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

Published: 25-01-2013
Last updated: 24-04-2024

Primary Objective:To compare the efficacy of pacritinib with that of Best Available Therapy (BAT) in patients with PMF, PPV-MF, or PET-MF; the efficacy measure for this analysis is the proportion of patients achieving a * 35% reduction in spleen...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Haematological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON41280

Source
ToetsingOnline

Brief title
The PERSIST-1 trial (PAC325)

Condition

- Haematological disorders NEC

Synonym
myelofibrosis, myeloproliferative diseases

Research involving

Human

Sponsors and support

Primary sponsor: CTI BioPharma Corp.
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: - Janus Kinase, - Myelofibrosis (MF), - Pacritinib, - Thrombocytopenia

Outcome measures

Primary outcome

Study objective:

Primary efficacy objective:

- The proportion of patients achieving a * 35% reduction in spleen volume from

baseline to Week 24 by MRI or CT.

Secondary outcome

The key secundary objective is the proportion of patients with 50% reduction

in total score from baseline to Week 24 on the Myeloproliferative Neoplasm

Symptom Assessment Form (MPN-SAF TSS2.0).

Other secundary objectives are:

- Proportion of patients with a baseline platelet count < 100,000/µL achieving

> 35% reduction in spleen volume from baseline to Week 24 as measured by MRI or

CT

- Proportion of patients with a baseline platelet count < 100,000/µL achieving

> 50% reduction in the TSS from baseline to Week 24

- Proportion of patients with a baseline platelet count < 50,000/µL achieving >

35% reduction in spleen volume from baseline to Week 24 as measured by MRI or CT

- Proportion of patients with a baseline platelet count < 50,000/µL achieving >

50% reduction in in the TSS from baseline to Week 24

Study description

Background summary

For a subgroup of patients with myelofibrosis (MF) with low platelet counts, the almost approved JAK inhibitor requires significant dose reduction and is less effective than in patients with normal platelet counts.
Data from two phase 2 trials show that pacritinib can be safely administered to patients with MF, including those who also have thrombocytopenia. Pacritinib led to clinically meaningful reduction in spleen size and volume in a substantial proportion of patients with MF. Pacritinib improved disease-related symptoms. These effects were observed in patients with thrombocytopenia, including those with platelet counts < 100,000/ul, as well in those with normal platelet counts. These findings warrant phase 3 investigation to confirm the efficacy and safety of pacritinib, both in patients with normal and those with low platelet counts.

Study objective

Primary Objective:
To compare the efficacy of pacritinib with that of Best Available Therapy (BAT) in patients with PMF, PPV-MF, or PET-MF; the efficacy measure for this analysis is the proportion of patients achieving a * 35% reduction in spleen volume from baseline to Week 24 by MRI or CT

Secundary Objective:
The key secundary objective is to compare pacritinib with BAT with respect to the proportion of patients with * 50% reduction in total score from baseline to Week 24 on the MPN-SAF TSS2.0.

Study design

This is an open randomized trial.

Intervention

The Pacritinib group:
The start dose is 4 x 100 mg capsules Pacritinib, once per day orally, at the

same time of day, with or without food.
A maximum of two dose reductions is allowed. The first dose reduction will be a 100-mg reduction from the original dose (reduction from 400 mg/day to 300 mg/day). The second dose reduction will be another 100-mg reduction (reduction from 300 mg/day to 200 mg/day). Once the dose is reduced, no re-escalation is allowed.

Best Available Therapy group:
Patients in the best available therapy group will NOT receive Pacritinib, but the research physician will chose the best available treatment. The treatment can be changed at any moment during the study and it is not allowed to use investigational drugs. At Week 24 or based on the test results patients my be eligible to cross over to the Pacritinib group during the study.

Study burden and risks

Pacritinib has been investigated in 130 patients with myelofibrosis, including PMF and Post PV/ET MF. The most common adverse events (in at least 10% of the patients) that do or do not have a relationship with the study medication are low platelet counts (thrombocytopenia), low red blood cell count (anemia), diarrhea, nausea, vomiting and fatigue. Many of these adverse events are also symptoms of the disease.
Possible adverse events of blood collection and bone marrow tests are pain, fatigue, bruising, painful and sensitivity of the collection spot and in rare cases an infection could occur.

Possible adverse events of the tape that is put on the skin when making an ECG are rash or mild irritation of the skin.

During a CT-scan of the abdomen patients are exposed to radiation. The dose of the radiation is approximately 10 mSv (millisievert), which is comparable with the exposure to natural background radiation during approximately 3 years. This exposure can slighly increase the risk of getting cancer. If the patient cannot have a MRI scan, the research physician can choose for a CT-scan instead of a MRI. In that case the research physician will be available to explain why a CT-scan is more suitable than an MRI-scan and to answer potential questions regarding the difference in risk between the two procedures.

Patients will be asked to come to the hospital at Screening, Baseline, Week 2, 4, 8, 12, 16, 20, 24 every 12 weken thereafter until progression of the disease. The normal visits will take approxmately 30 minutes. For patients in the Pacritinib arm and patients in the Best Available Therapy arm who went cross-over to Pacritinib an additional ECG has to be performed 4 hours after taking Pacritinib. at the Start of Week 1, 2 and 3 visits. The visits with a CT or MRI (at Baseline and then every 12 weeks until progression) will take approximately 1 hour.

Contacts

Public
CTI BioPharma Corp.

Suite 600, Western Avenue 3103
Seattle WA 98121
US
Scientific
CTI BioPharma Corp.

Suite 600, Western Avenue 3103
Seattle WA 98121
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1). Intermediate 1 or 2 or high-risk PMF, PPV-MF, or PET-MF (Passamonti et al 2010)
2). Palpable splenomegaly * 5 cm below LCM in midclavicular line by physical examination
3). Total Symptom Score (TSS) * 13 on the MPN-SAF-TSS2.0, not including te inactivity question.
4). Age * 18 years old
5). ECOG performance status 0-3
6). Peripheral blast count < 10%
7). Absolute neutrophil count > 500/*L
8). Patients who are platelet or red blood cell transfusion-dependent are eligible
9). Adequate liver and renal function, defined by liver transaminases (AST/SGOT and ALT/SGPT) * 3 × ULN (AST/ALT * 5 × ULN if transaminase elevation is related to MF), direct bilirubin * 4 x ULN, and creatinine * 2.5 mg/dL

10). At least 6 months from prior splenic irradiation
11). At least 12 months from prior 32P therapy
12). At least 1 week since prior treatment (most recent dose) with a potent CYP3A4 inhibitor
13). At least 4 weeks since any experimental treatment for PMF, PPV-MF, or PET-MF
14). At least 2 weeks since any treatment for PMF, PPV-MF, or PET-MF
15). If fertile, both males and females must agree to use effective birth control. Women of childbearing potential must use highly effective methods (defined as those resulting in a failure rate of <1% per year when used consistently and correctly) for the duration of study treatment and for 12 months after last dose of study drug. The contraceptive methods considered highly effective are intrauterine devices and hormonal contraceptives (contraceptive pills, implants, transdermal patches, hormonal vaginal devices, or injections with prolonged release).
16). Willingness to undergo and ability to tolerate frequent MRI or CT assessments on study
17). Ability to understand and willingness to complete symptom assessments using a patient reported outcomes instrument
18). Ability to understand and willingness to sign the informed consent form

Exclusion criteria

1). Any GI or metabolic condition that could interfere with absorption of oral medication
2). Life expectancy < 6 months
3). Prior treatment with a JAK2 inhibitor
4). Completed ASCT or eligible and willing to complete ASCT
5). History of splenectomy or planning to undergo splenectomy
6). Uncontrolled intercurrent illness, including but not limited to ongoing active infection or psychiatric illness or social situation that the treating physician judges would limit compliance with study requirements
7). Other malignancy within last 3 years other than curatively treated basal cell or squamous cell skin cancer, carcinoma in situ of the cervix, organ-confined or treated nonmetastatic prostate cancer with negative prostate-specific antigen, in situ breast carcinoma after complete surgical resection, or superficial transitional cell bladder carcinoma
8). Inflammatory or chronic functional bowel disorder such as Crohn disease, inflammatory bowel disease, chronic diarrhea, or constipation
9). Clinically symptomatic and uncontrolled cardiovascular disease
10). History of myocardial infarction, severe/unstable angina, or symptomatic congestive heart failure within 6 months prior to study randomization
11). New York Heart Association Class II, III, or IV congestive heart failure
12). Patients with CTCAE grade 2 cardiac dysrhythmias may be considered for inclusion, with approval of the medical monitor, if the arrhythmias are stable, aymptomatic and unlikely to affect patient safety. Ongoing cardiac dysrythmias of CTCAE * grade 3, corrected QTc prolongation > 450 ms or other factors that increase the risk for QT prolongation (eg, heart failure, serum potassium < 3.0 mEq/L, family history of long QT interval syndrome) are excluded.
13). Erythropoietic agent within 28 days prior to randomization
14). Thrombopoietic agent within 14 days prior to randomization

15). Known seropositivity for HIV
16). Known active hepatitis A, B, or C
17). Women who are pregnant or lactating

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-06-2013
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	niet van toepassing
Generic name:	Pacritinib

Ethics review

Approved WMO

Date:	25-01-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	10-04-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-06-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-09-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-10-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	06-11-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2012-004239-21-NL
CCMO	NL42821.029.12