Clinical trial results:
A Phase I, open-label, dose escalation study of ceritinib in pediatric patients with malignancies that have a genetic alteration in anaplastic lymphoma kinase (ALK)

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Summary

EudraCT number	2012-002074-31
Trial protocol	DE NL GB IT FR ES
Global end of trial date	26 April 2019

Results information

Result version number	v1 (current)
This version publication date	11 November 2019
First version publication date	11 November 2019

Trial information

Trial identification

Sponsor protocol code	CLDK378X2103

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01742286
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma, AG, +41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma, AG, +41 613241111, novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric	No

investigation plan (PIP)	
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	26 April 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Estimate the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of ceritinib as a single agent when administered orally to pediatric patients with ALK-activated tumors in fasting and fed states.

Fasted cohort: each daily dose of LDK378 (including days which involved PK blood sampling) was taken at least 2 hours after last meal & subjects did not eat until 1 hour after LDK378 was taken. Each daily dose of LDK378 was taken with 1-2 tablespoons (15-30 mL) of an appropriate food (such as applesauce or non-fat yogurt) & a glass of water

Fed cohort: each daily dose of LDK378 (including days which involved PK blood sampling) was taken with, or within 30 minutes after finishing a low-fat light snack containing 100-300 calories & 1.5-2 grams of fat.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 February 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Germany: 30

Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	83
EEA total number of subjects	67

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)	5
Children (2-11 years)	48
Adolescents (12-17 years)	30
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eighty-three subjects were treated at different dose levels in both fasted and fed states dose escalation and expansion groups. Forty subjects were treated with ceritinib in the dose escalation phase of the study. Twenty-five subjects were treated with ceritinib in fasted condition in dose escalation.

Pre-assignment

Screening details:

At least 15 subjects for the fasted dose escalation & 12 subjects for the fed dose escalation were expected to be treated. During the expansion part, approx. 45 subjects were planned to be treated on the preferred regimen, approx. 25 in group 1 (ALK-activated neuroblastoma) & approx. 20 in group 2 (other ALK-activated tumor such as IMT or ALCL).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Fasted: Ceritinib 300 mg/m2

Arm description:

Participants in the fasted group who took 300 mg of ceritinib

Arm type	Experimental
Investigational medicinal product name	Ceritinib
Investigational medicinal product code	LDK378
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use, Nasogastric use , Gastric use

Dosage and administration details:

300 mg/m2 Ceritinib was administered once daily by mouth, or by nasogastric tube or gastric tube.

Arm title	Fasted: Ceritinib 450 mg/m2

Arm description:

Participants in the fasted group who took 450 mg of ceritinib

Arm type	Experimental
Investigational medicinal product name	Ceritinib
Investigational medicinal product code	LDK378
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use, Nasogastric use , Gastric use

Dosage and administration details:

450 mg/m2 Ceritinib was administered once daily by mouth, or by nasogastric tube or gastric tube.

Arm title	Fasted: Ceritinib 510 mg/m2

Arm description:

Participants in the fasted group who took 510 mg of ceritinib

Arm type	Experimental

Investigational medicinal product name	Ceritinib
Investigational medicinal product code	LDK378
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use, Nasogastric use , Gastric use

Dosage and administration details:

510 mg/m2 Ceritinib was administered once daily by mouth, or by nasogastric tube or gastric tube.

Arm title	Fasted: Ceritinib 560 mg/m2

Arm description:

Participants in the fasted group who took 560 mg of ceritinib

Arm type	Experimental
Investigational medicinal product name	Ceritinib
Investigational medicinal product code	LDK378
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use, Nasogastric use , Gastric use

Dosage and administration details:

560 mg/m2 Ceritinib was administered once daily by mouth, or by nasogastric tube or gastric tube.

Arm title	Fed: Ceritinib 320 mg/m2

Arm description:

Participants in the fed group who took 320 mg of ceritinib

Arm type	Experimental
Investigational medicinal product name	Ceritinib
Investigational medicinal product code	LDK378
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use, Nasogastric use , Gastric use

Dosage and administration details:

320 mg/m2 Ceritinib was administered once daily by mouth, or by nasogastric tube or gastric tube.

Arm title	Fed: Ceritinib 400 mg/m2

Arm description:

Participants in the fed group who took 400 mg of ceritinib

Arm type	Experimental
Investigational medicinal product name	Ceritinib
Investigational medicinal product code	LDK378
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use, Nasogastric use , Gastric use

Dosage and administration details:

400 mg/m2 Ceritinib was administered once daily by mouth, or by nasogastric tube or gastric tube.

Arm title	Fed: Ceritinib 500 mg/m2

Arm description:

Participants in the fed group who took 500 mg of ceritinib

Arm type	Experimental
Investigational medicinal product name	Ceritinib
Investigational medicinal product code	LDK378
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use, Nasogastric use , Gastric use

Dosage and administration details:

500 mg/m2 Ceritinib was administered once daily by mouth, or by nasogastric tube or gastric tube.

Number of subjects in period 1	Fasted: Ceritinib 300 mg/m2	Fasted: Ceritinib 450 mg/m2	Fasted: Ceritinib 510 mg/m2
Started	5	12	13
Ended Treatment = Not Completed)	5	12	13
Completed	0	0	0
Not completed	5	12	13
Adverse event, serious fatal	-	-	-
Physician decision	-	3	4
Consent withdrawn by subject	-	-	-
Disease progression	3	7	7
Adverse event, non-fatal	-	1	2
Administrative problems	1	1	-
Patient/guardian decision	1	-	-

Number of subjects in period 1	Fasted: Ceritinib 560 mg/m2	Fed: Ceritinib 320 mg/m2	Fed: Ceritinib 400 mg/m2
Started	2	4	5
Ended Treatment = Not Completed)	2	4	5
Completed	0	0	0
Not completed	2	4	5
Adverse event, serious fatal	-	-	1
Physician decision	1	-	-
Consent withdrawn by subject	-	-	-
Disease progression	1	4	3
Adverse event, non-fatal	-	-	1
Administrative problems	-	-	-
Patient/guardian decision	-	-	-

Number of subjects in period 1	Fed: Ceritinib 500 mg/m2
Started	42
Ended Treatment = Not Completed)	42
Completed	0
Not completed	42
Adverse event, serious fatal	-
Physician decision	11

Consent withdrawn by subject	1
Disease progression	17
Adverse event, non-fatal	6
Administrative problems	7
Patient/guardian decision	-

Baseline characteristics

Reporting groups	
Reporting group title	Fasted: Ceritinib 300 mg/m2
Reporting group description:	
Participants in the fasted group who took 300 mg of ceritinib	
Reporting group title	Fasted: Ceritinib 450 mg/m2
Reporting group description:	
Participants in the fasted group who took 450 mg of ceritinib	
Reporting group title	Fasted: Ceritinib 510 mg/m2
Reporting group description:	
Participants in the fasted group who took 510 mg of ceritinib	
Reporting group title	Fasted: Ceritinib 560 mg/m2
Reporting group description:	
Participants in the fasted group who took 560 mg of ceritinib	
Reporting group title	Fed: Ceritinib 320 mg/m2
Reporting group description:	
Participants in the fed group who took 320 mg of ceritinib	
Reporting group title	Fed: Ceritinib 400 mg/m2
Reporting group description:	
Participants in the fed group who took 400 mg of ceritinib	
Reporting group title	Fed: Ceritinib 500 mg/m2
Reporting group description:	
Participants in the fed group who took 500 mg of ceritinib	

Reporting group values	Fasted: Ceritinib 300 mg/m2	Fasted: Ceritinib 450 mg/m2	Fasted: Ceritinib 510 mg/m2
Number of subjects	5	12	13
Age, Customized Units: Subjects			
1 - < 7 yrs	1	4	6
7 - < 12 yrs	2	2	1
12 - < 18 yrs	2	6	6
Age Continuous Units: years			
arithmetic mean	11.6	10.0	9.2
standard deviation	± 5.27	± 4.94	± 5.34
Sex: Female, Male Units: Subjects			
Female	3	3	5
Male	2	9	8
Race/Ethnicity, Customized Units: Subjects			
Asian	0	1	1
Black	0	1	0
Caucasian	5	7	11
Other	0	3	1
Native American	0	0	0

Reporting group values	Fasted: Ceritinib 560 mg/m2	Fed: Ceritinib 320 mg/m2	Fed: Ceritinib 400 mg/m2
Number of subjects	2	4	5
Age, Customized Units: Subjects			
1 - < 7 yrs	1	2	2
7 - < 12 yrs	0	0	1
12 - < 18 yrs	1	2	2
Age Continuous Units: years			
arithmetic mean	9.0	8.8	9.2
standard deviation	± 9.90	± 4.99	± 4.02
Sex: Female, Male Units: Subjects			
Female	1	1	3
Male	1	3	2
Race/Ethnicity, Customized Units: Subjects			
Asian	0	0	0
Black	0	0	0
Caucasian	2	4	3
Other	0	0	2
Native American	0	0	0

Reporting group values	Fed: Ceritinib 500 mg/m2	Total	
Number of subjects	42	83	
Age, Customized Units: Subjects			
1 - < 7 yrs	21	37	
7 - < 12 yrs	10	16	
12 - < 18 yrs	11	30	
Age Continuous Units: years			
arithmetic mean	7.3		
standard deviation	± 4.73	-	
Sex: Female, Male Units: Subjects			
Female	14	30	
Male	28	53	
Race/Ethnicity, Customized Units: Subjects			
Asian	3	5	
Black	0	1	
Caucasian	33	65	
Other	5	11	
Native American	1	1	

Subject analysis sets	
Subject analysis set title	ALK-activated Neuroblastoma
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with ALK-activated neuroblstoma enrolled in the expansion part of the study and were given ceritinib once daily, continuously

Subject analysis set title	ALK-activated Inflammatory myofibroblastic tumors (IMT)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with ALK-activated IMT enrolled in the expansion part of the study who were given ceritinib once daily, continuously

Subject analysis set title	ALK-activated Anaplastic large cell lymphoma (ALCL)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with ALK-activated ALCL enrolled in the expansion part of the study who were given ceritinib once daily, continuously

Subject analysis set title	ALK-activated Other
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with other ALK-activated tumors enrolled in the expansion part of the study who were given ceritinib once daily, continuously

Subject analysis set title	ALK-activated Neuroblastoma
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with ALK-activated neuroblstoma enrolled in the expansion part of the study and were given ceritinib once daily, continuously

Subject analysis set title	ALK-activated Inflammatory myofibroblastic tumors (IMT)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with ALK-activated IMT enrolled in the expansion part of the study who were given ceritinib once daily, continuously

Subject analysis set title	ALK-activated Anaplastic large cell lymphoma (ALCL)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with ALK-activated ALCL enrolled in the expansion part of the study who were given ceritinib once daily, continuously

Subject analysis set title	ALK-activated Other
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with other ALK-activated tumors enrolled in the expansion part of the study who were given ceritinib once daily, continuously

Reporting group values	ALK-activated Neuroblastoma	ALK-activated Inflammatory myofibroblastic tumors (IMT)	ALK-activated Anaplastic large cell lymphoma (ALCL)
Number of subjects	30	10	8
Age, Customized Units: Subjects			
1 - < 7 yrs			
7 - < 12 yrs			
12 - < 18 yrs			
Age Continuous Units: years			
arithmetic mean	20.0	70.0	75.0
standard deviation	±	±	±

Sex: Female, Male Units: Subjects			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
Asian Black Caucasian Other Native American			

Reporting group values	ALK-activated Other	ALK-activated Neuroblastoma	ALK-activated Inflammatory myofibroblastic tumors (IMT)
Number of subjects	7	6	7
Age, Customized Units: Subjects			
1 - < 7 yrs 7 - < 12 yrs 12 - < 18 yrs			
Age Continuous Units: years arithmetic mean standard deviation	 14.3 ±	 15.0 ±	 99.99 ±
Sex: Female, Male Units: Subjects			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
Asian Black Caucasian Other Native American			

Reporting group values	ALK-activated Anaplastic large cell lymphoma (ALCL)	ALK-activated Other	
Number of subjects	6	1	
Age, Customized Units: Subjects			
1 - < 7 yrs 7 - < 12 yrs 12 - < 18 yrs			
Age Continuous Units: years arithmetic mean standard deviation	 99.99 ±	 99.99 ±	

Sex: Female, Male Units: Subjects			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
Asian Black Caucasian Other Native American			

End points

End points reporting groups

Reporting group title	Fasted: Ceritinib 300 mg/m2
Reporting group description:	
Participants in the fasted group who took 300 mg of ceritinib	
Reporting group title	Fasted: Ceritinib 450 mg/m2
Reporting group description:	
Participants in the fasted group who took 450 mg of ceritinib	
Reporting group title	Fasted: Ceritinib 510 mg/m2
Reporting group description:	
Participants in the fasted group who took 510 mg of ceritinib	
Reporting group title	Fasted: Ceritinib 560 mg/m2
Reporting group description:	
Participants in the fasted group who took 560 mg of ceritinib	
Reporting group title	Fed: Ceritinib 320 mg/m2
Reporting group description:	
Participants in the fed group who took 320 mg of ceritinib	
Reporting group title	Fed: Ceritinib 400 mg/m2
Reporting group description:	
Participants in the fed group who took 400 mg of ceritinib	
Reporting group title	Fed: Ceritinib 500 mg/m2
Reporting group description:	
Participants in the fed group who took 500 mg of ceritinib	
Subject analysis set title	ALK-activated Neuroblastoma
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with ALK-activated neuroblstoma enrolled in the expansion part of the study and were given ceritinib once daily, continuously	
Subject analysis set title	ALK-activated Inflammatory myofibroblastic tumors (IMT)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with ALK-activated IMT enrolled in the expansion part of the study who were given ceritinib once daily, continuously	
Subject analysis set title	ALK-activated Anaplastic large cell lymphoma (ALCL)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with ALK-activated ALCL enrolled in the expansion part of the study who were given ceritinib once daily, continuously	
Subject analysis set title	ALK-activated Other
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with other ALK-activated tumors enrolled in the expansion part of the study who were given ceritinib once daily, continuously	
Subject analysis set title	ALK-activated Neuroblastoma
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with ALK-activated neuroblstoma enrolled in the expansion part of the study and were given ceritinib once daily, continuously	
Subject analysis set title	ALK-activated Inflammatory myofibroblastic tumors (IMT)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with ALK-activated IMT enrolled in the expansion part of the study who were given ceritinib once daily, continuously

Subject analysis set title	ALK-activated Anaplastic large cell lymphoma (ALCL)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with ALK-activated ALCL enrolled in the expansion part of the study who were given ceritinib once daily, continuously

Subject analysis set title	ALK-activated Other
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with other ALK-activated tumors enrolled in the expansion part of the study who were given ceritinib once daily, continuously

Primary: Incidence rate of Dose Limiting Toxicities (DLTs) occurring during first cycle of treatment

End point title	Incidence rate of Dose Limiting Toxicities (DLTs) occurring during first cycle of treatment[1]

End point description:

A DLT is defined as an adverse event or abnormal laboratory value assessed as unrelated to disease, disease progression, inter-current illness, or concomitant therapies that occurs within the first 21 days of treatment with LDK378 and meets a specified defined criteria. A participant with multiple occurrences of DLTs under one treatment is counted only once in the Adverse Event category for that treatment. A participant with multiple DLTs within a primary system organ class is counted only once in the total row.

End point type	Primary

End point timeframe:

up to day 21 after the patient's first dose; cycle = within the first 21 days of patient's first dose

Notes:

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

End point values	Fasted: Ceritinib 300 mg/m2	Fasted: Ceritinib 450 mg/m2	Fasted: Ceritinib 510 mg/m2	Fasted: Ceritinib 560 mg/m2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	12	6	2
Units: Participants				
Investigations: Alanine aminotransferase incr.	0	0	0	1
Gastrointestinal disorders: abdominal pain	0	0	0	1
Gastrointestinal disorders: Influenza	0	0	0	0
Total DLTs	0	0	0	2

End point values	Fed: Ceritinib 320 mg/m2	Fed: Ceritinib 400 mg/m2	Fed: Ceritinib 500 mg/m2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	5	
Units: Participants				
Investigations: Alanine aminotransferase incr.	0	1	0	
Gastrointestinal disorders: abdominal pain	0	0	0	

Gastrointestinal disorders: Influenza	0	0	1	
Total DLTs	0	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of best overall response by Overall response Rate (ORR) per Investigator assessment

End point title	Summary of best overall response by Overall response Rate (ORR) per Investigator assessment

End point description:

Assessed the anti-tumor activity of LDK378 per investigator assessment of disease status using RECIST 1.1 by treatment group.

End point type	Secondary

End point timeframe:

30 months

End point values	ALK-activated Neuroblastoma	ALK-activated Inflammatory myofibroblastic tumors (IMT)	ALK-activated Anaplastic large cell lymphoma (ALCL)	ALK-activated Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	10	8	7
Units: percentage of participants				
number (confidence interval 95%)	20.0 (7.7 to 38.6)	70.0 (34.8 to 93.3)	75.0 (34.9 to 96.8)	14.3 (0.4 to 57.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DoR) per investigator assessment

End point title	Duration of response (DoR) per investigator assessment

End point description:

Assess the anti-tumor activity of LDK378 per DOR by primary diagnosis of tumor

End point type	Secondary

End point timeframe:

30 months

End point values	ALK-activated Neuroblastoma	ALK-activated Inflammatory myofibroblastic tumors (IMT)	ALK-activated Anaplastic large cell lymphoma (ALCL)	ALK-activated Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	7	6	1
Units: months				
median (confidence interval 95%)	15.0 (5.8 to 22.2)	999 (3.5 to 999)	999 (2.8 to 999)	999 (999 to 999)

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS) based on investigator assessment

End point title	Progression free survival (PFS) based on investigator assessment

End point description:

Assess the anti-tumor activity of LDK378 as per RECIST 1.1 by PFS by primary diagnosis of tumor

End point type	Secondary

End point timeframe:

30 months

End point values	ALK-activated Neuroblastoma	ALK-activated Inflammatory myofibroblastic tumors (IMT)	ALK-activated Anaplastic large cell lymphoma (ALCL)	ALK-activated Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	10	6	1
Units: months				
median (confidence interval 95%)	2.4 (1.2 to 6.8)	999 (1.2 to 999)	999 (4.1 to 999)	1.9 (1.2 to 999)

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration time profiles by treatment group in escalation phase

End point title	Plasma concentration time profiles by treatment group in escalation phase

End point description:

Characterize single and multiple-dose PK of LDK378 in pediatric patients. Only PK plasma concentrations with non-missing sampling date and time, and for which the last dose date and time prior to the PK sample draw are non-missing, were included in the PK analysis.

End point type	Secondary

End point timeframe:

0hr pre-dose, 2hrs post-dose, 4hrs post-dose, 6hrs post-dose & 24hrs post-dose in Cycle1 Day1 & Cycle 2 day 1; 0hr pre-dose in Cycle 1 Day 15, Cycle 2 Day1, Cycle 2 Day 2, Cycle 3 day 1 & Cycle 4 Day 1

End point values	Fasted: Ceritinib 300 mg/m2	Fasted: Ceritinib 450 mg/m2	Fasted: Ceritinib 510 mg/m2	Fasted: Ceritinib 560 mg/m2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	12	13	2
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle1 Day1 (C1D1) 0 hr pre-dose(n=5,12,6,2,4,5,5)	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)
C1D1 2 hrs post-dose(n=5,11,6,2,4,5,5)	104 (± 97.9)	99.0 (± 94.7)	112 (± 90.6)	126 (± 0.6)
C1D1 4 hrs post-dose(n=5,11,6,2,4,5,5)	216 (± 39.6)	233 (± 69.0)	250 (± 93.5)	350 (± 54.7)
C1D1 6 hrs post-dose(n=5,11,6,2,4,5,4)	227 (± 33.8)	245 (± 78.1)	245 (± 97.2)	423 (± 74.2)
C1D1 24 hrs post-dose(n=5,11,6,2,4,5,4)	130 (± 66.3)	141 (± 89.9)	86.4 (± 117.2)	268 (± 73.6)
C1D2 0 hr pre-dose(n=5,11,6,2,4,5,4)	130 (± 66.3)	141 (± 89.9)	86.4 (± 117.2)	268 (± 73.6)
C1D15 0 hr pre-dose(n=5,12,6,2,3,4,5)	193 (± 99.6)	618 (± 64.6)	537 (± 49.9)	942 (± 5.1)
C2D1 0 hr pre-dose(n=5,12,5,2,3,4,3)	169 (± 299.5)	661 (± 53.5)	672 (± 45.4)	695 (± 152.7)
C2D1 2 hrs post-dose(n=5,12,5,2,3,4,3)	287 (± 85.4)	687 (± 61.6)	801 (± 45.9)	662 (± 99.6)
C2D1 4 hrs post-dose(n=5,12,5,2,3,4,3)	386 (± 47.6)	810 (± 51.9)	1000 (± 30.4)	1230 (± 30.1)
C2D1 6 hrs post-dose(n=5,12,5,2,3,4,2)	426 (± 38.4)	852 (± 47.8)	898 (± 37.6)	1260 (± 16.4)
C2D1 24 hrs post-dose(n=5,12,5,2,3,4,5)	247 (± 46.9)	651 (± 53.7)	714 (± 40.8)	847 (± 72.2)
C2D2 0 hr pre-dose(n=5,12,5,2,3,4,5)	247 (± 46.9)	651 (± 53.7)	714 (± 40.8)	847 (± 72.2)
C3D1 0 hr pre-dose(n=2,8,4,1,2,1,5)	399 (± 94.4)	810 (± 34.3)	415 (± 117.7)	1320 (± 0.0)
C4D1 0 hr pre-dose(n=2,8,4,1,1,1,3)	503 (± 35.1)	960 (± 36.2)	321 (± 874.8)	857 (± 0.0)

End point values	Fed: Ceritinib 320 mg/m2	Fed: Ceritinib 400 mg/m2	Fed: Ceritinib 500 mg/m2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	5	21	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle1 Day1 (C1D1) 0 hr pre-dose(n=5,12,6,2,4,5,5)	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)	
C1D1 2 hrs post-dose(n=5,11,6,2,4,5,5)	52.4 (± 138.1)	197 (± 58.3)	72.5 (± 82.3)	
C1D1 4 hrs post-dose(n=5,11,6,2,4,5,5)	166 (± 92.8)	311 (± 28.1)	153 (± 34.1)	
C1D1 6 hrs post-dose(n=5,11,6,2,4,5,4)	275 (± 35.3)	318 (± 36.7)	168 (± 68.9)	

C1D1 24 hrs post-dose(n=5,11,6,2,4,5,4)	98.5 (± 63.7)	126 (± 107.7)	161 (± 111.3)	
C1D2 0 hr pre-dose(n=5,11,6,2,4,5,4)	98.5 (± 63.7)	126 (± 107.7)	161 (± 111.3)	
C1D15 0 hr pre-dose(n=5,12,6,2,3,4,5)	262 (± 118.4)	379 (± 119.2)	461 (± 76.3)	
C2D1 0 hr pre-dose(n=5,12,5,2,3,4,3)	218 (± 103.7)	429 (± 73.8)	655 (± 12.4)	
C2D1 2 hrs post-dose(n=5,12,5,2,3,4,3)	196 (± 112.4)	475 (± 96.6)	718 (± 21.1)	
C2D1 4 hrs post-dose(n=5,12,5,2,3,4,3)	262 (± 133.9)	631 (± 86.6)	744 (± 13.2)	
C2D1 6 hrs post-dose(n=5,12,5,2,3,4,2)	300 (± 130.3)	648 (± 105.5)	786 (± 7.7)	
C2D1 24 hrs post-dose(n=5,12,5,2,3,4,5)	194 (± 106.5)	411 (± 147.3)	448 (± 43.9)	
C2D2 0 hr pre-dose(n=5,12,5,2,3,4,5)	194 (± 106.5)	411 (± 147.3)	448 (± 43.9)	
C3D1 0 hr pre-dose(n=2,8,4,1,2,1,5)	167 (± 218.3)	328 (± 0.0)	433 (± 128.5)	
C4D1 0 hr pre-dose(n=2,8,4,1,1,1,3)	403 (± 0.0)	1320 (± 0.0)	658 (± 27.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration time profiles by treatment group in expansion phase

End point title	Plasma concentration time profiles by treatment group in expansion phase

End point description:

Characterize single and multiple-dose PK of LDK378 in pediatric patients. Only PK plasma concentrations with non-missing sampling date and time, and for which thelast dose date and time prior to the PK sample draw are non-missing, were included in the PK analysis.

End point type	Secondary

End point timeframe:

0hr pre-dose Cycle 1 Day 1, cycle 1 Day 15; 0hr pre-dose, 2hrs post-dose, 4hrs post-dose, 6hrs post-dose & 24hrs post-dose in Cycle2 Day1; 0hr pre-dose in Cycle2 Day2, Cycle 3 Day 1 & Cycle 4 Day 1

End point values	Fasted: Ceritinib 300 mg/m2	Fasted: Ceritinib 450 mg/m2	Fasted: Ceritinib 510 mg/m2	Fasted: Ceritinib 560 mg/m2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	12	13	2
Units: mg/mg^2				
geometric mean (geometric coefficient of variation)				
C1D1 0 hr pre-dose(n=0,0,6,0,0,0,9)	999 (± 999)	999 (± 999)	0.0 (± 0.0)	999 (± 999)
C1D15 0 hr post-dose(n=0,0,1,0,0,0,0)	999 (± 999)	999 (± 999)	1190 (± 0.0)	999 (± 999)
C2D1 0 hr pre-dose(n=0,0,7,0,0,0,16)	999 (± 999)	999 (± 999)	529 (± 365.4)	999 (± 999)
C2D1 2 hrs post-dose(n=0,0,7,0,0,0,15)	999 (± 999)	999 (± 999)	798 (± 69.0)	999 (± 999)
C2D1 4 hrs post-dose(n=0,0,7,0,0,0,4)	999 (± 999)	999 (± 999)	863 (± 65.2)	999 (± 999)
C2D1 6 hrs post-dose(n=0,0,7,0,0,0,15)	999 (± 999)	999 (± 999)	939 (± 71.4)	999 (± 999)

C2D1 24 hrs post-dose(n=0,0,6,0,0,0,14)	999 (± 999)	999 (± 999)	615 (± 119.9)	999 (± 999)
C2D2 0 hr pre-dose(n=0,0,6,0,0,0,14)	999 (± 999)	999 (± 999)	615 (± 119.9)	999 (± 999)
C3D1 0 hr pre-dose(n=0,0,5,0,0,0,14)	999 (± 999)	999 (± 999)	836 (± 60.4)	999 (± 999)
C4D1 0 hr pre-dose(n=0,0,5,0,0,0,12)	999 (± 999)	999 (± 999)	834 (± 78.8)	999 (± 999)

End point values	Fed: Ceritinib 320 mg/m2	Fed: Ceritinib 400 mg/m2	Fed: Ceritinib 500 mg/m2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	5	21	
Units: mg/mg^2				
geometric mean (geometric coefficient of variation)				
C1D1 0 hr pre-dose(n=0,0,6,0,0,0,9)	999 (± 999)	999 (± 999)	0.0 (± 0.0)	
C1D15 0 hr post-dose(n=0,0,1,0,0,0,0)	999 (± 999)	999 (± 999)	999 (± 999)	
C2D1 0 hr pre-dose(n=0,0,7,0,0,0,16)	999 (± 999)	999 (± 999)	627 (± 93.6)	
C2D1 2 hrs post-dose(n=0,0,7,0,0,0,15)	999 (± 999)	999 (± 999)	729 (± 72.3)	
C2D1 4 hrs post-dose(n=0,0,7,0,0,0,4)	999 (± 999)	999 (± 999)	828 (± 47.9)	
C2D1 6 hrs post-dose(n=0,0,7,0,0,0,15)	999 (± 999)	999 (± 999)	870 (± 52.6)	
C2D1 24 hrs post-dose(n=0,0,6,0,0,0,14)	999 (± 999)	999 (± 999)	596 (± 75.5)	
C2D2 0 hr pre-dose(n=0,0,6,0,0,0,14)	999 (± 999)	999 (± 999)	596 (± 75.5)	
C3D1 0 hr pre-dose(n=0,0,5,0,0,0,14)	999 (± 999)	999 (± 999)	573 (± 134.2)	
C4D1 0 hr pre-dose(n=0,0,5,0,0,0,12)	999 (± 999)	999 (± 999)	622 (± 96.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) parameters: AUC0 - 24h & AUClast in Cycle 1 Day 1 - Dose escalation phase (single dose)

End point title	Pharmacokinetics (PK) parameters: AUC0 - 24h & AUClast in Cycle 1 Day 1 - Dose escalation phase (single dose)

End point description:

Characterize single and multiple-dose PK of LDK378 in pediatric patients. AUC: Area under the plasma (serum, or blood) concentration versus time curve AUClast: Area under the plasma (serum, or blood) concentration versus time curverea under the concentration-time curve from time zero to the last measureable concentration time AUC0-24h: AUC0-24h Area under the plasma concentration-time curve t=0-24 h

End point type	Secondary

End point timeframe:

0hr pre-dose, 2, 4, 6 & 24hrs post-dose

End point values	Fasted: Ceritinib 300 mg/m2	Fasted: Ceritinib 450 mg/m2	Fasted: Ceritinib 510 mg/m2	Fasted: Ceritinib 560 mg/m2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	12	10	2
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)				
AUC0-24h (n=4,3,2,0,1,1,2)	3920 (± 39.9)	5220 (± 58.0)	8750 (± 11.1)	999 (± 999)
AUClast (n= 5,9,3,1,3,4,3)	4260 (± 39.3)	4350 (± 91.8)	7670 (± 24.5)	4860 (± 0.0)

End point values	Fed: Ceritinib 320 mg/m2	Fed: Ceritinib 400 mg/m2	Fed: Ceritinib 500 mg/m2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	4	18	
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)				
AUC0-24h (n=4,3,2,0,1,1,2)	5720 (± 0.0)	7272 (± 0.0)	4730 (± 59.4)	
AUClast (n= 5,9,3,1,3,4,3)	3730 (± 48.6)	5760 (± 49.1)	4940 (± 32.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) parameters: AUC0 - 24h & AUClast in Cycle 2 Day 1 - Dose escalation phase (single dose)

End point title	Pharmacokinetics (PK) parameters: AUC0 - 24h & AUClast in Cycle 2 Day 1 - Dose escalation phase (single dose)

End point description:

Characterize single and multiple-dose PK of LDK378 in pediatric patients. AUC: Area under the plasma (serum, or blood) concentration versus time curve AUClast: Area under the plasma (serum, or blood) concentration versus time curverea under the concentration-time curve from time zero to the last measureable concentration time AUC0-24h: AUC0-24h Area under the plasma concentration-time curve t=0-24 h

End point type	Secondary

End point timeframe:

0hr pre-dose, 2, 4, 6 & 24hrs post-dose

End point values	Fasted: Ceritinib 300 mg/m2	Fasted: Ceritinib 450 mg/m2	Fasted: Ceritinib 510 mg/m2	Fasted: Ceritinib 560 mg/m2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	12	10	2
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)				
AUC0-24h (n=5,7,2,2,1,1,1)	8160 (± 44.0)	16900 (± 59.1)	21000 (± 20.8)	25300 (± 39.2)

AUClast (n= 5,12,5,2,3,4,2)	8210 (± 44.3)	18000 (± 50.0)	17200 (± 51.2)	25600 (± 39.0)

End point values	Fed: Ceritinib 320 mg/m2	Fed: Ceritinib 400 mg/m2	Fed: Ceritinib 500 mg/m2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	4	18	
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)				
AUC0-24h (n=5,7,2,2,1,1,1)	2100 (± 0.0)	30500 (± 0.0)	16500 (± 0.0)	
AUClast (n= 5,12,5,2,3,4,2)	5840 (± 118.4)	125000 (± 113.2)	16700 (± 1.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) parameters: AUC0 - 24h & AUClast in Cycle 2 Day 1 - Dose expansion phase (multiple dose)

End point title	Pharmacokinetics (PK) parameters: AUC0 - 24h & AUClast in Cycle 2 Day 1 - Dose expansion phase (multiple dose)[2]

End point description:

Characterize single and multiple-dose PK of LDK378 in pediatric patients. In this phase ceritinib was expanded at 500mg/m2 fed and 510mg/m2 fasted administered orally once daily and was assessed only at steady state, Cycle 2 Day 1. AUC: Area under the plasma (serum, or blood) concentration versus time curve AUClast: Area under the plasma (serum, or blood) concentration versus time curverea under the concentration-time curve from time zero to the last measureable concentration time AUC0-24h: AUC0-24h Area under the plasma concentration-time curve t=0-24 h

End point type	Secondary

End point timeframe:

0hr pre-dose, 2, 4, 6 & 24hrs post-dose

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Fasted: Ceritinib 510 mg/m2	Fed: Ceritinib 500 mg/m2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	18		
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)				
AUC0-24h (n = 0, 6)	999 (± 999)	15900 (± 93.8)		
AUClast (n = 4, 14)	24100 (± 38.9)	16100 (± 61.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Cmax in Cycle 1 Day 1 - Dose escalation phase (single dose)

End point title	PK parameter: Cmax in Cycle 1 Day 1 - Dose escalation phase (single dose)

End point description:

Characterize single and multiple-dose PK of LDK378 in pediatric patients. Cmax: Maximum (peak) concentration of drug

End point type	Secondary

End point timeframe:

0hr pre-dose, 2, 4, 6 & 24hrs post-dose

End point values	Fasted: Ceritinib 300 mg/m2	Fasted: Ceritinib 450 mg/m2	Fasted: Ceritinib 510 mg/m2	Fasted: Ceritinib 560 mg/m2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	12	10	2
Units: ng/mL				
geometric mean (geometric coefficient of variation)	258 (± 39.0)	270 (± 82.1)	537 (± 22.2)	265 (± 0.0)

End point values	Fed: Ceritinib 320 mg/m2	Fed: Ceritinib 400 mg/m2	Fed: Ceritinib 500 mg/m2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	4	18	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	251 (± 37.0)	341 (± 34.2)	204 (± 54.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Cmax in Cycle 2 Day 1 - Dose escalation phase (single dose)

End point title	PK parameter: Cmax in Cycle 2 Day 1 - Dose escalation phase (single dose)

End point description:

Characterize single and multiple-dose PK of LDK378 in pediatric patients. Cmax: Maximum (peak) concentration of drug.

End point type	Secondary

End point timeframe:

0hr pre-dose, 2, 4, 6 & 24hrs post-dose

End point values	Fasted: Ceritinib 300 mg/m2	Fasted: Ceritinib 450 mg/m2	Fasted: Ceritinib 510 mg/m2	Fasted: Ceritinib 560 mg/m2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	12	10	2
Units: ng/mL				
geometric mean (geometric coefficient of variation)	427 (± 38.5)	870 (± 48.7)	1020 (± 32.1)	1300 (± 21.4)

End point values	Fed: Ceritinib 320 mg/m2	Fed: Ceritinib 400 mg/m2	Fed: Ceritinib 500 mg/m2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	4	18	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	300 (± 130.3)	674 (± 93.8)	804 (± 10.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Cmax in Cycle 2 Day 1 - Dose expansion phase (multiple dose)

End point title	PK parameter: Cmax in Cycle 2 Day 1 - Dose expansion phase (multiple dose)[3]

End point description:

Characterize single and multiple-dose PK of LDK378 in pediatric patients. In this phase ceritinib was expanded at 500mg/m2 fed and 510mg/m2 fasted administered orally once daily and was assessed only at steady state, Cycle 2 Day 1. Cmax: Maximum (peak) concentration of drug

End point type	Secondary

End point timeframe:

0hr pre-dose, 2, 4, 6 & 24hrs post-dose

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Fasted: Ceritinib 510 mg/m2	Fed: Ceritinib 500 mg/m2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	18		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1220 (± 40.2)	890 (± 50.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Tmax in Cycle 1 Day 1 - Dose escalation phase (single dose)

End point title	PK parameter: Tmax in Cycle 1 Day 1 - Dose escalation phase (single dose)

End point description:

Characterize single and multiple-dose PK of LDK378 in pediatric patients. Tmax: The time to reach maximum plasma concentration

End point type	Secondary

End point timeframe:

0hr pre-dose, 2, 4, 6 & 24hrs post-dose

End point values	Fasted: Ceritinib 300 mg/m2	Fasted: Ceritinib 450 mg/m2	Fasted: Ceritinib 510 mg/m2	Fasted: Ceritinib 560 mg/m2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	12	10	2
Units: hour (hr)				
median (full range (min-max))	4.20 (1.90 to 24.0)	4.25 (0.00 to 6.10)	4.30 (4.10 to 6.00)	6.10 (6.10 to 6.10)

End point values	Fed: Ceritinib 320 mg/m2	Fed: Ceritinib 400 mg/m2	Fed: Ceritinib 500 mg/m2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	4	18	
Units: hour (hr)				
median (full range (min-max))	6.10 (5.70 to 6.30)	6.00 (4.30 to 6.20)	5.80 (4.10 to 6.10)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Tmax in Cycle 2 Day 1 - Dose escalation phase (single dose)

End point title	PK parameter: Tmax in Cycle 2 Day 1 - Dose escalation phase (single dose)

End point description:

Characterize single and multiple-dose PK of LDK378 in pediatric patients. Tmax: The time to reach maximum plasma concentration

End point type	Secondary

End point timeframe:

0hr pre-dose, 2, 4, 6 & 24hrs post-dose

End point values	Fasted: Ceritinib 300 mg/m2	Fasted: Ceritinib 450 mg/m2	Fasted: Ceritinib 510 mg/m2	Fasted: Ceritinib 560 mg/m2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	12	10	2
Units: hour (hr)				
median (full range (min-max))	6.00 (4.10 to 6.70)	5.10 (2.00 to 6.60)	4.00 (2.10 to 6.00)	3.95 (0.00 to 6.70)

End point values	Fed: Ceritinib 320 mg/m2	Fed: Ceritinib 400 mg/m2	Fed: Ceritinib 500 mg/m2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	4	18	
Units: hour (hr)				
median (full range (min-max))	5.90 (5.80 to 6.10)	6.00 (4.00 to 6.10)	2.20 (2.00 to 2.40)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Tmax in Cycle 2 Day 1 - Dose expansion phase (multiple dose)

End point title	PK parameter: Tmax in Cycle 2 Day 1 - Dose expansion phase (multiple dose)[4]

End point description:

Characterize single and multiple-dose PK of LDK378 in pediatric patients. In this phase ceritinib was expanded at 500mg/m2 fed and 510mg/m2 fasted administered orally once daily and was assessed only at steady state, Cycle 2 Day 1. Characterize single and multiple-dose PK of LDK378 in pediatric patients. Tmax: The time to reach maximum plasma concentration

End point type	Secondary

End point timeframe:

0hr pre-dose, 2, 4, 6 & 24hrs post-dose

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Fasted: Ceritinib 510 mg/m2	Fed: Ceritinib 500 mg/m2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	18		
Units: hour (hr)				
median (full range (min-max))	6.20 (3.80 to 23.8)	5.90 (1.90 to 23.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Racc in Dose escalation phase Cycle 2 Day 1

End point title	PK parameter: Racc in Dose escalation phase Cycle 2 Day 1

End point description:

Characterize single and multiple-dose PK of LDK378 in pediatric patients. Racc: Accumulation ratio

End point type	Secondary

End point timeframe:

0hr pre-dose, 2, 4, 6 & 24hrs post-dose

End point values	Fasted: Ceritinib 300 mg/m2	Fasted: Ceritinib 450 mg/m2	Fasted: Ceritinib 510 mg/m2	Fasted: Ceritinib 560 mg/m2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	12	10	2
Units: ratio				
geometric mean (geometric coefficient of variation)	41.6 (± 80.7)	30.3 (± 116.3)	22.8 (± 71.6)	15.5 (± 0.0)

End point values	Fed: Ceritinib 320 mg/m2	Fed: Ceritinib 400 mg/m2	Fed: Ceritinib 500 mg/m2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	4	18	
Units: ratio				
geometric mean (geometric coefficient of variation)	95.0 (± 0.0)	9.83 (± 0.0)	19.3 (± 118.4)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from first dose of study treatment until end of study treatment plus 30 days post treatment, up to maximum duration of 63.7 months.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Ceritinib@300 mg/m2

Reporting group description:

Ceritinib@300 mg/m2

Reporting group title	Ceritinib@450 mg/m2

Reporting group description:

Ceritinib@450 mg/m2

Reporting group title	Ceritinib@510 mg/m2

Reporting group description:

Ceritinib@510 mg/m2

Reporting group title	Ceritinib@560 mg/m2

Reporting group description:

Ceritinib@560 mg/m2

Reporting group title	Ceritinib@320 mg/m2

Reporting group description:

Ceritinib@320 mg/m2

Reporting group title	Ceritinib@400 mg/m2

Reporting group description:

Ceritinib@400 mg/m2

Reporting group title	Ceritinib@500 mg/m2

Reporting group description:

Ceritinib@500 mg/m2

Reporting group title	Fasted+Fed All Subjects

Reporting group description:

All participants in the Fasted and Fed groups

Serious adverse events	Ceritinib@300 mg/m2	Ceritinib@450 mg/m2	Ceritinib@510 mg/m2
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	4 / 12 (33.33%)	8 / 13 (61.54%)
number of deaths (all causes)	1	1	2
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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			
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchopleural fistula			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	2 / 13 (15.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lipase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	2 / 13 (15.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hemiplegia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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			
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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 bone marrow aplasia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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 neutropenia			

subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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 distension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dental caries			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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			
Acute hepatic failure			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovirus infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metapneumovirus infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
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			
Dehydration			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Ceritinib@560 mg/m2	Ceritinib@320 mg/m2	Ceritinib@400 mg/m2
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	3 / 4 (75.00%)	1 / 5 (20.00%)
number of deaths (all causes)	0	2	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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			
Hypotension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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			
Chest pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			

subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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			
Bronchopleural fistula			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Aspartate aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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 lactate dehydrogenase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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			
Hemiplegia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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			
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile bone marrow aplasia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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 distension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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			
subjects affected / exposed	1 / 2 (50.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dental caries			

subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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			
Acute hepatic failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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			
Acute kidney injury			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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			
Bone pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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			
Appendicitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovirus infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metapneumovirus infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
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 viral			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			

subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Ceritinib@500 mg/m2	Fasted+Fed All Subjects	
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 42 (50.00%)	40 / 83 (48.19%)	
number of deaths (all causes)	5	12	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 42 (0.00%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 42 (7.14%)	6 / 83 (7.23%)	
occurrences causally related to treatment / all	1 / 7	1 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchopleural fistula			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	2 / 42 (4.76%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 42 (4.76%)	4 / 83 (4.82%)	
occurrences causally related to treatment / all	3 / 3	6 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amylase increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 42 (2.38%)	4 / 83 (4.82%)	
occurrences causally related to treatment / all	2 / 2	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
subjects affected / exposed	0 / 42 (0.00%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			

subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hemiplegia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	2 / 42 (4.76%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
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	0 / 42 (0.00%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal pain			
subjects affected / exposed	1 / 42 (2.38%)	5 / 83 (6.02%)	
occurrences causally related to treatment / all	1 / 1	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
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 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal haemorrhage			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			

subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 42 (0.00%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
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	4 / 42 (9.52%)	4 / 83 (4.82%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear infection			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
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 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovirus infection			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastroenteritis			
subjects affected / exposed	2 / 42 (4.76%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	3 / 42 (7.14%)	3 / 83 (3.61%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metapneumovirus infection			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	3 / 42 (7.14%)	3 / 83 (3.61%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Septic shock			

subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 1	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	Ceritinib@300 mg/m2	Ceritinib@450 mg/m2	Ceritinib@510 mg/m2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	12 / 12 (100.00%)	13 / 13 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

Tumour pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pallor			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Catheter site pain			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	1 / 13 (7.69%)
occurrences (all)	0	2	1
Chest pain			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	1 / 13 (7.69%)
occurrences (all)	0	2	1
Fatigue			
subjects affected / exposed	3 / 5 (60.00%)	4 / 12 (33.33%)	3 / 13 (23.08%)
occurrences (all)	3	6	4
Gait disturbance			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
General physical health deterioration			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	3 / 5 (60.00%)	4 / 12 (33.33%)	6 / 13 (46.15%)
occurrences (all)	5	6	15
Secretion discharge			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Ulcer			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 5 (20.00%)	1 / 12 (8.33%)	2 / 13 (15.38%)
occurrences (all)	1	2	7
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Emphysema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	2
Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pleuritic pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	3	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Irritability			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Mental disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

Restlessness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	8 / 12 (66.67%)	8 / 13 (61.54%)
occurrences (all)	3	13	18
Amylase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	4	1
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	6 / 12 (50.00%)	7 / 13 (53.85%)
occurrences (all)	3	10	21
Blood albumin decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 5 (20.00%)	4 / 12 (33.33%)	0 / 13 (0.00%)
occurrences (all)	1	4	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Blood creatine increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	2 / 5 (40.00%)	4 / 12 (33.33%)	1 / 13 (7.69%)
occurrences (all)	5	5	1
Blood glucose increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	3 / 13 (23.08%)
occurrences (all)	0	3	4
Blood magnesium increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Blood urea increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	3 / 12 (25.00%)	3 / 13 (23.08%)
occurrences (all)	0	3	4
Haemoglobin decreased			

subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Lipase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Lymphocyte count decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	4	1
Neutrophil count decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	2	1
Platelet count decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	2	0	1
Prothrombin time prolonged			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Prothrombin time shortened			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Troponin increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Tumour marker increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	1 / 5 (20.00%)	2 / 12 (16.67%)	3 / 13 (23.08%)
occurrences (all)	1	2	3
White blood cell count decreased			
subjects affected / exposed	1 / 5 (20.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	1	2	0
White blood cell count increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural			

complications			
Contusion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hand fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Muscle injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Cardiac disorders			
Left ventricular dysfunction			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Pericardial effusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	1 / 13 (7.69%)
occurrences (all)	0	2	1
Dysaesthesia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Headache			

subjects affected / exposed	3 / 5 (60.00%)	4 / 12 (33.33%)	1 / 13 (7.69%)
occurrences (all)	3	8	1
Hypertonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Lethargy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 5 (20.00%)	3 / 12 (25.00%)	3 / 13 (23.08%)
occurrences (all)	2	4	5
Bone marrow disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Leukocytosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	2 / 13 (15.38%)
occurrences (all)	1	0	2

Lymphadenopathy			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 12 (8.33%)	3 / 13 (23.08%)
occurrences (all)	14	2	6
Thrombocytopenia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	2 / 13 (15.38%)
occurrences (all)	0	3	2
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
External ear inflammation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Hypoacusis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Eye swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Ocular discomfort			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 5 (20.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	5	1	0
Abdominal pain			

subjects affected / exposed	3 / 5 (60.00%)	6 / 12 (50.00%)	6 / 13 (46.15%)
occurrences (all)	6	17	12
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Anal fissure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Anal incontinence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Anal inflammation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	3 / 5 (60.00%)	2 / 12 (16.67%)	2 / 13 (15.38%)
occurrences (all)	4	3	2
Diarrhoea			
subjects affected / exposed	4 / 5 (80.00%)	12 / 12 (100.00%)	10 / 13 (76.92%)
occurrences (all)	11	30	21
Dyspepsia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Flatulence			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Gastrointestinal disorder			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Gingival pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Haematemesis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Haematochezia			

subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Nausea			
subjects affected / exposed	2 / 5 (40.00%)	8 / 12 (66.67%)	10 / 13 (76.92%)
occurrences (all)	3	8	20
Odynophagia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	5	0
Stomatitis			
subjects affected / exposed	1 / 5 (20.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	4 / 5 (80.00%)	10 / 12 (83.33%)	13 / 13 (100.00%)
occurrences (all)	11	25	33
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Alopecia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Eczema			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	2 / 13 (15.38%)
occurrences (all)	0	2	2
Rash			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	5	0
Rash erythematous			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 5 (0.00%)	3 / 12 (25.00%)	1 / 13 (7.69%)
occurrences (all)	0	3	1
Skin exfoliation			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Skin irritation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Swelling face			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Micturition urgency			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Delayed puberty			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	2	1
Back pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Bone pain			
subjects affected / exposed	1 / 5 (20.00%)	2 / 12 (16.67%)	0 / 13 (0.00%)
occurrences (all)	1	3	0
Groin pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Joint range of motion decreased			

subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	1 / 13 (7.69%)
occurrences (all)	0	4	1
Neck pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	1 / 5 (20.00%)	5 / 12 (41.67%)	0 / 13 (0.00%)
occurrences (all)	1	6	0
Torticollis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bacterial vulvovaginitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	0	3	1
Device related infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Ear infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Genital candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Human herpesvirus 6 infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	1 / 5 (20.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	5	1	0
Molluscum contagiosum			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Mycoplasma infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	2 / 5 (40.00%)	1 / 12 (8.33%)	2 / 13 (15.38%)
occurrences (all)	6	1	3
Oral herpes			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	1 / 13 (7.69%)
occurrences (all)	0	2	1

Sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	2 / 12 (16.67%)	3 / 13 (23.08%)
occurrences (all)	2	3	8
Urinary tract infection			
subjects affected / exposed	1 / 5 (20.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	3	1	0
Varicella			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Wound infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 5 (60.00%)	4 / 12 (33.33%)	0 / 13 (0.00%)
occurrences (all)	3	5	0
Dehydration			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	3	0	0
Electrolyte imbalance			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Fluid retention			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	3
Hypermagnesaemia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	1	2	1
Hypokalaemia			
subjects affected / exposed	3 / 5 (60.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	6	2	0
Hypomagnesaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	2 / 5 (40.00%)	1 / 12 (8.33%)	1 / 13 (7.69%)
occurrences (all)	2	2	1
Hypophosphataemia			
subjects affected / exposed	2 / 5 (40.00%)	2 / 12 (16.67%)	1 / 13 (7.69%)
occurrences (all)	4	2	1
Obesity			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 13 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Ceritinib@560 mg/m2	Ceritinib@320 mg/m2	Ceritinib@400 mg/m2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	4 / 4 (100.00%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			

Embolism			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pallor			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	3
Fatigue			
subjects affected / exposed	2 / 2 (100.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	2	2	0
Gait disturbance			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			

subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 2 (0.00%)	2 / 4 (50.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Pyrexia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Secretion discharge			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ulcer			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Dyspnoea exertional			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Emphysema			

subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pleuritic pain			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Irritability			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Mental disorder			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Sleep disorder			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 2 (100.00%)	3 / 4 (75.00%)	2 / 5 (40.00%)
occurrences (all)	2	5	2
Amylase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 2 (100.00%)	3 / 4 (75.00%)	1 / 5 (20.00%)
occurrences (all)	2	3	1
Blood albumin decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood creatine increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			

subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Blood magnesium increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 2 (50.00%)	2 / 4 (50.00%)	3 / 5 (60.00%)
occurrences (all)	1	2	3
Haemoglobin decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lipase increased			

subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Platelet count decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Prothrombin time prolonged			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Prothrombin time shortened			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Troponin increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tumour marker increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
White blood cell count decreased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
White blood cell count increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			

subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle injury			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Left ventricular dysfunction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Headache			

subjects affected / exposed	0 / 2 (0.00%)	2 / 4 (50.00%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Hypertonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Neuralgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 2 (50.00%)	3 / 4 (75.00%)	0 / 5 (0.00%)
occurrences (all)	1	5	0
Bone marrow disorder			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Leukopenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Lymphadenopathy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	2 / 2 (100.00%)	2 / 4 (50.00%)	0 / 5 (0.00%)
occurrences (all)	2	3	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
External ear inflammation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye swelling			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ocular discomfort			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			

subjects affected / exposed	2 / 2 (100.00%)	2 / 4 (50.00%)	1 / 5 (20.00%)
occurrences (all)	2	7	1
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Anal fissure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Anal inflammation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 2 (50.00%)	1 / 4 (25.00%)	1 / 5 (20.00%)
occurrences (all)	2	2	1
Diarrhoea			
subjects affected / exposed	2 / 2 (100.00%)	2 / 4 (50.00%)	3 / 5 (60.00%)
occurrences (all)	4	7	3
Dyspepsia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gastrointestinal disorder			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haematemesis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haematochezia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 2 (50.00%)	2 / 4 (50.00%)	3 / 5 (60.00%)
occurrences (all)	3	4	3
Odynophagia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	2 / 2 (100.00%)	4 / 4 (100.00%)	3 / 5 (60.00%)
occurrences (all)	4	7	3
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Alopecia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eczema			

subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Rash			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Skin lesion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Swelling face			

subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Delayed puberty			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Groin pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Joint range of motion decreased			

subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Torticollis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacterial vulvovaginitis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Ear infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Genital candidiasis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Human herpesvirus 6 infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Molluscum contagiosum			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Mycoplasma infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Oral herpes			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Sinusitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Varicella			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Wound infection			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 2 (100.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	3	1	0
Dehydration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Electrolyte imbalance			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypermagnesaemia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Hypomagnesaemia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Obesity			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Ceritinib@500 mg/m2	Fasted+Fed All Subjects	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 42 (100.00%)	83 / 83 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Tumour pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Vascular disorders			

Embolism			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Haematoma			
subjects affected / exposed	0 / 42 (0.00%)	2 / 83 (2.41%)	
occurrences (all)	0	2	
Hypertension			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Hypotension			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Pallor			
subjects affected / exposed	3 / 42 (7.14%)	3 / 83 (3.61%)	
occurrences (all)	3	3	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	9 / 42 (21.43%)	10 / 83 (12.05%)	
occurrences (all)	11	12	
Catheter site pain			
subjects affected / exposed	0 / 42 (0.00%)	3 / 83 (3.61%)	
occurrences (all)	0	3	
Chest pain			
subjects affected / exposed	6 / 42 (14.29%)	11 / 83 (13.25%)	
occurrences (all)	6	13	
Fatigue			
subjects affected / exposed	9 / 42 (21.43%)	22 / 83 (26.51%)	
occurrences (all)	14	31	
Gait disturbance			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
General physical health deterioration			
subjects affected / exposed	0 / 42 (0.00%)	2 / 83 (2.41%)	
occurrences (all)	0	2	
Influenza like illness			

subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	2	3	
Malaise			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Oedema peripheral			
subjects affected / exposed	2 / 42 (4.76%)	4 / 83 (4.82%)	
occurrences (all)	3	5	
Pyrexia			
subjects affected / exposed	20 / 42 (47.62%)	35 / 83 (42.17%)	
occurrences (all)	49	77	
Secretion discharge			
subjects affected / exposed	3 / 42 (7.14%)	3 / 83 (3.61%)	
occurrences (all)	3	3	
Ulcer			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	8 / 42 (19.05%)	13 / 83 (15.66%)	
occurrences (all)	16	27	
Dyspnoea			
subjects affected / exposed	4 / 42 (9.52%)	6 / 83 (7.23%)	
occurrences (all)	5	7	
Dyspnoea exertional			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Emphysema			

subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	2 / 42 (4.76%)	4 / 83 (4.82%)	
occurrences (all)	3	5	
Nasal congestion			
subjects affected / exposed	1 / 42 (2.38%)	3 / 83 (3.61%)	
occurrences (all)	1	3	
Oropharyngeal pain			
subjects affected / exposed	3 / 42 (7.14%)	5 / 83 (6.02%)	
occurrences (all)	4	7	
Pleural effusion			
subjects affected / exposed	2 / 42 (4.76%)	3 / 83 (3.61%)	
occurrences (all)	2	3	
Pleuritic pain			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Rhinorrhoea			
subjects affected / exposed	3 / 42 (7.14%)	4 / 83 (4.82%)	
occurrences (all)	5	8	
Upper-airway cough syndrome			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 42 (2.38%)	3 / 83 (3.61%)	
occurrences (all)	2	4	
Irritability			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Mental disorder			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Restlessness			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	

Sleep disorder			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	30 / 42 (71.43%)	54 / 83 (65.06%)	
occurrences (all)	72	115	
Amylase increased			
subjects affected / exposed	3 / 42 (7.14%)	6 / 83 (7.23%)	
occurrences (all)	5	11	
Aspartate aminotransferase increased			
subjects affected / exposed	28 / 42 (66.67%)	48 / 83 (57.83%)	
occurrences (all)	74	114	
Blood albumin decreased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 42 (9.52%)	10 / 83 (12.05%)	
occurrences (all)	4	10	
Blood bicarbonate decreased			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Blood bilirubin increased			
subjects affected / exposed	5 / 42 (11.90%)	8 / 83 (9.64%)	
occurrences (all)	9	12	
Blood creatine increased			
subjects affected / exposed	3 / 42 (7.14%)	3 / 83 (3.61%)	
occurrences (all)	4	4	
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Blood creatinine increased			

subjects affected / exposed	11 / 42 (26.19%)	18 / 83 (21.69%)	
occurrences (all)	17	28	
Blood glucose increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Blood lactate dehydrogenase increased			
subjects affected / exposed	5 / 42 (11.90%)	11 / 83 (13.25%)	
occurrences (all)	5	13	
Blood magnesium increased			
subjects affected / exposed	3 / 42 (7.14%)	3 / 83 (3.61%)	
occurrences (all)	4	4	
Blood pressure increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Blood urea increased			
subjects affected / exposed	3 / 42 (7.14%)	3 / 83 (3.61%)	
occurrences (all)	6	6	
Blood uric acid increased			
subjects affected / exposed	3 / 42 (7.14%)	4 / 83 (4.82%)	
occurrences (all)	3	4	
C-reactive protein increased			
subjects affected / exposed	4 / 42 (9.52%)	6 / 83 (7.23%)	
occurrences (all)	4	6	
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 42 (2.38%)	3 / 83 (3.61%)	
occurrences (all)	1	3	
Gamma-glutamyltransferase increased			
subjects affected / exposed	14 / 42 (33.33%)	26 / 83 (31.33%)	
occurrences (all)	21	34	
Haemoglobin decreased			
subjects affected / exposed	2 / 42 (4.76%)	3 / 83 (3.61%)	
occurrences (all)	2	3	
Lipase increased			

subjects affected / exposed	6 / 42 (14.29%)	9 / 83 (10.84%)	
occurrences (all)	9	12	
Lymphocyte count decreased			
subjects affected / exposed	2 / 42 (4.76%)	4 / 83 (4.82%)	
occurrences (all)	5	10	
Neutrophil count decreased			
subjects affected / exposed	2 / 42 (4.76%)	5 / 83 (6.02%)	
occurrences (all)	2	6	
Platelet count decreased			
subjects affected / exposed	1 / 42 (2.38%)	3 / 83 (3.61%)	
occurrences (all)	1	4	
Prothrombin time prolonged			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Prothrombin time shortened			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Troponin increased			
subjects affected / exposed	0 / 42 (0.00%)	2 / 83 (2.41%)	
occurrences (all)	0	2	
Tumour marker increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	6 / 42 (14.29%)	13 / 83 (15.66%)	
occurrences (all)	7	14	
White blood cell count decreased			
subjects affected / exposed	1 / 42 (2.38%)	4 / 83 (4.82%)	
occurrences (all)	1	5	
White blood cell count increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Contusion			

subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Hand fracture			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Muscle injury			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Cardiac disorders			
Left ventricular dysfunction			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Pericardial effusion			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Tachycardia			
subjects affected / exposed	2 / 42 (4.76%)	4 / 83 (4.82%)	
occurrences (all)	2	4	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 42 (4.76%)	5 / 83 (6.02%)	
occurrences (all)	3	6	
Dysaesthesia			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Dysgeusia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Headache			

subjects affected / exposed	8 / 42 (19.05%)	19 / 83 (22.89%)	
occurrences (all)	20	35	
Hypertonia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	2	
Lethargy			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Neuralgia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	1 / 42 (2.38%)	3 / 83 (3.61%)	
occurrences (all)	1	3	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 42 (26.19%)	22 / 83 (26.51%)	
occurrences (all)	14	31	
Bone marrow disorder			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Leukocytosis			
subjects affected / exposed	0 / 42 (0.00%)	2 / 83 (2.41%)	
occurrences (all)	0	2	
Leukopenia			
subjects affected / exposed	5 / 42 (11.90%)	8 / 83 (9.64%)	
occurrences (all)	7	10	

Lymphadenopathy			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Neutropenia			
subjects affected / exposed	5 / 42 (11.90%)	10 / 83 (12.05%)	
occurrences (all)	23	45	
Thrombocytopenia			
subjects affected / exposed	11 / 42 (26.19%)	19 / 83 (22.89%)	
occurrences (all)	16	26	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	3 / 42 (7.14%)	4 / 83 (4.82%)	
occurrences (all)	4	5	
External ear inflammation			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Hypoacusis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Eye swelling			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Ocular discomfort			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 42 (0.00%)	2 / 83 (2.41%)	
occurrences (all)	0	6	
Abdominal pain			

subjects affected / exposed	22 / 42 (52.38%)	42 / 83 (50.60%)	
occurrences (all)	56	101	
Abdominal pain upper			
subjects affected / exposed	3 / 42 (7.14%)	7 / 83 (8.43%)	
occurrences (all)	3	8	
Anal fissure			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Anal incontinence			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Anal inflammation			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	4 / 42 (9.52%)	14 / 83 (16.87%)	
occurrences (all)	4	18	
Diarrhoea			
subjects affected / exposed	32 / 42 (76.19%)	65 / 83 (78.31%)	
occurrences (all)	93	169	
Dyspepsia			
subjects affected / exposed	4 / 42 (9.52%)	6 / 83 (7.23%)	
occurrences (all)	6	8	
Flatulence			
subjects affected / exposed	1 / 42 (2.38%)	4 / 83 (4.82%)	
occurrences (all)	1	4	
Gastrointestinal disorder			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Gingival pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Haematemesis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Haematochezia			

subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	21 / 42 (50.00%)	47 / 83 (56.63%)	
occurrences (all)	32	73	
Odynophagia			
subjects affected / exposed	3 / 42 (7.14%)	3 / 83 (3.61%)	
occurrences (all)	3	3	
Proctalgia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Rectal haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	5	
Stomatitis			
subjects affected / exposed	3 / 42 (7.14%)	6 / 83 (7.23%)	
occurrences (all)	3	6	
Vomiting			
subjects affected / exposed	36 / 42 (85.71%)	72 / 83 (86.75%)	
occurrences (all)	72	155	
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	2	4	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 42 (4.76%)	4 / 83 (4.82%)	
occurrences (all)	2	4	
Alopecia			
subjects affected / exposed	1 / 42 (2.38%)	3 / 83 (3.61%)	
occurrences (all)	1	3	
Eczema			

subjects affected / exposed	3 / 42 (7.14%)	3 / 83 (3.61%)	
occurrences (all)	5	5	
Erythema			
subjects affected / exposed	4 / 42 (9.52%)	4 / 83 (4.82%)	
occurrences (all)	6	6	
Night sweats			
subjects affected / exposed	3 / 42 (7.14%)	3 / 83 (3.61%)	
occurrences (all)	3	3	
Pain of skin			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	1 / 42 (2.38%)	7 / 83 (8.43%)	
occurrences (all)	1	7	
Rash			
subjects affected / exposed	6 / 42 (14.29%)	8 / 83 (9.64%)	
occurrences (all)	10	15	
Rash erythematous			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Rash maculo-papular			
subjects affected / exposed	1 / 42 (2.38%)	5 / 83 (6.02%)	
occurrences (all)	1	5	
Skin exfoliation			
subjects affected / exposed	0 / 42 (0.00%)	2 / 83 (2.41%)	
occurrences (all)	0	2	
Skin hyperpigmentation			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Skin irritation			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Skin lesion			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Swelling face			

subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 42 (0.00%)	2 / 83 (2.41%)	
occurrences (all)	0	2	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	2	
Micturition urgency			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Endocrine disorders			
Delayed puberty			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Hypothyroidism			
subjects affected / exposed	0 / 42 (0.00%)	2 / 83 (2.41%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 42 (2.38%)	4 / 83 (4.82%)	
occurrences (all)	1	5	
Back pain			
subjects affected / exposed	4 / 42 (9.52%)	6 / 83 (7.23%)	
occurrences (all)	4	6	
Bone pain			
subjects affected / exposed	2 / 42 (4.76%)	6 / 83 (7.23%)	
occurrences (all)	2	7	
Groin pain			
subjects affected / exposed	1 / 42 (2.38%)	3 / 83 (3.61%)	
occurrences (all)	1	3	
Joint range of motion decreased			

subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Muscular weakness			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 42 (4.76%)	3 / 83 (3.61%)	
occurrences (all)	2	3	
Musculoskeletal pain			
subjects affected / exposed	2 / 42 (4.76%)	5 / 83 (6.02%)	
occurrences (all)	3	8	
Neck pain			
subjects affected / exposed	2 / 42 (4.76%)	3 / 83 (3.61%)	
occurrences (all)	2	4	
Pain in extremity			
subjects affected / exposed	5 / 42 (11.90%)	13 / 83 (15.66%)	
occurrences (all)	5	14	
Torticollis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Infections and infestations			
Bacterial vulvovaginitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	2 / 42 (4.76%)	3 / 83 (3.61%)	
occurrences (all)	2	3	
Conjunctivitis			
subjects affected / exposed	3 / 42 (7.14%)	5 / 83 (6.02%)	
occurrences (all)	3	7	
Device related infection			
subjects affected / exposed	3 / 42 (7.14%)	3 / 83 (3.61%)	
occurrences (all)	5	5	

Ear infection			
subjects affected / exposed	2 / 42 (4.76%)	3 / 83 (3.61%)	
occurrences (all)	2	3	
Gastroenteritis			
subjects affected / exposed	4 / 42 (9.52%)	4 / 83 (4.82%)	
occurrences (all)	5	5	
Genital candidiasis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	2	
Human herpesvirus 6 infection			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	2 / 42 (4.76%)	4 / 83 (4.82%)	
occurrences (all)	2	8	
Molluscum contagiosum			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Mycoplasma infection			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	4 / 42 (9.52%)	10 / 83 (12.05%)	
occurrences (all)	4	16	
Oral herpes			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Pneumonia			
subjects affected / exposed	3 / 42 (7.14%)	3 / 83 (3.61%)	
occurrences (all)	5	5	
Rhinitis			
subjects affected / exposed	8 / 42 (19.05%)	11 / 83 (13.25%)	
occurrences (all)	12	15	

Sinusitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	8 / 42 (19.05%)	15 / 83 (18.07%)	
occurrences (all)	20	34	
Urinary tract infection			
subjects affected / exposed	0 / 42 (0.00%)	3 / 83 (3.61%)	
occurrences (all)	0	5	
Varicella			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Viral infection			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Wound infection			
subjects affected / exposed	0 / 42 (0.00%)	2 / 83 (2.41%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	16 / 42 (38.10%)	26 / 83 (31.33%)	
occurrences (all)	17	29	
Dehydration			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	3	
Electrolyte imbalance			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	2	
Fluid retention			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Hyperkalaemia			
subjects affected / exposed	1 / 42 (2.38%)	2 / 83 (2.41%)	
occurrences (all)	1	4	
Hypermagnesaemia			

subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Hypoalbuminaemia			
subjects affected / exposed	4 / 42 (9.52%)	5 / 83 (6.02%)	
occurrences (all)	4	5	
Hypocalcaemia			
subjects affected / exposed	1 / 42 (2.38%)	4 / 83 (4.82%)	
occurrences (all)	1	5	
Hypokalaemia			
subjects affected / exposed	7 / 42 (16.67%)	12 / 83 (14.46%)	
occurrences (all)	9	19	
Hypomagnesaemia			
subjects affected / exposed	3 / 42 (7.14%)	5 / 83 (6.02%)	
occurrences (all)	4	6	
Hyponatraemia			
subjects affected / exposed	3 / 42 (7.14%)	7 / 83 (8.43%)	
occurrences (all)	3	8	
Hypophosphataemia			
subjects affected / exposed	2 / 42 (4.76%)	8 / 83 (9.64%)	
occurrences (all)	4	12	
Obesity			
subjects affected / exposed	0 / 42 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 March 2013	The following changes were requested by a Health Authority: In order to clarify the eligibility criteria in the protocol, a detailed definition of "a genetic alteration of ALK" has been added to the inclusion criteria. Due to the observation that ceritinib use is sometimes associated with hypophosphatemia, patients with abnormalities of phosphate as well as potassium, calcium or magnesium > CTCAE grade 1 are excluded from the study. The table defining dose-limiting toxicities was reorganized to clarify that any adverse event of CTCAE grade 3 or higher is a DLT, except as noted in the table. Due to the possibility that taking ceritinib mixed with a small amount of food may affect its bioavailability, the protocol has been modified to require that all patients take ceritinib with a small amount of food. If patients can swallow intact capsules, they must eat 1-2 tablespoons (15-30 mL) of food, such as apple sauce or non-fat yogurt at the time that they take ceritinib. If patients open the capsules, the contents are mixed with a food carrier, such as apple sauce or non-fat yogurt (or other carriers as defined in the separate instructions for patients who cannot swallow capsules). This prevented unexpected differences in bioavailability between those patients who swallow intact capsules and those who opened the capsules.
27 September 2013	The following changes were requested by Health Authorities: To address the management of QTc prolongation separately from the broader array of DLTs a specific approach including a detailed monitoring plan, need for physician evaluation, and recommendations for dose reduction or permanent discontinuation. Cases of pneumonitis/interstitial lung disease (ILD) have been reported with ceritinib in patients treated at the 750 mg dose level. Most cases improved or resolved with interruption of ceritinib and treatment with antibiotics and/or steroids. Fatal outcome of treatment-related pneumonitis was reported. Exclusion criteria, the definition of dose limiting toxicity, and the guidance for dose modification have been amended to address this newly observed risk
15 July 2014	The protocol was modified to include a fed state (low-fat light snack) dose escalation part following the determination of the fasted MTD/RDE. Further expansion at the fed MTD/RDE was allowed if the safety, PK or efficacy suggested that administering ceritinib with food was preferred. The age range in the inclusion criteria has been changed to 'up to 18' to make it clear that patients were eligible until they turn18 years of age.
13 May 2015	A consistent approach was implemented across ongoing studies with ceritinib to monitor and manage safety signals identified as the clinical experience with ceritinib has grown. Specifically, changes were made that addressed hepatic toxicity, pancreatitis and pneumonitis.
26 February 2016	The primary purpose of this amendment was to clarify the ceritinib dose modification recommendations, the guidelines for follow up of toxicities to ceritinib (including follow up evaluations for hepatic toxicities and work up guidelines for potential drug induced liver injury (DILI) cases) and the use of concomitant medications in order to optimize the patient safety. Furthermore, this amendment provided updated parameters for study visits for patients who were on study drug for more than 14 cycles. This was done in an effort to decrease the burden on the patient after a set number of cycles on study drug. In addition, the definition of highly effective contraception and the time period for using it have been updated, as well as the reporting period for pregnancy that has been revised to 3 months.

30 September 2016	The primary purpose of this amendment was to revise the dose reduction steps for The primary purpose of this amendment was to revise the dose reduction steps for ceritinib. Considering the recommended doses established for fed and fasted state were similar, the dose reduction schedule was revised to be applicable for both states. In addition, the schedule of assessments was revised to reduce frequency of on-site visits after cycle 16: on-site visits on day 1 of odd numbered cycles are replaced by phone calls and local laboratory tests for safety assessments Moreover, the pre-dose PK sample and the post-dose ECGs collection at Cycle 1 Day 1 have been removed in the expansion phase as they were no longer required at this time point as no correlation is planned in the expansion.
24 January 2017	The primary purpose of this amendment was to address Health Authorities' concerns regarding the cardiac safety monitoring conducted until Cycle 6 only and not afterwards for patient who remain on treatment, and the recent changes at Cycle 1 Day 1 (ECG monitoring at 4 and 6 hours post first dose of study drug) for the patients to be treated in the expansion phase of the study. Novartis decided to strengthen the cardiac safety monitoring: all patients were monitored with an ECG at Cycle 1 Day 1 (4-h post dose and 6-h post dose), and at each first day of every cycle of treatment. The ECG collection was expanded throughout the entire treatment duration. This was done in alignment with the ceritinib cardiovascular safety monitoring recommendations. In addition, guidelines for dose modification in case of Grade 3 transaminases elevation are clarified, allowing patients to stay in the study in case of a re-occurrence of Grade 3 ALT or AST elevation after a dose reduction as allowed across the ceritinib development program in adults patients. This was to avoid unnecessary withdrawal of patients who continued to derive clinical benefit from ceritinib. The guidelines in relation to concomitant medications use are also clarified to optimize the patient's safety. Moreover, ALK status inclusion criterion was clarified and it was specified that 15% threshold for rearrangement was applicable only when assessed by FISH. Furthermore the ALK tyrosine kinase domain (TKD) mutation inclusion criterion was simplified.
18 May 2018	The main purpose of this global amendment was to allow patients who were still deriving clinical benefit from study treatment as per the investigator to be transitioned to a separate rollover study or another option for continued treatment with ceritinib (i.e. managed access program), as soon as they become available. The end of study would occur once: All patients have discontinued study treatment and completed the required Study Evaluation Completion follow-up visit, or All patients have died, been lost to follow-up, have withdrawn consent, or the last patient has been enrolled into a separate rollover study (or other option for continued study treatment), whichever comes first As per original protocol, a primary analysis and CSR were planned after all patients had completed at least 6 cycles of treatment or discontinued the study. Given interim data presented previously, and at the time of this amendment all patients already completed at least 6 cycles of treatment and were allowed to transition into a separate rollover study (or other options for continued study treatment access), a single final analysis/CSR was planned once the end of study criteria are met.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Notes: