A phase II trial in patients with myelofibrosis (primary, post-ET or post PV-MF) treated with the selective JAK2 inhibitor Pacritinib before reduced-intensity conditioning allogeneic stem cell transplantation

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Improve allo-SCT transplant outcome using a uniform conditioning regimen and pacritinib pretreatment by means of the proportion of patients with a failure within 6 months post-transplant. Events that are considered a failure are: primary graft...

Ethical review	Approved WMO
Status	Completed
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON47477

Source
ToetsingOnline

Brief title
HOVON 134 MF

Condition

- Leukaemias

Synonym
Myelofibrosis, post-essential thrombocytosis, post-polycythemia vera, primary myelofibrosis

Research involving

Human

Sponsors and support

Primary sponsor: HOVON
Source(s) of monetary or material Support: KWF Kankerbestrijding;stichting HOVON;Neovii,Neovii

Intervention

Keyword: Myelofibrosis, Pacritinib

Outcome measures

Primary outcome

Among the patients who received an allo-SCT, the proportion of patients with

failure within or at D180 post-transplant. Events that are considered a failure

are:

o Primary graft failure;

o Acute graft versus host disease grade 3-4;

o Secondary graft failure

o Death, whatever the cause

Secondary outcome

• Adverse events

• Proportion of patients receiving allo-SCT

• Response rate (>= PR)

• Progression free survival

• Overall survival (OS) calculated from either registration or allo-SCT.

Patients still alive or lost to follow up are censored at the date they were

last known to be alive

• Relapse mortality (RM), i.e. death due to the disease or after progression

• Non-relapse mortality(NRM)

• Quality of Life during/after treatment

Study description

Background summary

The only curative treatment for patients with myelofibrosis (MF) is allogeneic stem cell transplantation (SCT). Treatment with JAK2 inhibitors like pacritinib improves condition of MF patients, decreases spleen size and might diminish graft-versus-host disease (GvHD), thereby improving the outcome of SCT

Study objective

Improve allo-SCT transplant outcome using a uniform conditioning regimen and pacritinib pretreatment by means of the proportion of patients with a failure within 6 months post-transplant. Events that are considered a failure are: primary graft failure; secondary graft failure; acute GvHD grade 3-4; death whatever the cause is.

Study design

Phase II, single arm multicenter

Intervention

Induction with 3-4 cycles pacritinib, followed by allo-SCT if suitable donor available. All patients will receive the same treatment.

Study burden and risks

Benefit for participating patients consists of improvement of MF-related symptoms before allo-SCT, decrease of spleen size and thereby improvement of clinical condition and transplantation outcome. Nevertheless, pacritinib treatment can be associated with side-effects (gastro-intestinal).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Patients with a confirmed diagnosis of post-ET, post-PV or primary myelofibrosis
- Intermediate-2 or high-risk according to DIPSS plus
- Age 18-70 years inclusive
- WHO performance status 0-2
- Platelet count >= 25 × 109/L without platelet support within 2 weeks before study entry.
- All men and women of childbearing potential must agree to use adequate contraception during the study
- Written informed consent
- Patient is capable of giving informed consent

Exclusion criteria

- Patients who have been treated with pacritinib as their previous JAK2 inhibitor treatment cannot participate in this study.
- Previous treatment with JAK2 inhbitors, other than pacritinib, is allowed

with the exception of high dose ruxolitinib (above 10 mg BID). For these patients taper the dose to 10 mg BID or lower at least 2 weeks before pacritinib treatment is allowed.
- Any GI or metabolic condition (e.g. inflammatory or chronic functional bowel disorder such as Crohn*s Disease, Inflammatory Bowel Disease, chronic diarrhea or constipation) that could interfere with absorption of oral medication
- Left ventricular cardiac ejection fraction of <= 45% by echocardiogram or multigated acquisition (MUGA) scan
- Impaired liver and renal function, defined by liver transaminases (aspartate aminotransferase [AST]/serum glutamic oxaloacetic transaminase [SGOT] and alanine aminotransferase [ALT]/serum glutamic pyruvic transaminase [SGPT]), >3 × the upper limit of normal (ULN) (AST/ALT >5 × ULN if transaminase elevation is related to MF), direct bilirubin >4× ULN, and creatinine clearance * 40 ml/min.
- Impaired coagulation function, defined by prothrombin time (PT)/international normalized ratio (INR), partial thromboplastin time (APTT)>1.5 x ULN.
- Experimental treatment within four weeks before inclusion for PMF, Post-PV, or Post-ET MF
- Severe pulmonary dysfunction (CTCAE grade III-IV, see appendix D)
- Treatment with a potent strong CYP3A4 inhibitor or a strong cytochrome P450 (CYP450) inducer within the last 2 weeks
- Treatment with anticoagulation or antiplatelet agents, except for aspirin dosages of <=100 mg per day, within the last 2 weeks
- New York Heart Association Class II, III, or IV congestive heart failure
- QTc prolongation >450 ms as assessed by ECG and corrected by Federicia method or other factors that increase the risk for QT interval prolongation (e.g., heart failure, hypokalemia [defined as serum potassium <3.0 mEq/L that is persistent and refractory to correction], family history of long QT interval syndrome, or concomitant use of medications that may prolong QT interval)
- Significant recent bleeding history defined as NCI CTCAE grade >=2 within the last 3 months, unless precipitated by an inciting event (e.g., surgery, trauma, injury)
- Any history of CTCAE grade >=2 non-dysrhythmia cardiac conditions within the last 6 months. Patients with asymptomatic grade 2 non-dysrhythmia cardiac conditions may be considered for inclusion, with the approval of the principal investigator, if stable and unlikely to affect patient safety.
- Any history of CTCAE grade *2 cardiac dysrhythmias within the last 6 months. Patients with non-QTc CTCAE grade 2 cardiac dysrhythmias may be considered for inclusion, with the approval of the principal investigator, if the dysrhythmias are stable, asymptomatic, and unlikely to affect patient safety.
- Patients with active, uncontrolled infections
- Patients known to be HIV (human immunodeficiency virus)-positive
- Active hepatitis A, B or C
- History of active malignancy during the past 3 years, except basal carcinoma of the skin or stage 0 cervical carcinoma
- Concurrent severe and/or uncontrolled medical condition (e.g. uncontrolled

diabetes, infection, hypertension, cancer, etc.)
- Pregnant or breastfeeding women
- Any psychological, familial, sociological and geographical condition
potentially hampering compliance with the study protocol and follow-up schedule

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	11-07-2018
Enrollment:	65
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	pacritinib

Ethics review

Approved WMO

Date:	03-02-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	18-08-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-12-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-01-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-02-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-03-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-09-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-09-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-09-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	27-09-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-03-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-04-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-09-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-08-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-08-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-12-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-06-2024

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-07-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2015-000195-98-NL
CCMO	NL52462.078.15

Study results

Date completed: 31-12-2024

Summary results
Trial ended prematurely