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Trial record **2 of 2** for: CQTI571A2301

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Imatinib (QTI571) in Pulmonary Arterial Hypertension (IMPRES)

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT00902174

First received: May 13, 2009
Last updated: February 16, 2016
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History of Changes

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Results First Received: April 16, 2013

Study Type:	Interventional
Study Design:	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Pulmonary Arterial Hypertension
Interventions:	Drug: imatinib mesylate Drug: Placebo

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
Overall, 326 participants were screened, 202 participants were randomized (103 to Imatinib and 99 to placebo). Out of 202 participants randomized 201 participants received study drug treatment (103 received imatinib mesylate, 98 received placebo). One participant was randomized to the placebo group but did not receive any study treatment.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
Participants were randomized in a 1:1 ratio to imatinib mesylate or placebo.

Reporting Groups

	Description
Imatinib Mesylate	Imatinib mesylate (QTI571) 200 mg once daily for two weeks, increased to 400 mg once daily if well tolerated. If 400 mg dose was not well tolerated, a down titration to 200 mg once daily was permitted.
Placebo	Placebo to imatinib mesylate taken once daily. Participants receiving placebo were allowed to receive already approved PAH treatments.

Participant Flow: Overall Study

	Imatinib Mesylate	Placebo
STARTED	**103**	**99**
COMPLETED	**69**	**81**
NOT COMPLETED	**34**	**18**
Adverse Event	**27**	**7**
Lack of Efficacy	**1**	**5**

Death	**2**	**2**
Withdrawal by Subject	**2**	**1**
Abnormal labs	**1**	**1**
Protocol Violation	**1**	**1**
Administration problem	**0**	**1**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Age set includes all randomized participants (202). Gender set includes all treated participants (201). One participant was randomized to placebo but did not receive stuy drug.

Reporting Groups

	Description
Imatinib Mesylate	Imatinib mesylate (QTI571) 200 mg once daily for two weeks, increased to 400 mg once daily if well tolerated. If 400 mg dose was not well tolerated, a down titration to 200 mg once daily was permitted.
Placebo	Placebo to imatinib mesylate taken once daily. Participants receiving placebo were allowed to receive already approved PAH treatments.
Total	Total of all reporting groups

Baseline Measures

	Imatinib Mesylate	Placebo	Total
Number of Participants [units: participants]	**103**	**99**	**202**

Age **[units: years]** **Mean (Standard Deviation)**	**50.0 (15.33)**	**46.5 (13.60)**	**48.3 (14.59)**
Gender [1] **[units: participants]**			
Female	**83**	**79**	**162**
Male	**20**	**19**	**39**

[1] One participant was randomized to placebo but did not receive study drug.

Outcome Measures

Hide All Outcome Measures

1. Primary: Difference in Six-minute Walk Distance Test (6MWD) Between Imatinib and Placebo at 24 Weeks [Time Frame: 24 weeks]

Measure Type	Primary
Measure Title	Difference in Six-minute Walk Distance Test (6MWD) Between Imatinib and Placebo at 24 Weeks
Measure Description	This standardized walk course was 30 meters in length. During the walk the participant was connected to a portable pulse oximeter via a finger probe. Participants were instructed to walk at a comfortable speed for as far as they could manage in 6 minutes. The total distance walked (in meters) was recorded. Results were compared between the 2 groups.
Time Frame	24 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

The Full Analysis Set includes all participants who received at least one dose of study drug and completed the 6MWD Six-minute walk test at week 24. Repeated measurement model was used for this analysis.

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Measured Values

	Imatinib	Placebo
Number of Participants Analyzed [units: participants]	**92**	**93**
Difference in Six-minute Walk Distance Test (6MWD) Between Imatinib and Placebo at 24 Weeks [units: meters] Least Squares Mean (Standard Error)	**382.94 (9.790)**	**351.18 (9.834)**

No statistical analysis provided for Difference in Six-minute Walk Distance Test (6MWD) Between Imatinib and Placebo at 24 Weeks

2. Secondary: Clinical Worsening Comparing Imatinib Versus Placebo for Adjudicated Cases [Time Frame: 24 weeks]

Measure Type	Secondary
Measure Title	Clinical Worsening Comparing Imatinib Versus Placebo for Adjudicated Cases
Measure Description	Clinical worsening per participant was measured by the onset of any adjudicated event (all cause mortality; overnight hospitalization for worsening of Pulmonary Arterial Hypertension (PAH); worsening of WHO functional class by one level; 15% decline in Six Minute Walk Distance (6MWD) measured on two consecutive occasions) at 24 weeks treatment, comparing imatinib to placebo groups. A cox regression analysis model was used.
Time Frame	24 weeks

Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Full Analysis Set included all participants who received at least one dose of study drug and experienced an adjudicated event. A cox regression analysis model was used.

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Measured Values

	Imatinib	**Placebo**
Number of Participants Analyzed [units: participants]	**37**	**32**
Clinical Worsening Comparing Imatinib Versus Placebo for Adjudicated Cases [units: percentage of participants]	**35.9**	**32.7**

No statistical analysis provided for Clinical Worsening Comparing Imatinib Versus Placebo for Adjudicated Cases

3. Secondary: Change From Baseline in Right Atrial Pressure [Time Frame: baseline and week 24]

Measure Type	Secondary
Measure Title	Change From Baseline in Right Atrial Pressure
Measure Description	Change from baseline in right atrial pressure (mmHg) was measured via right heart catheterization according to the

	local hospital procedures. The right atrial pressure was assessed when the participant was in a stable hemodynamic rest state. A higher right atrial pressure number indicates worsening.
Time Frame	baseline and week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the Full Analysis Set, defined as all randomized participants who received at least one dose of study drug, with data available for analysis.

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Measured Values

	Imatinib	**Placebo**
Number of Participants Analyzed [units: participants]	**73**	**81**
Change From Baseline in Right Atrial Pressure [units: mm Hg] Least Squares Mean (Standard Error)	**-1.02 (0.851)**	**0.68 (0.855)**

No statistical analysis provided for Change From Baseline in Right Atrial Pressure

4. Secondary: Change From Baseline in Mean Pulmonary Arterial Pressure [Time Frame: baseline and week 24]

Measure Type	Secondary
Measure Title	Change From Baseline in Mean Pulmonary Arterial Pressure
Measure Description	Change from baseline in mean pulmonary arterial pressure (mmHg) was measured via right heart catheterization according to the local hospital procedures. The mean pulmonary arterial pressure was assessed when the participant was in a stable hemodynamic rest state. A higher mean pulmonary arterial pressure number indicates worsening.
Time Frame	baseline and week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the Full Analysis Set, defined as all randomized participants who received at least one dose of study drug, with data available for analysis

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Measured Values

	Imatinib	**Placebo**
Number of Participants Analyzed [units: participants]	**75**	**82**
Change From Baseline in Mean Pulmonary Arterial Pressure [units: mm Hg] Least Squares Mean (Standard Error)	**-3.54 (1.585)**	**1.63 (1.586)**

No statistical analysis provided for Change From Baseline in Mean Pulmonary Arterial Pressure

5. Secondary: Change From Baseline in Mean Pulmonary Capillary Wedge Pressure [Time Frame: baseline and week 24]

Measure Type	Secondary
Measure Title	Change From Baseline in Mean Pulmonary Capillary Wedge Pressure
Measure Description	Change from baseline in mean pulmonary capillary wedge pressure (mmHg)was measured via right heart catheterization according to the local hospital procedures. The right atrial mean pulmonary capillary wedge pressure was assessed when the participant was in a stable hemodynamic rest state.
Time Frame	baseline and week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the Full Analysis Set, defined as all randomized participants who received at least one dose of study drug, with data available for analysis.

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Measured Values

	Imatinib	**Placebo**
Number of Participants Analyzed [units: participants]	**74**	**80**

Change From Baseline in Mean Pulmonary Capillary Wedge Pressure [units: mm Hg] Least Squares Mean (Standard Error)	**0.92 (0.693)**	**-0.05 (0.701)**

No statistical analysis provided for Change From Baseline in Mean Pulmonary Capillary Wedge Pressure

6. Secondary: Change From Baseline in Systemic Vascular Resistance [Time Frame: baseline and week 24]

Measure Type	Secondary
Measure Title	Change From Baseline in Systemic Vascular Resistance
Measure Description	Change from baseline in systemic vascular resistance (dynes*sec*cm^-5) was measured via right heart catheterization according to the local hospital procedures. The systemic vascular resistance was assessed when the participant was in a stable hemodynamic rest state. Reduction from baseline in mean systemic vascular resistance indicates improvement.
Time Frame	baseline and week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the Full Analysis Set, defined as all randomized participants who received at least one dose of study drug, with data available for analysis.

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Measured Values

	Imatinib	Placebo
Number of Participants Analyzed [units: participants]	**71**	**76**
Change From Baseline in Systemic Vascular Resistance [units: dynes*sec*cm^-5] Least Squares Mean (Standard Error)	**-467.84 (78.577)**	**-88.10 (77.183)**

No statistical analysis provided for Change From Baseline in Systemic Vascular Resistance

7. Secondary: Change From Baseline in Pulmonary Vascular Resistance [Time Frame: baseline and week 24]

Measure Type	Secondary
Measure Title	Change From Baseline in Pulmonary Vascular Resistance
Measure Description	Change from baseline in pulmonary vascular resistance (dynes*sec*cm^-5) was measured via right heart catheterization according to the local hospital procedures. The pulmonary vascular resistance was assessed when the participant was in a stable hemodynamic rest state. Reduction from baseline in pulmonary vascular resistance indicates improvement.
Time Frame	baseline and week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the Full Analysis Set, defined as all randomized participants who received at least one dose of study drug, with data available for analysis.

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Measured Values

	Imatinib	Placebo
Number of Participants Analyzed [units: participants]	**74**	**80**
Change From Baseline in Pulmonary Vascular Resistance [units: dynes*sec*cm^-5] Least Squares Mean (Standard Error)	**-366.47 (67.673)**	**12.12 (68.963)**

No statistical analysis provided for Change From Baseline in Pulmonary Vascular Resistance

8. Secondary: Change From Baseline in Pulmonary Resistance Index [Time Frame: baseline and week 24]

Measure Type	Secondary
Measure Title	Change From Baseline in Pulmonary Resistance Index
Measure Description	Change from baseline in pulmonary resistance index (dynes*sec*cm^-5/m2) was measured via right heart catheterization according to the local hospital procedures. The pulmonary resistance index was assessed when the participant was in a stable hemodynamic rest state. A reduction from baseline in pulmonary resistance index indicates improvement.
Time Frame	baseline and week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the Full Analysis Set, defined as all randomized participants who received at least one dose of study drug, with data available for analysis.

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Measured Values

	Imatinib	**Placebo**
Number of Participants Analyzed [units: participants]	**74**	**80**
Change From Baseline in Pulmonary Resistance Index [units: dynes*sec*cm^-5/m2] Least Squares Mean (Standard Error)	**-221.29 (47.355)**	**21.92 (48.247)**

No statistical analysis provided for Change From Baseline in Pulmonary Resistance Index

9. Secondary: Change From Baseline in Cardiac Output [Time Frame: 24 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Cardiac Output
Measure Description	Change from baseline in cardiac output (L/min) was measured via right heart catheterization according to the local hospital procedures. The cardiac output was assessed when the participant was in a stable hemodynamic rest state. An increase from baseline (higher number) in cardiac output indicates improvement.

Time Frame	24 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the Full Analysis Set, defined as all randomized participants who received at least one dose of study drug, with data available for analysis.

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Measured Values

	Imatinib	**Placebo**
Number of Participants Analyzed [units: participants]	**75**	**81**
Change From Baseline in Cardiac Output [units: Liters/minute] Least Squares Mean (Standard Error)	**1.17 (0.182)**	**0.29 (0.186)**

No statistical analysis provided for Change From Baseline in Cardiac Output

10. Secondary: Change From Baseline in Systolic Arterial Blood Pressure [Time Frame: baseline and week 24]

Measure Type	Secondary

Measure Title	Change From Baseline in Systolic Arterial Blood Pressure
Measure Description	Change from baseline in systolic arterial blood pressure (mmHg) was measured via right heart catheterization according to the local hospital procedures. The systolic arterial blood was assessed when the participant was in a stable hemodynamic rest state.
Time Frame	baseline and week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the Full Analysis Set, defined as all randomized participants who received at least one dose of study drug, with data available for analysis.

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Measured Values

	Imatinib	**Placebo**
Number of Participants Analyzed [units: participants]	**73**	**78**
Change From Baseline in Systolic Arterial Blood Pressure [units: mm Hg] Least Squares Mean (Standard Error)	**-2.92 (2.298)**	**-1.15 (2.227)**

No statistical analysis provided for Change From Baseline in Systolic Arterial Blood Pressure

11. Secondary: Change From Baseline in Diastolic Arterial Blood Pressure [Time Frame: baseline and week 24]

Measure Type	Secondary
Measure Title	Change From Baseline in Diastolic Arterial Blood Pressure
Measure Description	Change from baseline in diastolic arterial blood pressure (mmHg) was measured via right heart catheterization according to the local hospital procedures. The diastolic arterial blood pressure was assessed when the participant was in a stable hemodynamic rest state.
Time Frame	baseline and week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the Full Analysis Set, defined as all randomized participants who received at least one dose of study drug, with data available for analysis.

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Measured Values

	Imatinib	**Placebo**
Number of Participants Analyzed [units: participants]	**72**	**78**
Change From Baseline in Diastolic Arterial Blood Pressure [units: mm Hg]	**-3.81 (1.958)**	**-1.48 (1.909)**

Least Squares Mean (Standard Error)		

No statistical analysis provided for Change From Baseline in Diastolic Arterial Blood Pressure

12. Secondary: Change From Baseline in Heart Rate [Time Frame: 24 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Heart Rate
Measure Description	Change from baseline in heart rate (bpm) was measured via right heart catheterization according to the local hospital procedures. The heart rate was assessed when the participant was in a stable hemodynamic rest state.
Time Frame	24 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the Full Analysis Set, defined as all randomized participants who received at least one dose of study drug, with data available for analysis.

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Measured Values

	Imatinib	**Placebo**

Number of Participants Analyzed [units: participants]	**73**	**77**
Change From Baseline in Heart Rate [units: bpm] Least Squares Mean (Standard Error)	**0.38 (12.63)**	**0.73 (2.255)**

No statistical analysis provided for Change From Baseline in Heart Rate

13. Secondary: Change in Borg Dyspnea Score During 6-minute Walk Test [Time Frame: week 24]

Measure Type	Secondary
Measure Title	Change in Borg Dyspnea Score During 6-minute Walk Test
Measure Description	Change in Borg scale was measured at different time points at week 24. The Borg Scale consists of scale range of 0 to 10. Participants pointed to indicate their level of dyspnea before and at the end of exercise testing (where 0 indicates no breathlessness at all and 10 indicates maximum breathlessness). A reduction in this score indicates an improvement.
Time Frame	week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the Full Analysis Set, defined as all randomized participants who received at least one dose of study drug, with data available for analysis.

Reporting Groups

	Description
Imatinib	imatinib mesylate

Placebo	Placebo to imatinib

Measured Values

	Imatinib	Placebo
Number of Participants Analyzed [units: participants]	**92**	**91**
Change in Borg Dyspnea Score During 6-minute Walk Test [units: units on a scale] Mean (Standard Deviation)		
Resting (n= 86 imatinib; 89 placebo)	**-0.06 (1.097)**	**-0.12 (1.142)**
End of test (n= 92 imatinib; 91 placebo)	**-0.38 (2.009)**	**-0.24 (2.093)**
2 min after end (n= 82 imatinib; 81 placebo)	**-0.37 (1.409)**	**-0.18 (1.550)**
End of test - Resting (n= 81 imatinib; 81 placebo)	**-0.24 (1.193)**	**-0.29 (1.279)**
2 min after end - end of test (n= 82 ima; 81plb)	**-0.07 (1.533)**	**-0.03 (1.743)**

No statistical analysis provided for Change in Borg Dyspnea Score During 6-minute Walk Test

14. Secondary: Covariance of End of Study CAMPHOR Score [Time Frame: Week 24]

Measure Type	Secondary
Measure Title	Covariance of End of Study CAMPHOR Score
Measure Description	The CAMPHOR test consists of 65 items and 3 scales. Two scales measure Health Related Quality of Life. 1) Symptoms: consists of 25 items measuring loss or abnormality of psychological, physiological or anatomical structure or function; further sub-divided into 3 subscales (energy, breathlessness and mood), 2) Disability: consists of 15 items measuring any restriction or lack of ability to perform an activity. 3) Quality of Life (QOL): consists of 25 items defining how individuals perceived ability and capacity to satisfy their needs. The 25-item symptom and QOL scales score from 0-25 where a higher score indicates the presence of more symptoms and poor QOL, respectively. The 15-item

	functioning scale scores 0-30; a higher score indicates poor functioning.
Time Frame	Week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the Full Analysis Set, defined as all randomized participants who received at least one dose of study drug, with data available for analysis.

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Measured Values

	Imatinib	Placebo
Number of Participants Analyzed [units: participants]	**45**	**44**
Covariance of End of Study CAMPHOR Score [units: units on a scale] Least Squares Mean (Standard Error)		
Symptoms score	**7.93 (1.372)**	**9.03 (1.431)**
Activity score	**8.99 (1.177)**	**10.55 (1.223)**
Quality of life score	**7.45 (1.026)**	**7.13 (1.066)**

No statistical analysis provided for Covariance of End of Study CAMPHOR Score

15. Secondary: Plasma Concentration of QTI571 200 mg and Its Metabolite (GCP74588) Pre-dose and Between 0 Hour to 3 Hour Post-dose Per Participant [Time Frame: predose and between 0 hour to 3 hour post dose at day 1, day 14, day 28 and day 168]

Measure Type	Secondary
Measure Title	Plasma Concentration of QTI571 200 mg and Its Metabolite (GCP74588) Pre-dose and Between 0 Hour to 3 Hour Post-dose Per Participant
Measure Description	Blood samples were taken from each subject participating in the study (placebo group and active treatment group) once predose and once between 0 hour to 3 hour post dose at day 1 (baseline), day 14, day 28 and day 168. The parent compound QTI571 and its active metabolite, GCP74588, were measured in plasma by validated liquid chromatography-mass spectrometry (HPLC-MS/MS) assay.
Time Frame	predose and between 0 hour to 3 hour post dose at day 1, day 14, day 28 and day 168
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Full Analysis Set includes all patients who received at least one dose of study drug with available blood samples for analysis.

Reporting Groups

	Description
Imatinib 200 mg	imatinib mesylate 200 mg once daily
GCP74588	imatinib metabolite

Measured Values

	Imatinib 200 mg	**GCP74588**

Number of Participants Analyzed [units: participants]	**77**	**77**
Plasma Concentration of QTI571 200 mg and Its Metabolite (GCP74588) Pre-dose and Between 0 Hour to 3 Hour Post-dose Per Participant [units: ng/mL] Mean (Standard Deviation)		
Day 1 - predose (n=77 imat; n=77 GCP)	**0 (0)**	**0 (0)**
Day 1 - 0-3h post-dose (n=77 imat; n=77 GCP)	**471.9 (560.1)**	**61.8 (77.6)**
Day 14 - predose (n=18 imat; n=18 GCP)	**579.6 (384.9)**	**178.8 (122.8)**
Day 14 - 0-3h post-dose (n=19 imat; n=19 GCP)	**1005.7 (665.6)**	**233.8 (170.9)**
Day 28 - predose (n=20 imat; n=20 GCP)	**658.8 (450.3)**	**228.6 (121.4)**
Day 28 - 0-3h post-dose (n=19 imat; n=19 GCP)	**1438.6 (924.4)**	**323.9 (150.6)**
Day 168 predose (n=24 imat; n=24 GCP)	**398.6 (415.5)**	**126.6 (83.3)**
Day 168- 0-3h post-dose (n=23 imat; n=23 GCP)	**710.8 (639.7)**	**166.1 (103.1)**

No statistical analysis provided for Plasma Concentration of QTI571 200 mg and Its Metabolite (GCP74588) Pre-dose and Between 0 Hour to 3 Hour Post-dose Per Participant

16. Secondary: Plasma Concentration of QTI571 400 mg and Its Metabolite (GCP74588) Pre-dose and Between 0 Hour to 3 Hour Post-dose Per Participant [Time Frame: predose and between 0 hour to 3 hour post dose at day 1, day 14, day 28 and day 168]

Measure Type	Secondary

Measure Title	Plasma Concentration of QTI571 400 mg and Its Metabolite (GCP74588) Pre-dose and Between 0 Hour to 3 Hour Post-dose Per Participant
Measure Description	Blood samples were taken from each subject participating in the study (placebo group and active treatment group) once predose and once between 0 hour to 3 hour post dose at day 1 (baseline), day 14, day 28 and day 168. The parent compound QTI571 and its active metabolite, GCP74588, were measured in plasma by validated liquid chromatography-mass spectrometry (HPLC-MS/MS) assay.
Time Frame	predose and between 0 hour to 3 hour post dose at day 1, day 14, day 28 and day 168
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Full Analysis Set includes all patients who received at least one dose of study drug with available blood samples for analysis.

Reporting Groups

	Description
Imatinib 400 mg	imatinib mesylate 400 mg once daily
GCP74588	imatinib metabolite

Measured Values

	Imatinib 400 mg	**GCP74588**
Number of Participants Analyzed **[units: participants]**	**62**	**62**
Plasma Concentration of QTI571 400 mg and Its Metabolite (GCP74588) Pre-dose and Between 0 Hour to 3 Hour Post-dose Per Participant **[units: ng/mL]** **Mean (Standard Deviation)**		

Day 1 - predose (n=12 imat; n=12 GCP)	**0 (0)**	**0 (0)**
Day 1 - 0-3h post-dose (n=13 imat; n=13 GCP)	**843.2 (788.9)**	**109.9 (132.4)**
Day 14 - predose (n=62 imat; n=62 GCP)	**516.5 (405.2)**	**155.1 (101.1)**
Day 14 - 0-3h post-dose (n=62 imat; n=62 GCP)	**1172.8 (1088.9)**	**233.7 (165.6)**
Day 28 - predose (n=55 imat; n=55 GCP)	**829.8 (482.6)**	**248.2 (125.2)**
Day 28 - 0-3h post-dose (n=58 imat; n=58 GCP)	**1335.3 (817.9)**	**320.7 (154.8)**
Day 168 predose (n=36 imat; n=36 GCP)	**869.9 (407.8)**	**241.4 (91.9)**
Day 168- 0-3h post-dose (n=35 imat; n=35 GCP)	**1616.1 (787.6)**	**348.0 (119.1)**

No statistical analysis provided for Plasma Concentration of QTI571 400 mg and Its Metabolite (GCP74588) Pre-dose and Between 0 Hour to 3 Hour Post-dose Per Participant

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	202 participants were randomized (103 imatinib & 99 placebo; however, one participant who was randomized to the placebo group did not receive study drug and was excluded from this analysis set. The safety set includes all participants who received study drug = 201 (103 imatinib, 98 placebo).

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Serious Adverse Events

	Imatinib	Placebo
Total, serious adverse events		
# participants affected / at risk	**45/103 (43.69%)**	**29/98 (29.59%)**
Blood and lymphatic system disorders		
Anaemia † [1]		
# participants affected / at risk	**7/103 (6.80%)**	**1/98 (1.02%)**
Coagulopathy † [1]		
# participants affected / at risk	**1/103 (0.97%)**	**0/98 (0.00%)**
Neutropenia † [1]		
# participants affected / at risk	**2/103 (1.94%)**	**0/98 (0.00%)**
Thrombocytopenia † [1]		
# participants affected / at risk	**2/103 (1.94%)**	**0/98 (0.00%)**
Cardiac disorders		
Angina pectoris † [1]		
# participants affected / at risk	**2/103 (1.94%)**	**0/98 (0.00%)**
Atrial fibrillation † [1]		
# participants affected / at risk	**1/103 (0.97%)**	**1/98 (1.02%)**
Atrial flutter † [1]		
# participants affected / at risk	**2/103 (1.94%)**	**1/98 (1.02%)**
Cardiac failure † [1]		

# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Nodal arrhythmia † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Right ventricular failure † 1		
# participants affected / at risk	2/103 (1.94%)	2/98 (2.04%)
Tricuspid valve incompetence † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Eye disorders		
Periorbital oedema † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Retinal detachment † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Gastrointestinal disorders		
Abdominal pain † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Diarrhoea † 1		
# participants affected / at risk	3/103 (2.91%)	2/98 (2.04%)
Gastritis † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Gastrointestinal haemorrhage † 1		
# participants affected / at risk	1/103 (0.97%)	1/98 (1.02%)
Haemorrhoidal haemorrhage † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Melaena † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)

Nausea † [1]		
# participants affected / at risk	**2/103 (1.94%)**	**1/98 (1.02%)**
Vomiting † [1]		
# participants affected / at risk	**1/103 (0.97%)**	**0/98 (0.00%)**
General disorders		
Catheter site haemorrhage † [1]		
# participants affected / at risk	**1/103 (0.97%)**	**0/98 (0.00%)**
Device leakage † [1]		
# participants affected / at risk	**0/103 (0.00%)**	**1/98 (1.02%)**
Face oedema † [1]		
# participants affected / at risk	**1/103 (0.97%)**	**0/98 (0.00%)**
Fatigue † [1]		
# participants affected / at risk	**1/103 (0.97%)**	**0/98 (0.00%)**
Injection site extravasation † [1]		
# participants affected / at risk	**0/103 (0.00%)**	**1/98 (1.02%)**
Medical device complication † [1]		
# participants affected / at risk	**1/103 (0.97%)**	**1/98 (1.02%)**
Non-cardiac chest pain † [1]		
# participants affected / at risk	**0/103 (0.00%)**	**2/98 (2.04%)**
Oedema peripheral † [1]		
# participants affected / at risk	**6/103 (5.83%)**	**0/98 (0.00%)**
Pyrexia † [1]		
# participants affected / at risk	**0/103 (0.00%)**	**1/98 (1.02%)**
Hepatobiliary disorders		
Hepatic congestion † [1]		

# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Jaundice † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Infections and infestations		
Bacteraemia † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Campylobacter infection † 1		
# participants affected / at risk	0/103 (0.00%)	1/98 (1.02%)
Clostridial infection † 1		
# participants affected / at risk	0/103 (0.00%)	1/98 (1.02%)
Device related infection † 1		
# participants affected / at risk	3/103 (2.91%)	0/98 (0.00%)
Enterocolitis infectious † 1		
# participants affected / at risk	0/103 (0.00%)	1/98 (1.02%)
Gastroenteritis † 1		
# participants affected / at risk	0/103 (0.00%)	2/98 (2.04%)
Gastroenteritis bacterial † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Infection † 1		
# participants affected / at risk	0/103 (0.00%)	1/98 (1.02%)
Lower respiratory tract infection † 1		
# participants affected / at risk	0/103 (0.00%)	1/98 (1.02%)
Lung infection † 1		
# participants affected / at risk	0/103 (0.00%)	1/98 (1.02%)
Pneumonia † 1		
# participants affected / at risk	1/103 (0.97%)	2/98 (2.04%)

Pneumonia primary atypical † 1		
# participants affected / at risk	**0/103 (0.00%)**	**1/98 (1.02%)**
Pyelonephritis acute † 1		
# participants affected / at risk	**1/103 (0.97%)**	**0/98 (0.00%)**
Respiratory tract infection † 1		
# participants affected / at risk	**0/103 (0.00%)**	**1/98 (1.02%)**
Sepsis † 1		
# participants affected / at risk	**2/103 (1.94%)**	**0/98 (0.00%)**
Injury, poisoning and procedural complications		
Accidental overdose † 1		
# participants affected / at risk	**1/103 (0.97%)**	**0/98 (0.00%)**
Fall † 1		
# participants affected / at risk	**1/103 (0.97%)**	**0/98 (0.00%)**
Head injury † 1		
# participants affected / at risk	**1/103 (0.97%)**	**0/98 (0.00%)**
Subdural haematoma † 1		
# participants affected / at risk	**1/103 (0.97%)**	**0/98 (0.00%)**
Subdural haemorrhage † 1		
# participants affected / at risk	**1/103 (0.97%)**	**0/98 (0.00%)**
Investigations		
Cardiac output decreased † 1		
# participants affected / at risk	**0/103 (0.00%)**	**1/98 (1.02%)**
International normalised ratio increased † 1		
# participants affected / at risk	**1/103 (0.97%)**	**0/98 (0.00%)**
Right atrial pressure increased † 1		

# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Metabolism and nutrition disorders		
Electrolyte imbalance † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Fluid overload † 1		
# participants affected / at risk	1/103 (0.97%)	1/98 (1.02%)
Hypervolaemia † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Hypokalaemia † 1		
# participants affected / at risk	2/103 (1.94%)	0/98 (0.00%)
Hyponatraemia † 1		
# participants affected / at risk	1/103 (0.97%)	1/98 (1.02%)
Hypovolaemia † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Musculoskeletal and connective tissue disorders		
Arthralgia † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Myalgia † 1		
# participants affected / at risk	0/103 (0.00%)	1/98 (1.02%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Breast cancer † 1		
# participants affected / at risk	0/103 (0.00%)	1/98 (1.02%)
Nervous system disorders		
Dizziness † 1		

# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Headache † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Presyncope † 1		
# participants affected / at risk	5/103 (4.85%)	0/98 (0.00%)
Syncope † 1		
# participants affected / at risk	1/103 (0.97%)	5/98 (5.10%)
Renal and urinary disorders		
Renal failure † 1		
# participants affected / at risk	1/103 (0.97%)	1/98 (1.02%)
Renal failure acute † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Renal impairment † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Reproductive system and breast disorders		
Menorrhagia † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Uterine haemorrhage † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Respiratory, thoracic and mediastinal disorders		
Atelectasis † 1		
# participants affected / at risk	0/103 (0.00%)	1/98 (1.02%)
Bronchial haemorrhage † 1		
# participants affected / at risk	0/103 (0.00%)	1/98 (1.02%)
Dyspnoea † 1		

# participants affected / at risk	6/103 (5.83%)	2/98 (2.04%)
Epistaxis † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Haemoptysis † 1		
# participants affected / at risk	0/103 (0.00%)	2/98 (2.04%)
Hypoxia † 1		
# participants affected / at risk	1/103 (0.97%)	1/98 (1.02%)
Pleural effusion † 1		
# participants affected / at risk	2/103 (1.94%)	1/98 (1.02%)
Pneumonitis † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Pulmonary arterial hypertension † 1		
# participants affected / at risk	4/103 (3.88%)	4/98 (4.08%)
Pulmonary fibrosis † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Pulmonary hypertension † 1		
# participants affected / at risk	2/103 (1.94%)	4/98 (4.08%)
Pulmonary veno-occlusive disease † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Respiratory failure † 1		
# participants affected / at risk	1/103 (0.97%)	2/98 (2.04%)
Vascular disorders		
Haematoma † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)
Hypertension † 1		
# participants affected / at risk	1/103 (0.97%)	0/98 (0.00%)

Hypertensive crisis † 1		
# participants affected / at risk	**0/103 (0.00%)**	**1/98 (1.02%)**
Hypoperfusion † 1		
# participants affected / at risk	**1/103 (0.97%)**	**0/98 (0.00%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	202 participants were randomized (103 imatinib & 99 placebo; however, one participant who was randomized to the placebo group did not receive study drug and was excluded from this analysis set. The safety set includes all participants who received study drug = 201 (103 imatinib, 98 placebo).

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Imatinib	imatinib mesylate
Placebo	Placebo to imatinib

Other Adverse Events

	Imatinib	**Placebo**
Total, other (not including serious) adverse events		

# participants affected / at risk	96/103 (93.20%)	80/98 (81.63%)
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	8/103 (7.77%)	2/98 (2.04%)
Cardiac disorders		
Palpitations † 1		
# participants affected / at risk	4/103 (3.88%)	7/98 (7.14%)
Eye disorders		
Periorbital oedema † 1		
# participants affected / at risk	30/103 (29.13%)	7/98 (7.14%)
Gastrointestinal disorders		
Abdominal distension † 1		
# participants affected / at risk	9/103 (8.74%)	3/98 (3.06%)
Abdominal pain † 1		
# participants affected / at risk	6/103 (5.83%)	3/98 (3.06%)
Abdominal pain upper † 1		
# participants affected / at risk	2/103 (1.94%)	6/98 (6.12%)
Diarrhoea † 1		
# participants affected / at risk	33/103 (32.04%)	18/98 (18.37%)
Dyspepsia † 1		
# participants affected / at risk	8/103 (7.77%)	5/98 (5.10%)
Nausea † 1		
# participants affected / at risk	56/103 (54.37%)	23/98 (23.47%)
Vomiting † 1		
# participants affected / at risk	30/103 (29.13%)	10/98 (10.20%)

General disorders		
Face oedema † 1		
# participants affected / at risk	**9/103 (8.74%)**	**1/98 (1.02%)**
Fatigue † 1		
# participants affected / at risk	**10/103 (9.71%)**	**7/98 (7.14%)**
Non-cardiac chest pain † 1		
# participants affected / at risk	**3/103 (2.91%)**	**5/98 (5.10%)**
Oedema peripheral † 1		
# participants affected / at risk	**41/103 (39.81%)**	**20/98 (20.41%)**
Pyrexia † 1		
# participants affected / at risk	**7/103 (6.80%)**	**3/98 (3.06%)**
Infections and infestations		
Device related infection † 1		
# participants affected / at risk	**1/103 (0.97%)**	**5/98 (5.10%)**
Influenza † 1		
# participants affected / at risk	**2/103 (1.94%)**	**5/98 (5.10%)**
Nasopharyngitis † 1		
# participants affected / at risk	**18/103 (17.48%)**	**19/98 (19.39%)**
Respiratory tract infection † 1		
# participants affected / at risk	**3/103 (2.91%)**	**7/98 (7.14%)**
Sinusitis † 1		
# participants affected / at risk	**2/103 (1.94%)**	**6/98 (6.12%)**
Upper respiratory tract infection † 1		
# participants affected / at risk	**5/103 (4.85%)**	**7/98 (7.14%)**
Urinary tract infection † 1		

# participants affected / at risk	4/103 (3.88%)	5/98 (5.10%)
Investigations		
Blood creatinine increased † [1]		
# participants affected / at risk	9/103 (8.74%)	1/98 (1.02%)
Metabolism and nutrition disorders		
Hypokalaemia † [1]		
# participants affected / at risk	14/103 (13.59%)	3/98 (3.06%)
Musculoskeletal and connective tissue disorders		
Muscle spasms † [1]		
# participants affected / at risk	10/103 (9.71%)	2/98 (2.04%)
Pain in extremity † [1]		
# participants affected / at risk	5/103 (4.85%)	6/98 (6.12%)
Nervous system disorders		
Dizziness † [1]		
# participants affected / at risk	8/103 (7.77%)	5/98 (5.10%)
Headache † [1]		
# participants affected / at risk	25/103 (24.27%)	22/98 (22.45%)
Respiratory, thoracic and mediastinal disorders		
Cough † [1]		
# participants affected / at risk	11/103 (10.68%)	15/98 (15.31%)
Dyspnoea † [1]		
# participants affected / at risk	13/103 (12.62%)	11/98 (11.22%)
Epistaxis † [1]		
# participants affected / at risk	7/103 (6.80%)	7/98 (7.14%)
Nasal congestion † [1]		

# participants affected / at risk	**6/103 (5.83%)**	**4/98 (4.08%)**
Oropharyngeal pain † 1		
# participants affected / at risk	**9/103 (8.74%)**	**6/98 (6.12%)**
Skin and subcutaneous tissue disorders		
Alopecia † 1		
# participants affected / at risk	**7/103 (6.80%)**	**1/98 (1.02%)**
Pruritus † 1		
# participants affected / at risk	**3/103 (2.91%)**	**5/98 (5.10%)**
Rash † 1		
# participants affected / at risk	**9/103 (8.74%)**	**2/98 (2.04%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** The terms and conditions of Novartis' agreements with its investigators may vary. However, Novartis does not prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of the pooled data (i.e., data from all sites) in the clinical trial or disclosure of trial results in their entirety.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
phone: 862-778-8300

No publications provided by Novartis

Publications automatically indexed to this study:

Querejeta Roca G, Campbell P, Claggett B, Solomon SD, Shah AM. Right Atrial Function in Pulmonary Arterial Hypertension. Circ Cardiovasc Imaging. 2015 Nov;8(11):e003521; discussion e003521. doi: 10.1161/CIRCIMAGING.115.003521.

Querejeta Roca G, Campbell P, Claggett B, Vazir A, Quinn D, Solomon SD, Shah AM. Impact of lowering pulmonary vascular resistance on right and left ventricular deformation in pulmonary arterial hypertension. Eur J Heart Fail. 2015 Jan;17(1):63-73. doi: 10.1002/ejhf.177. Epub 2014 Nov 4.

Shah AM, Campbell P, Rocha GQ, Peacock A, Barst RJ, Quinn D, Solomon SD; IMPRES Investigators. Effect of imatinib as add-on therapy on echocardiographic measures of right ventricular function in patients with significant pulmonary arterial hypertension. Eur Heart J. 2015 Mar

7;36(10):623-32. doi: 10.1093/eurheartj/ehu035. Epub 2014 Feb 23.

Hoeper MM, Barst RJ, Bourge RC, Feldman J, Frost AE, Galié N, Gómez-Sánchez MA, Grimminger F, Grünig E, Hassoun PM, Morrell NW, Peacock AJ, Satoh T, Simonneau G, Tapson VF, Torres F, Lawrence D, Quinn DA, Ghofrani HA. Imatinib mesylate as add-on therapy for pulmonary arterial hypertension: results of the randomized IMPRES study. Circulation. 2013 Mar 12;127(10):1128-38. doi: 10.1161/CIRCULATIONAHA.112.000765. Epub 2013 Feb 12.

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT00902174 History of Changes
Other Study ID Numbers:	**CQTI571A2301**
Study First Received:	May 13, 2009
Results First Received:	April 16, 2013
Last Updated:	February 16, 2016
Health Authority:	United States: Food and Drug Administration Austria: Federal Office for Safety in Health Care Belgium: Federal Agency for Medicinal Products and Health Products France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) Germany: Federal Institute for Drugs and Medical Devices Italy: The Italian Medicines Agency Netherlands: The Central Committee on Research Involving Human Subjects (CCMO) Spain: Spanish Agency of Medicines Sweden: Medical Products Agency United Kingdom: Medicines and Healthcare Products Regulatory Agency Switzerland: Swissmedic Korea: Food and Drug Administration Japan: Pharmaceuticals and Medical Devices Agency Canada: Health Canada