



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 | v2 (current) |
| This version publication date | 20 October 2021 |
| First version publication date | 01 August 2015 |
| Version creation reason | <ul style="list-style-type: none">• New data added to full data set• Changes to summary attachments full results attached |
| Summary attachment (see zip file) | Full results (CQTI571A2102_CTR_29Mar2021protected.pdf) |

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 | United Kingdom: 1 |
| Country: Number of subjects enrolled | United States: 1 |
| Country: Number of subjects enrolled | Australia: 3 |
| 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: no statistical analysis were specified | |

| 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 400mg |
|-----------------------|--------------|

Reporting group description:

QTI571 400mg

| | |
|-----------------------|--------------|
| Reporting group title | QTI571 200mg |
|-----------------------|--------------|

Reporting group description:

QTI571 200mg

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

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

| | | | |
|---|----------------|----------------|--|
| Salivary gland cyst | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 4 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 4 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary mass | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 4 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Catatonia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 4 (25.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Urethral haemorrhage | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 4 (25.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure acute | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 4 (25.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 4 (25.00%) | |
| 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 | 1 / 13 (7.69%) | 0 / 4 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 4 (25.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 4 (25.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 4 (25.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

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

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

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

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

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

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

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

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: