Clinical trial results:
A Randomized Controlled Phase 3 Study of Oral Pacritinib versus Best Available Therapy in Patients with Primary Myelofibrosis, Post-Polycythemia Vera Myelofibrosis, or Post-Essential Thrombocythemia Myelofibrosis.

Summary

EudraCT number	2012-004239-21
Trial protocol	BE GB CZ HU DE IT
Global end of trial date	22 April 2016

Results information

Result version number	v1 (current)
This version publication date	02 August 2018
First version publication date	02 August 2018

Trial information

Trial identification

Sponsor protocol code	PAC325

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01773187
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CTI Life Sciences Ltd.
Sponsor organisation address	Highlands House, Basingstoke Road, Spencers Wood, Reading, Berkshire, United Kingdom, RG7 1NT
Public contact	Bruce Seeley Director, CTILS, CTI Life Sciences Ltd., +1 206-272-4260, bseeley@ctibiopharma.com
Scientific contact	Bruce Seeley Director, CTILS, CTI Life Sciences Ltd., +1 206-272-4260, bseeley@ctibiopharma.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 June 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 April 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the PERSIST-1 study was to compare the efficacy of pacritinib with that of BAT in subjects with PMF, PPV-MF, or PET-MF. The primary efficacy measure for this analysis was the proportion of subjects achieving a ≥35% reduction in spleen volume from baseline to Week 24, as measured by magnetic resonance imaging (MRI) or computed tomography (CT) scan

Protection of trial subjects:

This trial was conducted in compliance with International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines, US FDA regulations 21 Code of Federal Regulations Parts 50, 56, and 312, and with the laws and regulations of the country in which the research was conducted, whichever affords the greatest protection to the study subject.
No trial procedures were performed on trial participants until written consent had been obtained from them. The informed consent form (ICF), protocol, and amendments for this trial were submitted to and approved by the Ethics committee.
Routine monitoring was performed to verify that rights and well being of patients were protected. Also, any medication considered necessary for the patient's safety and well-being was given at the discretion of the Investigator.

Background therapy:

The most common concomitant medications by ATC class in the pacritinib and BAT arms, were Antipropulsives (49.1% and 48.1%, respectively), Proton Pump Inhibitors (33.6% and 50.9 %, respectively), Preparations Inhibiting Uric Acid Production (32.7% and 42.5%, respectively), Platelet Aggregation Inhibitors Excluding Heparin (32.7% and 37.7%, respectively), and Anilides (35.0% and 40.6%, respectively).

Evidence for comparator:

The control arm of the study consisted of best available therapies (BAT) , which was the same control arm used in the COMFORT-II phase 3 study of the currently approved JAK2 inhibitor, ruxolitinib. Due to the limitations in the approved indications for ruxolitinib and its regulatory and economic availability on a world-wide basis at the time this study was conducted, ruxolitinib was not included in the BAT treatment arm. Placebo control was deemed inappropriate for these subjects, given the likelihood of efficacy shown in early phase pacritinib clinical studies, as well as the proven efficacy of the approved ruxolitinib agent, which also inhibits the JAK2 pathway.
As with the completed phase 3 registrational ruxolitinib COMFORT studies, subjects were permitted to cross over from BAT to pacritinib. This was deemed essential to achieve appropriate equipoise for the participating subjects and to encourage participation given the lack of BAT agents approved for treatment of these MF patients. Crossover provided further scientific benefit as it enabled comparison of safety and efficacy with BAT treatment prior to crossover versus pacritinib treatment after crossover.

Actual start date of recruitment	08 January 2013
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	Netherlands: 21
Country: Number of subjects enrolled	United Kingdom: 25
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Czech Republic: 18
Country: Number of subjects enrolled	France: 35
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Hungary: 70
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	United States: 5
Country: Number of subjects enrolled	Russian Federation: 53
Country: Number of subjects enrolled	Australia: 46
Country: Number of subjects enrolled	New Zealand: 20
Worldwide total number of subjects	327
EEA total number of subjects	203

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)	137
From 65 to 84 years	189
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

327 patients from 12 countries (8 EU countries, US, Russia and Australia and New Zealand) were enrolled. Enrolment started on 08 January 2013. Last patient visit was on 22 April 2016.

Pre-assignment

Screening details:

Participants had a washout period (day -35 to day -7) and screening evaluations between day -14 to day -5 before entering treatment.

Period 1

Period 1 title	overall period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Investigators, site personnel, subjects, clinical monitors, and a designated field CRA were unblinded to individual study treatment assignment. Except certain CTI personnel responsible for pharmacovigilance activities, regulatory submissions, supply chain, and GCP compliance, the sponsor and independent radiographic assessors were blinded throughout the entire study. The sponsor remained blinded to individual study treatment assignment until the database lock for primary analysis.

Arms

Are arms mutually exclusive?	Yes
Arm title	Pacritinib

Arm description:

Subjects who received pacritinib were to self-administer four 100 mg capsules per day orally, once a day (400 mg daily), at the same time of day, with or without food.

Arm type	Experimental
Investigational medicinal product name	Pacritinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who received pacritinib were to self-administer four 100 mg capsules per day orally, once a day (400 mg daily), at the same time of day, with or without food.

Arm title	Best available Therapies (BAT)

Arm description:

Best available Therapies (BAT): Subjects receiving BAT were treated on a schedule commensurate with the therapy(ies) chosen by the investigator. BAT agents could be administered as monotherapy or in combinations, and could be changed (eg, new dose, new schedule, new regimen) as clinically indicated without limitation. Best available therapies may have included any physician-selected treatment for PMF, PPV-MF, or PET-MF, with the exclusion of JAK inhibitors, and may have included any treatment received before study entry. Best available therapies also could have included no treatment (watch and wait) or symptom-directed treatment without MF-specific treatment. BAT therapies could not be co-administered to subjects in the pacritinib arm for treatment of MF.

Arm type	Active comparator

Investigational medicinal product name	Hydroxyurea, prednisone, interferon-alpha, thalidomide, danazole, prednisolone, busulfan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Solution for injection, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

BAT agents could be administered as monotherapy or in combinations, and could be changed (eg, new dose, new schedule, new regimen) as clinically indicated without limitation. The pharmaceutical forms and routes of administration depend on the specific product and its clinical indication. Examples of the most used products, their pharmaceutical form and route of administration are shown above.

Number of subjects in period 1	Pacritinib	Best available Therapies (BAT)
Started	220	107
Completed	167	75
Not completed	53	32
Adverse event, serious fatal	1	1
Physician decision	7	18
Consent withdrawn by subject	18	2
Adverse event, non-fatal	20	2
Other	4	-
progressive disease	3	9

Baseline characteristics

Reporting groups	
Reporting group title	Pacritinib
Reporting group description:	
Subjects who received pacritinib were to self-administer four 100 mg capsules per day orally, once a day (400 mg daily), at the same time of day, with or without food.	
Reporting group title	Best available Therapies (BAT)
Reporting group description:	
Best available Therapies (BAT): Subjects receiving BAT were treated on a schedule commensurate with the therapy(ies) chosen by the investigator. BAT agents could be administered as monotherapy or in combinations, and could be changed (eg, new dose, new schedule, new regimen) as clinically indicated without limitation. Best available therapies may have included any physician-selected treatment for PMF, PPV-MF, or PET-MF, with the exclusion of JAK inhibitors, and may have included any treatment received before study entry. Best available therapies also could have included no treatment (watch and wait) or symptom-directed treatment without MF-specific treatment. BAT therapies could not be co-administered to subjects in the pacritinib arm for treatment of MF.	

Reporting group values	Pacritinib	Best available Therapies (BAT)	Total
Number of subjects	220	107	327
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	85	52	137
From 65-84 years	134	55	189
85 years and over	1	0	1
Age continuous Units: years			
arithmetic mean	65.5	64.8	
standard deviation	± 10.85	± 9.12	-
Gender categorical Units: Subjects			
Female	95	47	142
Male	125	60	185
Race Units: Subjects			
Asian	2	1	3
Black	2	0	2
White	191	98	289
Not reported	23	8	31
Other	2	0	2

End points

End points reporting groups

Reporting group title	Pacritinib

Reporting group description:

Subjects who received pacritinib were to self-administer four 100 mg capsules per day orally, once a day (400 mg daily), at the same time of day, with or without food.

Reporting group title	Best available Therapies (BAT)

Reporting group description:

Best available Therapies (BAT): Subjects receiving BAT were treated on a schedule commensurate with the therapy(ies) chosen by the investigator. BAT agents could be administered as monotherapy or in combinations, and could be changed (eg, new dose, new schedule, new regimen) as clinically indicated without limitation. Best available therapies may have included any physician-selected treatment for PMF, PPV-MF, or PET-MF, with the exclusion of JAK inhibitors, and may have included any treatment received before study entry. Best available therapies also could have included no treatment (watch and wait) or symptom-directed treatment without MF-specific treatment. BAT therapies could not be co-administered to subjects in the pacritinib arm for treatment of MF.

Primary: ≥35% Spleen Volume Reduction

End point title	≥35% Spleen Volume Reduction

End point description:

The primary efficacy endpoint was the proportion of subjects achieving a ≥35% spleen volume reduction (SVR) from baseline to Week 24, as measured by MRI or CT scan.
For each subject, the same imaging modality was to have been used throughout the study. Splenic progression was followed for subjects who discontinued treatment but did not progress. Subjects with progressive disease documented prior to week 24 who opted to continue on study treatment did not undergo week 24 imaging if the date of progression was at week 20 or later. For subjects who crossed over after week 24, an MRI was done within 30 days prior to the start of pacritinib treatment.

End point type	Primary

End point timeframe:

MRI or CT scan (without contrast agents) was performed prior to randomization (days -10 to -4). MRI or CT scan was performed at the end of week 12 ± 7 days and every 12 weeks thereafter, and at treatment termination.

End point values	Pacritinib	Best available Therapies (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	107		
Units: patient number (n)				
Overall (n)	42	5		

Statistical analyses

Statistical analysis title	Primary endpoint statistics
Comparison groups	Pacritinib v Best available Therapies (BAT)

Number of subjects included in analysis	327
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003
Method	Fisher exact
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.1
upper limit	24.9

Secondary: > 50% TSS reduction on MPN-SAF TSS 2.0

End point title	> 50% TSS reduction on MPN-SAF TSS 2.0

End point description:

The secondary endpoint in the study was the proportion of subjects with a ≥50% reduction from baseline to Week 24 in the subject reported outcome instrument, MPN-SAF TSS 2.0. The original version of this instrument (MPN-SAF TSS) was administered to the first 179 subjects enrolled in the study. However, after discussion with FDA, agreement was reached on modified questions to be included in the instrument. The new version (termed MPN-SAF TSS 2.0) was administered to all subsequently enrolled subjects throughout their participation in the study.
A total of 148 subjects (100 pacritinib, 48 BAT) were tested with the MPN-SAF TSS 2.0 and comprise the ITT population for this endpoint. Responses (on a scale from 0 [absent] to 10 [worst imaginable]) to questions about the symptoms of tiredness, early satiety, abdominal discomfort, night sweats, pruritus, bone pain, and pain under the ribs on the left side were used to compute the MPN-SAF TSS 2.0 results.

End point type	Secondary

End point timeframe:

Daily after receiving eDiary and throughout treatment. Subject-reported symptoms on MPN-SAF TSS 2.0: daily for 7 to 10 consecutive days prior to start of study treatment + daily from day 1 through week 48 or until subject discontinuation.

End point values	Pacritinib	Best available Therapies (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	48		
Units: number of patients (n)				
Overall	19	5		

Statistical analyses

Statistical analysis title	Statistics - secondary endpoint
Comparison groups	Best available Therapies (BAT) v Pacritinib

Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2368
Method	Fisher exact

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Subjects were evaluated from the time of signing informed consent through 30 d after the last study treatment.

Adverse event reporting additional description:

The data display threshold for SAEs is set to 1% or more, that of AEs is set to 5% or more.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Pacritinib

Reporting group description:

Subjects who received pacritinib were to self-administer four 100 mg capsules per day orally, once a day (400 mg daily), at the same time of day, with or without food.

Reporting group title	Best available therapies (BAT) safety population

Reporting group description:

Subgroup of the ITT population representing subjects who received any dose of study treatment.

Serious adverse events	Pacritinib	Best available therapies (BAT) safety population	
Total subjects affected by serious adverse events			
subjects affected / exposed	110 / 220 (50.00%)	8 / 106 (7.55%)	
number of deaths (all causes)	8	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	6 / 220 (2.73%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	4 / 220 (1.82%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myeloid leukaemia			
subjects affected / exposed	3 / 220 (1.36%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Squamous cell carcinoma of skin			
subjects affected / exposed	3 / 220 (1.36%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	7 / 220 (3.18%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	4 / 220 (1.82%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	3 / 220 (1.36%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	16 / 220 (7.27%)	4 / 106 (3.77%)	
occurrences causally related to treatment / all	9 / 16	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	4 / 220 (1.82%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	3 / 220 (1.36%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			

subjects affected / exposed	6 / 220 (2.73%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 5	0 / 0	
Pyrexia			
subjects affected / exposed	6 / 220 (2.73%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	3 / 220 (1.36%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 220 (1.82%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	3 / 220 (1.36%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 220 (1.36%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	5 / 220 (2.27%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 220 (0.00%)	2 / 106 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	4 / 220 (1.82%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	16 / 220 (7.27%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	7 / 16	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	4 / 220 (1.82%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	3 / 220 (1.36%)	0 / 106 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 220 (0.00%)	2 / 106 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pacritinib	Best available therapies (BAT) safety population	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	207 / 220 (94.09%)	81 / 106 (76.42%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 220 (5.00%)	0 / 106 (0.00%)	
occurrences (all)	11	0	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	33 / 220 (15.00%)	9 / 106 (8.49%)	
occurrences (all)	33	9	
Oedema peripheral			
subjects affected / exposed	24 / 220 (10.91%)	16 / 106 (15.09%)	
occurrences (all)	24	16	
Pyrexia			
subjects affected / exposed	17 / 220 (7.73%)	11 / 106 (10.38%)	
occurrences (all)	17	11	
Asthenia			
subjects affected / exposed	16 / 220 (7.27%)	7 / 106 (6.60%)	
occurrences (all)	16	7	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	20 / 220 (9.09%)	9 / 106 (8.49%)	
occurrences (all)	20	9	
Epistaxis			
subjects affected / exposed	17 / 220 (7.73%)	10 / 106 (9.43%)	
occurrences (all)	17	10	
Cough			
subjects affected / exposed	18 / 220 (8.18%)	8 / 106 (7.55%)	
occurrences (all)	18	8	
Oropharyngeal pain			
subjects affected / exposed	13 / 220 (5.91%)	0 / 106 (0.00%)	
occurrences (all)	13	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	13 / 220 (5.91%)	0 / 106 (0.00%)	
occurrences (all)	13	0	
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	12 / 220 (5.45%)	0 / 106 (0.00%)	
occurrences (all)	12	0	
Injury, poisoning and procedural complications			
Contusion			

subjects affected / exposed	11 / 220 (5.00%)	0 / 106 (0.00%)	
occurrences (all)	11	0	
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 220 (5.45%)	0 / 106 (0.00%)	
occurrences (all)	12	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	58 / 220 (26.36%)	18 / 106 (16.98%)	
occurrences (all)	58	18	
Thrombocytopenia			
subjects affected / exposed	48 / 220 (21.82%)	15 / 106 (14.15%)	
occurrences (all)	48	15	
Neutropenia			
subjects affected / exposed	12 / 220 (5.45%)	0 / 106 (0.00%)	
occurrences (all)	12	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	142 / 220 (64.55%)	14 / 106 (13.21%)	
occurrences (all)	142	14	
Nausea			
subjects affected / exposed	70 / 220 (31.82%)	7 / 106 (6.60%)	
occurrences (all)	70	7	
Vomiting			
subjects affected / exposed	46 / 220 (20.91%)	7 / 106 (6.60%)	
occurrences (all)	46	7	
Abdominal pain			
subjects affected / exposed	29 / 220 (13.18%)	11 / 106 (10.38%)	
occurrences (all)	29	11	
Constipation			
subjects affected / exposed	22 / 220 (10.00%)	8 / 106 (7.55%)	
occurrences (all)	22	8	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	14 / 220 (6.36%)	0 / 106 (0.00%)	
occurrences (all)	14	0	
Rash			

subjects affected / exposed	12 / 220 (5.45%)	0 / 106 (0.00%)	
occurrences (all)	12	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	13 / 220 (5.91%)	0 / 106 (0.00%)	
occurrences (all)	13	0	
Pain in extremity			
subjects affected / exposed	11 / 220 (5.00%)	9 / 106 (8.49%)	
occurrences (all)	11	9	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	16 / 220 (7.27%)	6 / 106 (5.66%)	
occurrences (all)	16	6	
Urinary tract infection			
subjects affected / exposed	12 / 220 (5.45%)	0 / 106 (0.00%)	
occurrences (all)	12	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	21 / 220 (9.55%)	0 / 106 (0.00%)	
occurrences (all)	21	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 September 2012	Amendment 1 included the following changes: - addition of a new inclusion criterion - addition of dose management guidelines for QTc interval prolongation - clarification to dose reduction for pacritinib-related, nonhematologic toxicities - change of timepoints for spleen size assessments.
16 March 2013	Amendment 2 included the following changes: - revision of secondary and exploratory objectives - addition of a crossover section from BAT to pacritinib including criteria - revision of inclusion and exclusion criteria - addition of a section for withdrawal from study procedures - revision of the method of treatment assignment - addition of explanation of QTc calculation and recalculation - addition of provision of prescription for loperamide (and instructions for use) - AE section was expanded - amendment of spleen volume measurement by MRI or CT - a modified ITT population was added - the PP population definition was revised - the Data Monitoring Committee was changed to an IDMC - major changes to study assessments.
15 August 2013	Amendment 3 included the following changes: - revision of inclusion and exclusion criteria - update of statistical methods section - revision of study design - revision of period of blinding for independent radiographic assessors - replacement of MPN-SAF TSS with MPN-SAF TSS 2.0 for subjects randomized under protocol Amendment 3 - revision of the endpoint for collection of AEs and SAEs to the last day of study participation - amendments and changes to the ITT population - Major changes to the study assessments.
30 January 2014	Amendment 4 included the following changes: - revision of sample size of randomized subjects - revision of statistical methods section - clarification of PK and PD assessments - clarification and correction of inconsistencies regarding the timing of the administration of the PGIA, MPN-SAF TSS (all versions), pain medication log, and QoL assessments; clarification regarding use of the MPN-SAF TSS (all versions) - amendment of timepoints prior to start of study treatment - revision of the SAE collection time period.
21 February 2014	Amendment 4a: - revision of sample size of randomized subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date

08 February 2016	PERSIST-1 was placed on Partial Clinical Hold by FDA on 2016 FEB 04 and then on Full Clinical Hold 2016 FEB 08. At the time of the FDA Partial Clinical Hold, no PERSIST-1 subjects were permitted to start pacritinib as initial or crossover treatment, and subjects not deriving benefit after 30 weeks of pacritinib treatment were to stop pacritinib. When the FDA Full Clinical Hold was imposed, all PERSIST-1 subjects discontinued pacritinib study treatment and no subjects were allowed to start pacritinib as initial or crossover treatment. Subjects continued to be followed for OS.	-

Notes:

Limitations and caveats

None reported