of randomization to the date of death due to any cause, up to approximately 3 years after enrollment	

End point values	Quizartinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268[1]	271		
Units: months				
median (confidence interval 95%)				
Overall survival	31.9 (21.0 to 99.9)	15.1 (13.2 to 26.2)		

Notes:

[1] - 99.9=NA, Upper CI was not estimable due to insufficient number of events.

Statistical analyses

Statistical analysis title	Quizartinib vs placebo
Comparison groups	Quizartinib v Placebo
Number of subjects included in analysis	539
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0324 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.776

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.615
upper limit	0.979

Notes:

[2] - Stratification factors include region, age, and WBC count at the time of diagnosis of AML.

Secondary: Event-free Survival in Participants With Newly Diagnosed FLT3-ITD (+) Acute Myeloid Leukemia

End point title	Event-free Survival in Participants With Newly Diagnosed FLT3-ITD (+) Acute Myeloid Leukemia

End point description:

Event-free survival (EFS) is the time from randomization to the earliest date of either refractory disease (or treatment failure [TF]), relapse, or death from any cause. Refractory disease is defined as complete remission never achieved during Induction (CR: >1000 neutrophils, >100,000 platelets, <5% blasts, and other [defined as absence of extramedullary disease [EMD], blasts with rods, and leukemic blasts]). For refractory disease, EFS event date is Day 1 (randomization). Relapse after CR is defined as ≥5% blasts, leukemic blasts, extramedullary leukemia, and presence of rods. This analysis is based on a response assessment with TF defined as not achieving response of CR, using a 42-day window from the start of the last cycle in Induction for CR evaluation.

End point type	Secondary

End point timeframe:

Date of randomization to the date of refractory disease, relapse, or death, up to approximately 3 years after enrollment

End point values	Quizartinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	271		
Units: months				
median (confidence interval 95%)				
Event-free survival	0.03 (0.03 to 0.95)	0.71 (0.03 to 3.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Remission (CR) Rate at the End of Induction in Participants With Newly Diagnosed FLT3-ITD (+) Acute Myeloid Leukemia

End point title	Complete Remission (CR) Rate at the End of Induction in Participants With Newly Diagnosed FLT3-ITD (+) Acute Myeloid Leukemia

End point description:

Complete remission (CR) rate is defined as the percentage of participants achieving CR, defined as a disappearance of all target lesions, after Induction.

End point type	Secondary

End point timeframe:

Approximately Cycle 1 Day 21 (Induction) to end of Induction, up to approximately 120 days (each Induction cycle is up to 60 days)

End point values	Quizartinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	271		
Units: number of patients				
number (not applicable)				
Complete remission (CR) rate	147	150		

Statistical analyses

No statistical analyses for this end point

Secondary: Composite CR Rate at the End of Induction in Participants With Newly Diagnosed FLT3-ITD (+) Acute Myeloid Leukemia

End point title	Composite CR Rate at the End of Induction in Participants With Newly Diagnosed FLT3-ITD (+) Acute Myeloid Leukemia

End point description:

Composite complete remission (CRc) rate is defined as the percentage of participants whose best response is complete remission (CR), defined as a disappearance of all target lesions, or CR with incomplete neutrophil or platelet recovery (CRi) at the end of first Induction cycle.

End point type	Secondary

End point timeframe:

Approximately Cycle 1 Day 21 (Induction) to end of Induction, up to approximately 120 days (each Induction cycle is up to 60 days)

End point values	Quizartinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	271		
Units: number of patients				
number (not applicable)				
Composite CR rate	192	176		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-emergent Adverse Events Occurring in ≥10% Participants With Newly Diagnosed FLT3-ITD (+) Acute Myeloid Leukemia

End point title	Number of Participants With Treatment-emergent Adverse Events Occurring in ≥10% Participants With Newly Diagnosed FLT3-ITD (+) Acute Myeloid Leukemia

End point description:

A treatment-emergent adverse event (TEAE) is defined as an adverse event that occur, having been absent before first dose of quizartinib or placebo, or have worsened in severity after initiating quizartinib or placebo. Adverse events collected more than 30 days after the last dose of quizartinib/placebo will not be considered TEAEs unless they are considered drug-related.

End point type	Secondary

End point timeframe:

Date of first dose up to 30 days after last dose, up to 36 cycles following continuation (approximately 6 years 11 months, each cycle is 28 days)

End point values	Quizartinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	268		
Units: number of patients				
number (not applicable)				
Any TEAE	264	265		
Gastrointestinal disorders	215	209		
Diarrhoea	98	94		
Nausea	90	84		
Vomiting	65	53		
Stomatitis	57	56		
Constipation	56	69		
Abdominal pain	46	38		
Dyspepsia	30	23		
Abdominal pain upper	29	25		
Infections and infestations	204	188		
Pneumonia	39	41		
Sepsis	15	28		
General disorders and administration site disorder	177	173		
Pyrexia	112	109		
Oedema peripheral	30	37		
Fatigue	29	23		
Blood and lymphatic system disorders	168	143		
Febrile neutropenia	117	113		
Neutropenia	54	27		
Thrombocytopenia	30	30		
Anaemia	29	19		
Metabolism and nutrition disorders	165	153		
Hypokalaemia	93	96		
Decreased appetite	46	36		
Hypomagnesaemia	30	30		
Hypophosphataemia	27	24		
Hypocalcaemia	26	29		
Skin and subcutaneous tissue disorders	152	158		
Rash	69	66		
Pruritus	35	40		
Investigations	140	105		
Alanine aminotransferase increased	42	27		
Electrocardiogram QT prolonged	36	11		

Aspartate aminotransferase increased	28	19		
Neutrophil count decreased	27	12		
Respiratory, thoracic, and mediastinal disorders	123	115		
Cough	50	44		
Epistaxis	40	29		
Oropharyngeal pain	27	18		
Nervous system disorders	103	97		
Headache	73	53		
Musculoskeletal and connective tissue disorders	91	108		
Arthralgia	29	35		
Back pain	19	28		
Vascular disorders	71	70		
Hypertension	29	33		
Psychiatric disorders	57	50		
Insomnia	37	30		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events were collected from date of first dose up to 30 days after last dose, up to 36 cycles following continuation phase (approximately 6 years 11 months, each cycle is 28 days).

Adverse event reporting additional description:

In the all-cause mortality section, all deaths due to any cause during the study period (from the date of first dose to 30 days after last dose, up to 36 cycles following continuation (approximately 6 years 11 months, each cycle is 28 days) are reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Quizartinib

Reporting group description:

Participants who were randomized to receive quizartinib treatment regimen.

Reporting group title	Placebo

Reporting group description:

Participants who were randomized to receive placebo treatment regimen.

Serious adverse events	Quizartinib	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	143 / 265 (53.96%)	123 / 268 (45.90%)	
number of deaths (all causes)	32	25	
number of deaths resulting from adverse events	31	25	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acanthoma			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma gastric			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Breast neoplasm			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post transplant lymphoproliferative disorder			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 265 (0.38%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyst rupture			

subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fat necrosis			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 265 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 3	
Generalised oedema			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-cardiac chest pain			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	8 / 265 (3.02%)	5 / 268 (1.87%)	
occurrences causally related to treatment / all	1 / 8	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Graft versus host disease			

subjects affected / exposed	1 / 265 (0.38%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	4 / 265 (1.51%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 265 (0.75%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 265 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung infiltration			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumomediastinum			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
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	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 2	0 / 0	
Pulmonary haemorrhage			

subjects affected / exposed	0 / 265 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	
Pulmonary oedema			
subjects affected / exposed	2 / 265 (0.75%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	3 / 265 (1.13%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	1 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Acid base balance abnormal			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 265 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood magnesium increased			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			

subjects affected / exposed	4 / 265 (1.51%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			

subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transfusion reaction			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 265 (0.38%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	2 / 265 (0.75%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 265 (0.75%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiotoxicity			

subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 265 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 265 (0.00%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular dysfunction			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ventricular fibrillation			

subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain oedema			
subjects affected / exposed	2 / 265 (0.75%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cerebellar syndrome			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 265 (0.00%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cognitive disorder			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 265 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemorrhagic stroke			

subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hemiplegia			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 265 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 265 (0.75%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune haemolytic anaemia			
subjects affected / exposed	2 / 265 (0.75%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			

subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	29 / 265 (10.94%)	22 / 268 (8.21%)	
occurrences causally related to treatment / all	7 / 29	4 / 22	
deaths causally related to treatment / all	0 / 1	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 265 (0.00%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphopenia			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelosuppression			
subjects affected / exposed	3 / 265 (1.13%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	4 / 265 (1.51%)	5 / 268 (1.87%)	
occurrences causally related to treatment / all	3 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	2 / 265 (0.75%)	8 / 268 (2.99%)	
occurrences causally related to treatment / all	1 / 2	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Allergic otitis externa			

subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Anal fistula			
subjects affected / exposed	4 / 265 (1.51%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	3 / 265 (1.13%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	1 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental caries			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			

subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal ulcer			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic colitis			
subjects affected / exposed	2 / 265 (0.75%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			

subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Stomatitis			
subjects affected / exposed	1 / 265 (0.38%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toothache			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 265 (0.75%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	2 / 265 (0.75%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cytolysis			
subjects affected / exposed	0 / 265 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash papular			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous emphysema			

subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic skin eruption			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	4 / 265 (1.51%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	1 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 265 (0.38%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
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			
Back pain			
subjects affected / exposed	0 / 265 (0.00%)	2 / 268 (0.75%)	
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	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Haematoma muscle			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	2 / 265 (0.75%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal infection			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			

subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspergillus infection			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BK virus infection			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	2 / 265 (0.75%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	3 / 265 (1.13%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida sepsis			

subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Catheter site cellulitis			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site infection			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 265 (0.75%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium colitis			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus chorioretinitis			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			

subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 265 (0.00%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated varicella zoster virus infection			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	0 / 265 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Endocarditis			
subjects affected / exposed	1 / 265 (0.38%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal bacteraemia			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal sepsis			
subjects affected / exposed	1 / 265 (0.38%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection reactivation			

subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 265 (0.38%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal sepsis			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital herpes			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genitourinary tract infection			

subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatosplenic candidiasis			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	5 / 265 (1.89%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			
subjects affected / exposed	2 / 265 (0.75%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	7 / 265 (2.64%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 7	1 / 1	
deaths causally related to treatment / all	0 / 3	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection fungal			

subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucormycosis			
subjects affected / exposed	2 / 265 (0.75%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 3	0 / 0	
Oral herpes			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	17 / 265 (6.42%)	15 / 268 (5.60%)	
occurrences causally related to treatment / all	4 / 17	2 / 15	
deaths causally related to treatment / all	0 / 1	1 / 5	
Pneumonia fungal			
subjects affected / exposed	4 / 265 (1.51%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pseudomonal			

subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
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	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	2 / 265 (0.75%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 265 (0.38%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	10 / 265 (3.77%)	14 / 268 (5.22%)	
occurrences causally related to treatment / all	0 / 10	3 / 14	
deaths causally related to treatment / all	0 / 4	0 / 2	
Septic shock			
subjects affected / exposed	11 / 265 (4.15%)	8 / 268 (2.99%)	
occurrences causally related to treatment / all	1 / 11	0 / 8	
deaths causally related to treatment / all	1 / 8	0 / 3	
Soft tissue infection			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 265 (0.38%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 265 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 265 (0.38%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stenotrophomonas sepsis			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	2 / 265 (0.75%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			

subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic candida			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic mycosis			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 2	
Upper respiratory tract infection			
subjects affected / exposed	2 / 265 (0.75%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 265 (1.13%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella zoster virus infection			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular device infection			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Acid-base balance disorder mixed			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			

subjects affected / exposed	2 / 265 (0.75%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	1 / 265 (0.38%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour lysis syndrome			
subjects affected / exposed	0 / 265 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Quizartinib	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	264 / 265 (99.62%)	265 / 268 (98.88%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	29 / 265 (10.94%)	33 / 268 (12.31%)	
occurrences (all)	29	33	
Hypotension			
subjects affected / exposed	23 / 265 (8.68%)	17 / 268 (6.34%)	
occurrences (all)	23	17	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	16 / 265 (6.04%)	21 / 268 (7.84%)	
occurrences (all)	16	21	
Chills			
subjects affected / exposed	8 / 265 (3.02%)	14 / 268 (5.22%)	
occurrences (all)	8	14	
Fatigue			
subjects affected / exposed	29 / 265 (10.94%)	23 / 268 (8.58%)	
occurrences (all)	29	23	
Non-cardiac chest pain			

subjects affected / exposed	14 / 265 (5.28%)	5 / 268 (1.87%)	
occurrences (all)	14	5	
Oedema peripheral			
subjects affected / exposed	30 / 265 (11.32%)	37 / 268 (13.81%)	
occurrences (all)	30	37	
Pyrexia			
subjects affected / exposed	112 / 265 (42.26%)	109 / 268 (40.67%)	
occurrences (all)	112	109	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	50 / 265 (18.87%)	44 / 268 (16.42%)	
occurrences (all)	50	44	
Dyspnoea			
subjects affected / exposed	14 / 265 (5.28%)	21 / 268 (7.84%)	
occurrences (all)	14	21	
Epistaxis			
subjects affected / exposed	40 / 265 (15.09%)	29 / 268 (10.82%)	
occurrences (all)	40	29	
Oropharyngeal pain			
subjects affected / exposed	27 / 265 (10.19%)	18 / 268 (6.72%)	
occurrences (all)	27	18	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	15 / 265 (5.66%)	12 / 268 (4.48%)	
occurrences (all)	15	12	
Insomnia			
subjects affected / exposed	37 / 265 (13.96%)	30 / 268 (11.19%)	
occurrences (all)	37	30	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	42 / 265 (15.85%)	27 / 268 (10.07%)	
occurrences (all)	42	27	
Aspartate aminotransferase increased			
subjects affected / exposed	28 / 265 (10.57%)	19 / 268 (7.09%)	
occurrences (all)	28	19	
Blood bilirubin increased			

subjects affected / exposed	16 / 265 (6.04%)	14 / 268 (5.22%)	
occurrences (all)	16	14	
Electrocardiogram QT prolonged			
subjects affected / exposed	36 / 265 (13.58%)	11 / 268 (4.10%)	
occurrences (all)	36	11	
Gamma-glutamyltransferase increased			
subjects affected / exposed	24 / 265 (9.06%)	25 / 268 (9.33%)	
occurrences (all)	24	25	
Neutrophil count decreased			
subjects affected / exposed	27 / 265 (10.19%)	12 / 268 (4.48%)	
occurrences (all)	27	12	
Platelet count decreased			
subjects affected / exposed	18 / 265 (6.79%)	8 / 268 (2.99%)	
occurrences (all)	18	8	
Injury, poisoning and procedural complications			
Transfusion reaction			
subjects affected / exposed	11 / 265 (4.15%)	19 / 268 (7.09%)	
occurrences (all)	11	19	
Nervous system disorders			
Dizziness			
subjects affected / exposed	16 / 265 (6.04%)	19 / 268 (7.09%)	
occurrences (all)	16	19	
Headache			
subjects affected / exposed	73 / 265 (27.55%)	53 / 268 (19.78%)	
occurrences (all)	73	53	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	29 / 265 (10.94%)	19 / 268 (7.09%)	
occurrences (all)	29	19	
Febrile neutropenia			
subjects affected / exposed	117 / 265 (44.15%)	113 / 268 (42.16%)	
occurrences (all)	117	113	
Neutropenia			
subjects affected / exposed	54 / 265 (20.38%)	27 / 268 (10.07%)	
occurrences (all)	54	27	
Thrombocytopenia			

subjects affected / exposed	30 / 265 (11.32%)	30 / 268 (11.19%)	
occurrences (all)	30	30	
Eye disorders			
Dry eye			
subjects affected / exposed	22 / 265 (8.30%)	13 / 268 (4.85%)	
occurrences (all)	22	13	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	46 / 265 (17.36%)	38 / 268 (14.18%)	
occurrences (all)	46	38	
Abdominal pain upper			
subjects affected / exposed	29 / 265 (10.94%)	25 / 268 (9.33%)	
occurrences (all)	29	25	
Constipation			
subjects affected / exposed	56 / 265 (21.13%)	69 / 268 (25.75%)	
occurrences (all)	56	69	
Diarrhoea			
subjects affected / exposed	98 / 265 (36.98%)	94 / 268 (35.07%)	
occurrences (all)	98	94	
Dyspepsia			
subjects affected / exposed	30 / 265 (11.32%)	23 / 268 (8.58%)	
occurrences (all)	30	23	
Gingival bleeding			
subjects affected / exposed	14 / 265 (5.28%)	13 / 268 (4.85%)	
occurrences (all)	14	13	
Haemorrhoids			
subjects affected / exposed	25 / 265 (9.43%)	20 / 268 (7.46%)	
occurrences (all)	25	20	
Nausea			
subjects affected / exposed	90 / 265 (33.96%)	84 / 268 (31.34%)	
occurrences (all)	90	84	
Stomatitis			
subjects affected / exposed	57 / 265 (21.51%)	56 / 268 (20.90%)	
occurrences (all)	57	56	
Vomiting			

subjects affected / exposed	65 / 265 (24.53%)	53 / 268 (19.78%)	
occurrences (all)	65	53	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	18 / 265 (6.79%)	9 / 268 (3.36%)	
occurrences (all)	18	9	
Erythema			
subjects affected / exposed	17 / 265 (6.42%)	14 / 268 (5.22%)	
occurrences (all)	17	14	
Pruritus			
subjects affected / exposed	35 / 265 (13.21%)	40 / 268 (14.93%)	
occurrences (all)	35	40	
Rash			
subjects affected / exposed	69 / 265 (26.04%)	66 / 268 (24.63%)	
occurrences (all)	69	66	
Urticaria			
subjects affected / exposed	16 / 265 (6.04%)	11 / 268 (4.10%)	
occurrences (all)	16	11	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	14 / 265 (5.28%)	9 / 268 (3.36%)	
occurrences (all)	14	9	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	29 / 265 (10.94%)	35 / 268 (13.06%)	
occurrences (all)	29	35	
Back pain			
subjects affected / exposed	19 / 265 (7.17%)	28 / 268 (10.45%)	
occurrences (all)	19	28	
Myalgia			
subjects affected / exposed	16 / 265 (6.04%)	17 / 268 (6.34%)	
occurrences (all)	16	17	
Pain in extremity			
subjects affected / exposed	17 / 265 (6.42%)	22 / 268 (8.21%)	
occurrences (all)	17	22	
Infections and infestations			

Bacteraemia			
subjects affected / exposed	16 / 265 (6.04%)	6 / 268 (2.24%)	
occurrences (all)	16	6	
Conjunctivitis			
subjects affected / exposed	16 / 265 (6.04%)	8 / 268 (2.99%)	
occurrences (all)	16	8	
Folliculitis			
subjects affected / exposed	14 / 265 (5.28%)	4 / 268 (1.49%)	
occurrences (all)	14	4	
Oral herpes			
subjects affected / exposed	18 / 265 (6.79%)	12 / 268 (4.48%)	
occurrences (all)	18	12	
Pneumonia			
subjects affected / exposed	39 / 265 (14.72%)	41 / 268 (15.30%)	
occurrences (all)	39	41	
Sepsis			
subjects affected / exposed	15 / 265 (5.66%)	28 / 268 (10.45%)	
occurrences (all)	15	28	
Upper respiratory tract infection			
subjects affected / exposed	21 / 265 (7.92%)	15 / 268 (5.60%)	
occurrences (all)	21	15	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	46 / 265 (17.36%)	36 / 268 (13.43%)	
occurrences (all)	46	36	
Hyperglycaemia			
subjects affected / exposed	12 / 265 (4.53%)	15 / 268 (5.60%)	
occurrences (all)	12	15	
Hypoalbuminaemia			
subjects affected / exposed	23 / 265 (8.68%)	23 / 268 (8.58%)	
occurrences (all)	23	23	
Hypocalcaemia			
subjects affected / exposed	26 / 265 (9.81%)	29 / 268 (10.82%)	
occurrences (all)	26	29	
Hypokalaemia			

subjects affected / exposed	93 / 265 (35.09%)	96 / 268 (35.82%)	
occurrences (all)	93	96	
Hypomagnesaemia			
subjects affected / exposed	30 / 265 (11.32%)	30 / 268 (11.19%)	
occurrences (all)	30	30	
Hyponatraemia			
subjects affected / exposed	10 / 265 (3.77%)	15 / 268 (5.60%)	
occurrences (all)	10	15	
Hypophosphataemia			
subjects affected / exposed	27 / 265 (10.19%)	24 / 268 (8.96%)	
occurrences (all)	27	24	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 April 2017	Updated information for quizartinib and updated quizartinib dosing instructions, modified the cytarabine regimen in induction, added clarification regarding subjects who will receive second cycle of induction, increased the maximum length of each induction and consolidation cycle, changed the schedule for collecting bone marrow aspirate specimens in induction and increased the window for the bone marrow procedures, updated eligibility criteria, updated language surrounding contraception, pregnancy, and childbearing potential, added language allowing dose adjustment for chemotherapy, revised prohibition of concomitant medication use, added predose QTcF requirement, updated schedule of minimal or measurable residual disease assessments in the Maintenance Phase, added a clarification regarding event-free survival analysis, and removed CRp and updated the definition of other response criteria.
20 November 2018	Changed the duration of double-blind therapy in the Continuation Phase (formerly the Maintenance Phase), added clarification regarding restarting continuation therapy, and updated collection schedule of Health Economic and Outcome Research data
26 June 2019	Specified examples of mutations to be assessed, added additional exploratory objectives, revised schedule for HSCT for consolidation to be performed, modified the inclusion criterion for total bilirubin, clarified rationale for the normal range for serum electrolytes, clarified requirements of an echocardiogram or multi-gated acquisition scan, clarified requirements for subjects who discontinued continuation therapy and then restarted continuation therapy, added text requiring permanent discontinuation of study drug for recurrent QTcF >500 ms, added text regarding management of electrolyte abnormalities, modified the instructions for study drug dose reduction in case of myelosuppression, changed text describing disease history; added cytogenetic risk classification, and the reference for the cytogenetic risk classification being used, clarified ECG testing procedures, added text for activities to be performed from Day 21 up to Day 56 ± 3 days in Cycles 1 and 2 of the Induction Phase, added chemistry where missing, added requirement for subjects who permanently discontinued study drug, restarted on study drug, and completed 36 cycles, revised text to indicate that automated QTcF values should be used to guide decisions regarding dose reduction, escalation, or interruption, and added formula for correcting serum calcium for hypoalbuminemia.
07 April 2020	Changed primary objective/endpoint from EFS to dual primary endpoints of EFS and overall survival (OS), clarified statistical significance for EFS or OS analysis, changed leukemia-free survival to relapse-free survival (RFS), revised the study duration, clarified the definition of the primary completion date, increased target number of EFS events required, added that the OS analysis will be performed when 287 OS events are observed, changed log-rank test methodology, corrected bone marrow exam procedures, clarified "withdrawal by subject" definition, added the collection of Karnofsky performance status prior to the start of the conditioning regimen, added additional timepoints for the collection of graft versus host disease information, corrected Per-protocol Analysis Set, and added adverse events of special interest to the type of safety data that is to be listed.
28 October 2020	Moved EFS to secondary objectives/endpoints, updated the definition of RFS, updated duration of complete response, clarified bone marrow aspirate/biopsy procedures, updated GVHD data collection requirements, clarified procedures for outcomes and remission status after subsequent antileukemic treatments, clarified IRC involvement in assessing response, added that EFS based on investigator's response assessment will also be analyzed, added the definition of CR that will be used by the IRC for assessment of response, and added a new section and tables for acute GVHD grading and staging, percent body surfaces, and chronic GVHD organ scoring.

26 May 2021	Changed the statistical testing order of the secondary endpoints and clarified that the EFS analysis which uses the IRC assessment will be based on the EFS definition in recent health authority acute myeloid leukemia guidance documents.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported