Clinical trial results:
An open-label extension study to CQTI571A2102 to evaluate the long-term safety, tolerability and efficacy of QTI571 (imatinib) in the treatment of severe pulmonary arterial hypertension

Summary

EudraCT number	2010-021960-14
Trial protocol	DE IT
Global end of trial date	26 March 2014

Results information

Result version number	v1
This version publication date	13 July 2016
First version publication date	01 August 2015

Trial information

Trial identification

Sponsor protocol code	CQTI571A2102E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01392495
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,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 March 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 March 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

• To evaluate the long-term safety and tolerability of QTI571 in patients with severe pulmonary arterial hypertension

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.

Subjects who experience worsening of PAH requiring hospitalization may require the use of diuretics and supplemental oxygen. If severe, subjects may require intensive care treatment and use of vasopressors. PAH therapies, not used at time of enrollment, such as subcutaneous, oral, inhaled or intravenous prostacyclin derivatives, should only be added if the subject meets a TTCW event, including overnight hospitalization for worsening of PAH, worsening of WHO functional class by one or more levels, or a decrease in 6MWD of 15% measured on two occasions. Subjects who have a TTCW event may remain in the study and perform assessments per the visit schedule.

Background therapy:

Specific PAH medications include: all endothelin receptor antagonists, phosphodiesterase 5 inhibitors and inhaled, oral, intravenous, or subcutaneous prostacyclin analogues.

Background PAH therapies include: oxygen, digoxin, all diuretics, and calcium channel blockers. Background PAH therapies may be adjusted as necessary during the study.

Evidence for comparator:

Open label

Actual start date of recruitment	22 June 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	United States: 1
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Lithuania: 2
Worldwide total number of subjects	17
EEA total number of subjects	13

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)	12
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study population was composed of patients with PAH who completed the CQTI571A2102 study, did not meet withdrawal criteria for safety reasons during study conduct, and met the eligibility criteria for the current study.

Pre-assignment

Screening details:

Subjects were enrolled from the Core study CQTI571A2102.

Period 1

Period 1 title	Open Label 400 or 200 mg (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	QTI571 200 mg

Arm description:

QTI571 200 mg (highest tolerated dose in CQTI571A2102).

Arm type	Experimental
Investigational medicinal product name	Imatinib mesylate
Investigational medicinal product code	QTI571
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were instructed to take 2 100 mg tablets (highest tolerated dose in core study) once daily with a meal and a 200 mL glass of water and to swallow the tablet whole. If at any time, the dose of 200 mg q.d was not tolerated, treatment was to be discontinued and patient was to be discontinued from the study.
Dosing was to be stopped immediately for unacceptable values (defined in protocol) of thrombocytopenia, neutropenia, all events of syncope, receipt of lung transplant, and significant arrhythmia or LV dysfunction.

Arm title	QTI571 400 mg

Arm description:

QTI571 400 mg (highest tolerated dose in CQTI571A2102).

Arm type	Experimental
Investigational medicinal product name	Imatinib mesylate
Investigational medicinal product code	QTI571
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were instructed to take 4 100 mg tablets (highest tolerated dose in core study) once daily with a meal and a 200 mL glass of water and to swallow the tablet whole. For patients unable to tolerate 400mg q.d, based on specific criteria outlined in the protocol, a dose reduction to 200mg q.d was to have taken place . If criteria persisted after two weeks of dose reduction, patient was to have been discontinued. After a dose reduction, dose escalation back to 400 mg was permitted if it was safe to do so in the investigator's clinical judgment.
Dosing was to be stopped immediately for unacceptable values (defined in protocol) of thrombocytopenia, neutropenia, all events of syncope, receipt of lung transplant, and significant arrhythmia or LV dysfunction.

Number of subjects in period 1	QTI571 200 mg	QTI571 400 mg
Started	4	13
Completed	0	1
Not completed	4	12
Consent withdrawn by subject	-	2
Adverse event, non-fatal	1	2
Death	2	1
Administrative problems	1	7

Baseline characteristics

Reporting groups	
Reporting group title	Open Label 400 or 200 mg

Reporting group description: -

Reporting group values	Open Label 400 or 200 mg	Total	
Number of subjects	17	17	
Age categorical Units: Subjects			
Adults (18-64 years)	12	12	
From 65-84 years	5	5	
Age continuous Units: years			
arithmetic mean	53.5		
standard deviation	± 14.3	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	6	6	

End points

End points reporting groups

Reporting group title	QTI571 200 mg
Reporting group description:	
QTI571 200 mg (highest tolerated dose in CQTI571A2102).	
Reporting group title	QTI571 400 mg
Reporting group description:	
QTI571 400 mg (highest tolerated dose in CQTI571A2102).	

Primary: Number of patients with adverse events, serious adverse events and deaths

End point title	Number of patients with adverse events, serious adverse events and deaths[1]
End point description:	
Adverse event monitoring was conducted throughout the trial. Safety Analysis Set: The safety analysis set included all participants who received at least one dose of study drug during the extension and had at least one post-baseline safety assessment.	
End point type	Primary
End point timeframe:	
144 weeks	

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: Study was terminated and statistical analysis was not performed.

End point values	QTI571 200 mg	QTI571 400 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	13		
Units: Patients				
Adverse Events (serious and non-serious)	4	13		
Serious Adverse Events	4	5		
Deaths	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in the six minute walk distance (6MWD)

End point title	Change from baseline in the six minute walk distance (6MWD)
End point description:	
Efficacy outcomes were not powered for statistical analysis due to insufficient data resulting from early termination. No data displayed because Outcome Measure has zero total participants analyzed.	
End point type	Secondary
End point timeframe:	
baseline, 144 weeks	

End point values	QTI571 200 mg	QTI571 400 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Meters				
arithmetic mean (standard deviation)	()	()		

Notes:

[2] - Efficacy outcomes were not powered for statistical analysis due to early termination of trial.

[3] - No data displayed because Outcome Measure has zero total participants analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to clinical worsening (TTCW) endpoints

End point title	Time to clinical worsening (TTCW) endpoints

End point description:

Efficacy outcomes were not powered for statistical analysis due to insufficient data resulting from early termination. No data displayed because Outcome Measure has zero total participants analyzed.

End point type	Secondary

End point timeframe:

144 weeks

End point values	QTI571 200 mg	QTI571 400 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: events				

Notes:

[4] - No data displayed because Outcome Measure has zero total participants analyzed.

[5] - No data displayed because Outcome Measure has zero total participants analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Medical resource utilization

End point title	Medical resource utilization

End point description:

Efficacy outcomes were not powered for statistical analysis due to insufficient data resulting from termination of the study. No data displayed because Outcome Measure has zero total participants analyzed.

End point type	Secondary

End point timeframe:

144 weeks

End point values	QTI571 200 mg	QTI571 400 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: Events				

Notes:

[6] - No data displayed because Outcome Measure had zero total participants analyzed.

[7] - No data displayed because Outcome Measure had zero total participants analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV).

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	16.1

Reporting groups

Reporting group title	QTI571 200mg
Reporting group description:	
QTI571 200mg	
Reporting group title	QTI571 400mg
Reporting group description:	
QTI571 400mg	

Serious adverse events	QTI571 200mg	QTI571 400mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	5 / 13 (38.46%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Right ventricular failure			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood and lymphatic system disorders			
Iron deficiency anaemia			

subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (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	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric panniculitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Salivary gland cyst			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
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			
Pulmonary mass			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Catatonia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urethral haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	1 / 4 (25.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			

subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	QTI571 200mg	QTI571 400mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	13 / 13 (100.00%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Oedema peripheral			
subjects affected / exposed	1 / 4 (25.00%)	3 / 13 (23.08%)	
occurrences (all)	1	3	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	0 / 4 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Dysphonia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	0 / 4 (0.00%)	3 / 13 (23.08%)	
occurrences (all)	0	4	
Haemoptysis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Respiratory distress			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	3	
Sleep disorder			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Blood potassium decreased			

subjects affected / exposed	0 / 4 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Blood sodium decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
International normalised ratio increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Leukopenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Anaemia			

subjects affected / exposed	2 / 4 (50.00%)	3 / 13 (23.08%)	
occurrences (all)	2	3	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Periorbital oedema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 4 (25.00%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	6 / 13 (46.15%)	
occurrences (all)	0	6	
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	3 / 13 (23.08%)	
occurrences (all)	0	4	
Large intestine polyp			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Gastritis			

subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	1 / 4 (25.00%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	4 / 13 (30.77%)	
occurrences (all)	0	7	
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Proteinuria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Renal failure			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Renal impairment			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Scleroderma			

subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	3	
Infections and infestations			
Bacteriuria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Ear infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Haemophilus infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	6 / 13 (46.15%)	
occurrences (all)	0	7	
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Otitis externa			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences (all)	1	0	

Staphylococcal skin infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	3 / 13 (23.08%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	0 / 4 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Hypercholesterolaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hypoglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Iron deficiency			
subjects affected / exposed	1 / 4 (25.00%)	0 / 13 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 November 2010	The protocol was amended to specify an end date for the study and to clarify an exclusion criterion for female contraception requirements.
17 December 2010	The protocol was amended to remove the requirements for reporting pregnancy outcome from the male participant's partner. Mandatory collection of the information could be an unwarranted intrusion into the privacy of the male participant's partner.
23 June 2012	Relevant Data Summary was added to include the currently available clinical data, safety and tolerability data related to imatinib. Corrections of visit numbers in Section 6-Visit schedule and assessments were done. Fluid retention information for imatinib and the requirements for weight measurement and edema assessment were added. References were updated.
14 December 2012	This study has been designed to run over the course of three years. However, the current protocol mistakenly does not provide for study site visits during the final year. These visits have now been added to the assessment schedule. Patients will return to their study site twice during this period. This is an open label and requirement for an independent statistician and programmer was removed.

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.

In 2013, Novartis discontinued the development program of imatinib in pulmonary arterial hypertension (PAH) due to requirement of regulatory authorities for additional data to secure marketing approval; all global extension studies were closed.

Notes: