Clinical trial results:
A Phase 3, Interventional, Double-Blind, Placebo-Controlled study to assess the safety and efficacy of DCC-2618 in Patients with Advanced Gastrointestinal Stromal Tumors who have received treatment with Prior Anticancer Therapies

Summary

EudraCT number	2017-002446-76
Trial protocol	GB DE FR NL BE ES PL FI IT
Global end of trial date	11 May 2022

Results information

Result version number	v1 (current)
This version publication date	23 June 2023
First version publication date	23 June 2023

Trial information

Trial identification

Sponsor protocol code	DCC-2618-03-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03353653
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Deciphera Pharmaceuticals, LLC
Sponsor organisation address	200 Smith Street , Waltham, MA , United States, 02451
Public contact	Priyanka Kamath, Deciphera Pharmaceuticals, LLC, 001 7812096400, clinicaltrials@deciphera.com
Scientific contact	Priyanka Kamath, Deciphera Pharmaceuticals, LLC, 001 7812096400, clinicaltrials@deciphera.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	13 November 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 May 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the efficacy (progression-free survival [PFS]) of DCC-2618 (ripretinib) by independent radiologic review in patients with advanced gastrointestinal stromal tumors (GIST) who have received prior therapies

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH), Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which the study was conducted
All study subjects were required to read and sign an Informed Consent Form
Subjects were randomized to either ripretinib (DCC-2618) or placebo and best supportive care in both arms

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 January 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Singapore: 6
Country: Number of subjects enrolled	United States: 60
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Italy: 2
Worldwide total number of subjects	129
EEA total number of subjects	47

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	79
From 65 to 84 years	50
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

129 participants were enrolled and randomized in the double-blind period in the ITT population. Of the 129 participants randomized in the double-blind period (ITT population), 85 participants were randomized to the ripretinib arm and 44 participants were randomized to the placebo arm. One participant was randomized to placebo but was never treated

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ripretinib

Arm description:

DCC-2618 (ripretinib) was supplied as 50 mg strength tablets for oral administration in repeated 28-day cycles. Patients were instructed to take their assigned dose at the same time each day. If a patient dose escalates to 150 mg BID, patients were instructed take the study drug twice a day, at least 6 hours apart, and at the same time each day. On days of scheduled visits, the dose of study drug must be administered at the site after pre-dose assessments have been completed.

Arm type	Experimental
Investigational medicinal product name	DCC-2618
Investigational medicinal product code	
Other name	Ripretinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

DCC-2618 was supplied as 50 mg strength tablets for oral administration. Patients received 150 mg QD or if patient dose escalated 150 mg BID. Patients were instructed to swallow the tablets whole. Tablets must not be crushed, chewed, or dissolved in liquid or food

Arm title	Placebo

Arm description:

Placebo supplied as identically sized and color-matched tablets

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

Dosage and administration details:

Placebo supplied as identically sized and color-matched tablets

Number of subjects in period 1	Ripretinib	Placebo
Started	85	44
Completed	64	30
Not completed	21	14
Clinical progression	4	3
termination of study by sponsor	1	-
Physician decision	1	1
Consent withdrawn by subject	3	1
Adverse event, non-fatal	3	2
progressive disease by Investigator assessment	3	-
Death	4	4
progressive disease by independent radiologist	1	2
not specified	1	-
Not treated	-	1

Period 2	
Period 2 title	Open label period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	No
Arm title	crossed-over to ripretinib

Arm description:

participants who received placebo in the double-blind period crossed-over to receive ripretinib 150 mg QD in the open-label period

Arm type	Experimental
Investigational medicinal product name	DCC-2618
Investigational medicinal product code	
Other name	Ripretinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

DCC-2618 was supplied as 50 mg strength tablets for oral administration. Patients received 150 mg QD or if patient dose escalated 150 mg BID. Patients were instructed to swallow the tablets whole. Tablets must not be crushed, chewed, or dissolved in liquid or food

Arm title	Ripretinib 150 mg QD

Arm description:

Ripretinib 150 mg QD (originally received ripretinib in double-blind period)

Arm type	Experimental

Investigational medicinal product name	DCC-2618
Investigational medicinal product code	
Other name	Ripretinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

DCC-2618 was supplied as 50 mg strength tablets for oral administration. Patients received 150 mg QD or if patient dose escalated 150 mg BID. Patients were instructed to swallow the tablets whole. Tablets must not be crushed, chewed, or dissolved in liquid or food

Arm title	Ripretinib 150 mg BID

Arm description:

participants who dose escalated and received ripretinib 150 mg BID in the open-label period

Arm type	Experimental
Investigational medicinal product name	DCC-2618
Investigational medicinal product code	
Other name	Ripretinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

DCC-2618 was supplied as 50 mg strength tablets for oral administration. Patients received 150 mg QD or if patient dose escalated 150 mg BID. Patients were instructed to swallow the tablets whole. Tablets must not be crushed, chewed, or dissolved in liquid or food

Number of subjects in period 2	crossed-over to ripretinib	Ripretinib 150 mg QD	Ripretinib 150 mg BID
Started	30	18	62
Completed	16	0	0
Not completed	14	18	62
Clinical progression	4	2	11
termination of study by sponsor	2	2	2
Consent withdrawn by subject	2	3	3
Physician decision	-	1	3
Adverse event, non-fatal	1	-	9
progressive disease by Investigator assessment	5	3	28
Death	-	1	3
progressive disease by independent radiologist	-	5	1
not specified	-	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Ripretinib
Reporting group description:	
DCC-2618 (ripretinib) was supplied as 50 mg strength tablets for oral administration in repeated 28-day cycles. Patients were instructed to take their assigned dose at the same time each day. If a patient dose escalates to 150 mg BID, patients were instructed take the study drug twice a day, at least 6 hours apart, and at the same time each day. On days of scheduled visits, the dose of study drug must be administered at the site after pre-dose assessments have been completed.	
Reporting group title	Placebo
Reporting group description:	
Placebo supplied as identically sized and color-matched tablets	

Reporting group values	Ripretinib	Placebo	Total
Number of subjects	85	44	129
Age categorical			
Age at Informed Consent			
Units: Subjects			
Adults (18-64 years)	57	22	79
85 years and over	28	22	50
Age continuous			
Age at Informed Consent			
Units: years			
arithmetic mean	59.1	62.0	
standard deviation	± 10.84	± 13.50	-
Gender categorical			
Units: Subjects			
Female	38	18	56
Male	47	26	73
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	4	5	9
Black or African American	8	2	10
Native Hawaiian or Other Pacific Islander	0	0	0
White	64	33	97
Not Reported	8	4	12
Other	1	0	1
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	76	38	114
Not Reported	5	5	10
Unknown	3	1	4
ECOG Score at Screening			
Units: Subjects			
Score = 0	37	17	54
Score = 1	40	24	64

Score = 2	8	3	11
Number of Prior Systemic Anticancer Treatments Units: Subjects			
Number = 3	54	27	81
Number >= 4	31	17	48
Height Units: cm			
arithmetic mean	169.7	169.7	
standard deviation	± 10.38	± 11.72	-
Weight Units: kg			
arithmetic mean	73.9	71.4	
standard deviation	± 19.02	± 18.04	-
Body Mass Index Units: kg/m^2			
arithmetic mean	25.6	24.5	
standard deviation	± 6.22	± 5.08	-

Subject analysis sets

Subject analysis set title	ITT Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients who signed the informed consent and were randomised.

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients who received at least 1 dose of study drug.

Subject analysis set title	PK Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All randomised subjects who received at least 1 dose of DCC-2618 and had at least 1 non-missing PK concentration in plasma reported for DCC-2618 or DP-5439.

Subject analysis set title	PP Population
Subject analysis set type	Per protocol

Subject analysis set description:

Patients in the ITT population who do not have protocol violations that are expected to compromise the efficacy and/or safety assessments.

Reporting group values	ITT Population	Safety Population	PK Population
Number of subjects	129	128	114
Age categorical			
Age at Informed Consent			
Units: Subjects			
Adults (18-64 years)	79	79	
85 years and over	50	49	
Age continuous			
Age at Informed Consent			
Units: years			
arithmetic mean	60.1	60.0	
standard deviation	± 11.84	± 11.78	±

Gender categorical Units: Subjects			
Female	56	56	
Male	73	72	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	9	9	
Black or African American	10	10	
Native Hawaiian or Other Pacific Islander	0	0	
White	97	96	
Not Reported	12	12	
Other	1	1	
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	114	113	
Not Reported	10	10	
Unknown	4	4	
ECOG Score at Screening Units: Subjects			
Score = 0	54	54	
Score = 1	64	63	
Score = 2	11	11	
Number of Prior Systemic Anticancer Treatments Units: Subjects			
Number = 3	81	81	
Number >= 4	48	47	
Height Units: cm			
arithmetic mean	169.7	169.7	
standard deviation	± 10.80	± 10.80	±
Weight Units: kg			
arithmetic mean	73.1	73.1	
standard deviation	± 18.67	± 18.67	±
Body Mass Index Units: kg/m^2			
arithmetic mean	25.3	25.3	
standard deviation	± 5.87	± 5.87	±

Reporting group values	PP Population		
Number of subjects	70		
Age categorical			
Age at Informed Consent			
Units: Subjects			
Adults (18-64 years) 85 years and over			

Age continuous			
Age at Informed Consent			
Units: years arithmetic mean standard deviation	±		
Gender categorical Units: Subjects			
Female Male			
Race Units: Subjects			
American Indian or Alaska Native Asian Black or African American Native Hawaiian or Other Pacific Islander White Not Reported Other			
Ethnicity Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Not Reported Unknown			
ECOG Score at Screening Units: Subjects			
Score = 0 Score = 1 Score = 2			
Number of Prior Systemic Anticancer Treatments Units: Subjects			
Number = 3 Number >= 4			
Height Units: cm arithmetic mean standard deviation	±		
Weight Units: kg arithmetic mean standard deviation	±		
Body Mass Index Units: kg/m^2 arithmetic mean standard deviation	±		

End points

End points reporting groups

Reporting group title	Ripretinib
Reporting group description:	
DCC-2618 (ripretinib) was supplied as 50 mg strength tablets for oral administration in repeated 28-day cycles. Patients were instructed to take their assigned dose at the same time each day. If a patient dose escalates to 150 mg BID, patients were instructed take the study drug twice a day, at least 6 hours apart, and at the same time each day. On days of scheduled visits, the dose of study drug must be administered at the site after pre-dose assessments have been completed.	
Reporting group title	Placebo
Reporting group description:	
Placebo supplied as identically sized and color-matched tablets	
Reporting group title	crossed-over to ripretinib
Reporting group description:	
participants who received placebo in the double-blind period crossed-over to receive ripretinib 150 mg QD in the open-label period	
Reporting group title	Ripretinib 150 mg QD
Reporting group description:	
Ripretinib 150 mg QD (originally received ripretinib in double-blind period)	
Reporting group title	Ripretinib 150 mg BID
Reporting group description:	
participants who dose escalated and received ripretinib 150 mg BID in the open-label period	
Subject analysis set title	ITT Population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients who signed the informed consent and were randomised.	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received at least 1 dose of study drug.	
Subject analysis set title	PK Population
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All randomised subjects who received at least 1 dose of DCC-2618 and had at least 1 non-missing PK concentration in plasma reported for DCC-2618 or DP-5439.	
Subject analysis set title	PP Population
Subject analysis set type	Per protocol
Subject analysis set description:	
Patients in the ITT population who do not have protocol violations that are expected to compromise the efficacy and/or safety assessments.	

Primary: Progression Free Survival

End point title	Progression Free Survival
End point description:	
The interval between the date of randomization and the earliest documented evidence of disease progression based on the independent radiologic review, or death due to any cause on initially assigned study treatment, whichever comes earlier.	
End point type	Primary
End point timeframe:	
Double-Blind Treatment Period	

End point values	Ripretinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	44		
Units: Weeks				
median (confidence interval 95%)	27.6 (20.0 to 29.9)	4.1 (4.0 to 7.3)		

Statistical analyses

Statistical analysis title	Cox Proportional Regression Model
Comparison groups	Ripretinib v Placebo
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	0.25

Secondary: Objective Response Rate

End point title	Objective Response Rate

End point description:

The proportion of patients with a confirmed Complete Response or Partial Response based on the independent radiologic review and during the double-blind phase.

End point type	Secondary

End point timeframe:

Double-Blind Treatment Period

End point values	Ripretinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	44		
Units: Subjects				
Complete Response	0	0		
Partial Response	8	0		
Stable Disease (≥ 6 Weeks)	56	9		

Progressive Disease	16	28		
Not Evaluable	4	3		
No Response Assessment	1	4		

Statistical analyses

Statistical analysis title	Difference in ORR
Comparison groups	Ripretinib v Placebo
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0504
Method	Fisher exact
Parameter estimate	Difference in ORR (%)
Point estimate	9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	17.5

Secondary: Overall Survival

End point title	Overall Survival
End point description:	
The time interval between the date of randomization until the date of death or the date of last follow-up.	
End point type	Secondary
End point timeframe:	
Double-Blind Treatment Period	

End point values	Ripretinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	44		
Units: Weeks				
median (confidence interval 95%)	65.6 (53.6 to 65.6)	28.6 (17.9 to 50.4)		

Statistical analyses

Statistical analysis title	Cox Proportional Regression Model
Comparison groups	Ripretinib v Placebo

Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	0.62

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Double-Blind Treatment Period

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Ripretinib

Reporting group description:

DCC-2618 (ripretinib) was supplied as 50 mg strength tablets for oral administration in repeated 28-day cycles. Patients were instructed to take their assigned dose at the same time each day. If a patient dose escalates to 150 mg BID, patients were instructed take the study drug twice a day, at least 6 hours apart, and at the same time each day. On days of scheduled visits, the dose of study drug must be administered at the site after pre-dose assessments have been completed.

Reporting group title	Placebo

Reporting group description:

Placebo supplied as identically sized and color-matched tablets

Serious adverse events	Ripretinib	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 85 (30.59%)	19 / 43 (44.19%)	
number of deaths (all causes)	12	13	
number of deaths resulting from adverse events	5	10	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			

subjects affected / exposed	3 / 85 (3.53%)	4 / 43 (9.30%)	
occurrences causally related to treatment / all	1 / 3	0 / 4	
deaths causally related to treatment / all	1 / 3	0 / 4	
General physical health deterioration			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asthenia			
subjects affected / exposed	0 / 85 (0.00%)	2 / 43 (4.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyrexia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Psychiatric disorders			

Hallucinations, mixed			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	3 / 85 (3.53%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 85 (4.71%)	2 / 43 (4.65%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nausea			
subjects affected / exposed	2 / 85 (2.35%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 85 (2.35%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 85 (1.18%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal fistula			

subjects affected / exposed	1 / 85 (1.18%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 85 (1.18%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal perforation			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 85 (1.18%)	2 / 43 (4.65%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Urinary retention			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Liver abscess			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 85 (1.18%)	2 / 43 (4.65%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 85 (1.18%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 85 (1.18%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypophosphataemia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dehydration			
subjects affected / exposed	0 / 85 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ripretinib	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	84 / 85 (98.82%)	41 / 43 (95.35%)	
Investigations			
Weight decreased			
subjects affected / exposed	16 / 85 (18.82%)	5 / 43 (11.63%)	
occurrences (all)	18	5	
Blood bilirubin increased			
subjects affected / exposed	14 / 85 (16.47%)	0 / 43 (0.00%)	
occurrences (all)	16	0	
Lipase increased			
subjects affected / exposed	9 / 85 (10.59%)	0 / 43 (0.00%)	
occurrences (all)	12	0	
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 85 (7.06%)	2 / 43 (4.65%)	
occurrences (all)	8	3	
Blood alkaline phosphatase increased			
subjects affected / exposed	6 / 85 (7.06%)	1 / 43 (2.33%)	
occurrences (all)	8	2	
Vascular disorders			
Hypertension			
subjects affected / exposed	12 / 85 (14.12%)	2 / 43 (4.65%)	
occurrences (all)	19	2	
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 85 (18.82%)	2 / 43 (4.65%)	
occurrences (all)	16	2	
Dizziness			

subjects affected / exposed	7 / 85 (8.24%)	3 / 43 (6.98%)	
occurrences (all)	8	3	
Peripheral sensory neuropathy			
subjects affected / exposed	6 / 85 (7.06%)	1 / 43 (2.33%)	
occurrences (all)	6	1	
Dysgeusia			
subjects affected / exposed	3 / 85 (3.53%)	4 / 43 (9.30%)	
occurrences (all)	4	4	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 85 (12.94%)	7 / 43 (16.28%)	
occurrences (all)	13	12	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	36 / 85 (42.35%)	10 / 43 (23.26%)	
occurrences (all)	47	12	
Oedema peripheral			
subjects affected / exposed	14 / 85 (16.47%)	3 / 43 (6.98%)	
occurrences (all)	14	4	
Asthenia			
subjects affected / exposed	11 / 85 (12.94%)	5 / 43 (11.63%)	
occurrences (all)	14	6	
Pyrexia			
subjects affected / exposed	6 / 85 (7.06%)	2 / 43 (4.65%)	
occurrences (all)	6	2	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	32 / 85 (37.65%)	5 / 43 (11.63%)	
occurrences (all)	38	5	
Constipation			
subjects affected / exposed	29 / 85 (34.12%)	8 / 43 (18.60%)	
occurrences (all)	38	8	
Abdominal pain			
subjects affected / exposed	28 / 85 (32.94%)	12 / 43 (27.91%)	
occurrences (all)	31	14	
Diarrhoea			

subjects affected / exposed	24 / 85 (28.24%)	6 / 43 (13.95%)	
occurrences (all)	30	9	
Vomiting			
subjects affected / exposed	17 / 85 (20.00%)	3 / 43 (6.98%)	
occurrences (all)	19	3	
Abdominal pain upper			
subjects affected / exposed	8 / 85 (9.41%)	2 / 43 (4.65%)	
occurrences (all)	11	2	
Stomatitis			
subjects affected / exposed	9 / 85 (10.59%)	0 / 43 (0.00%)	
occurrences (all)	9	0	
Dyspepsia			
subjects affected / exposed	7 / 85 (8.24%)	6 / 43 (13.95%)	
occurrences (all)	8	7	
Abdominal distension			
subjects affected / exposed	3 / 85 (3.53%)	5 / 43 (11.63%)	
occurrences (all)	5	5	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	10 / 85 (11.76%)	0 / 43 (0.00%)	
occurrences (all)	13	0	
Cough			
subjects affected / exposed	6 / 85 (7.06%)	1 / 43 (2.33%)	
occurrences (all)	7	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	44 / 85 (51.76%)	2 / 43 (4.65%)	
occurrences (all)	54	2	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	18 / 85 (21.18%)	0 / 43 (0.00%)	
occurrences (all)	23	0	
Dry skin			
subjects affected / exposed	11 / 85 (12.94%)	3 / 43 (6.98%)	
occurrences (all)	11	3	
Pruritus			

subjects affected / exposed	9 / 85 (10.59%)	2 / 43 (4.65%)	
occurrences (all)	9	2	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	8 / 85 (9.41%)	6 / 43 (13.95%)	
occurrences (all)	9	6	
Anxiety			
subjects affected / exposed	7 / 85 (8.24%)	4 / 43 (9.30%)	
occurrences (all)	8	4	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	27 / 85 (31.76%)	5 / 43 (11.63%)	
occurrences (all)	37	6	
Arthralgia			
subjects affected / exposed	15 / 85 (17.65%)	2 / 43 (4.65%)	
occurrences (all)	23	2	
Muscle spasms			
subjects affected / exposed	13 / 85 (15.29%)	2 / 43 (4.65%)	
occurrences (all)	16	2	
Back pain			
subjects affected / exposed	8 / 85 (9.41%)	2 / 43 (4.65%)	
occurrences (all)	8	2	
Pain in extremity			
subjects affected / exposed	8 / 85 (9.41%)	2 / 43 (4.65%)	
occurrences (all)	9	2	
Musculoskeletal pain			
subjects affected / exposed	5 / 85 (5.88%)	3 / 43 (6.98%)	
occurrences (all)	5	3	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	23 / 85 (27.06%)	9 / 43 (20.93%)	
occurrences (all)	30	9	
Hypophosphataemia			
subjects affected / exposed	8 / 85 (9.41%)	0 / 43 (0.00%)	
occurrences (all)	12	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 November 2017	Incorporate changes suggested by the US FDA
01 March 2018	Updates and clarifications to assessments and dosing schedule, and sample collection. Revision of inclusion/exclusion criteria and guidance on dose escalation
22 March 2018	Revision of inclusion criteria and clarification on contraception for male patients and concomitant medications
27 August 2018	Clarifications to inclusion criteria, TEAEs and storage conditions
30 October 2018	Updates to the statistical analysis for this study
06 March 2020	Updates to frequency of assessments, collection of samples, and use of concomitant medications for patients who have been on DCC-2618. Clarification to the adverse events section.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported