A Phase 3, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Study of Fostamatinib Disodium in the Treatment of Persistent/Chronic Immune Thrombocytopenic Purpura

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

Summary

ID

NL-OMON42185

Source
ToetsingOnline

Brief title
Rigel-047

Condition

- Platelet disorders

Synonym
immune thrombocytopenic purpura

Research involving
Human

Sponsors and support

Primary sponsor: INC Research
Source(s) of monetary or material Support: Industry

Intervention

Keyword: fostamatinib

Outcome measures

Primary outcome

The primary efficacy endpoint is achieving a stable thrombocyte response in week 24, defined as a thrombocyte count of at least 50,000/µl during at least 4 out of the 6 visits between week 14*24. Subjects who discontinue the treatment prior to week 24 due to a lack of efficacy or a side effect, or who receive an emergency treatment after 10 weeks, are considered as non-responders.

Secondary outcome

The secondary efficacy endpoints of this study are:

• Achieving a thrombocyte response (a thrombocyte count of at least 50,000/µl) in week 12.

• Achieving a thrombocyte response (a thrombocyte count of at least 50,000/ µl) in week 24.

• In subjects with a thrombocyte count at baseline < 15,000/µl, achieving a count >= 30,000/µl, and at least 20,000/µl above baseline, in week 12.

• In subjects with a thrombocyte count at baseline < 15,000/µl, achieving a count >= 30,000/µl, and at least 20,000/µl above baseline, in week 24.

• Frequency and severity of the bleeding according to the ITP Bleeding Score

(IBLS) during the study period of 24 weeks.

• Frequency and severity of the bleeding according to the bleeding scale of the

World Health Organization (WHO) during the study period of 24 weeks.

Study description

Background summary

Fostamatinib is an investigational drug which is being tested for persistent/chronic immune thrombocytopenic purpura (ITP), a disorder manifested by immune mediated platelet destruction. ITP is a disorder that results when your platelets are destroyed by your immune system. Your ITP is considered to be persistent/chronic if your platelet count has regularly been below 30,000/µL for at least 3 months and you don*t have any other conditions that are causing your platelets to be destroyed.

The purpose of this research study is to see how effective fostamatinib is at increasing your platelet count, by measuring whether the number of platelets you have increases when the study drug is taken.

Study objective

• The primary objective of this study is to establish the efficacy of fostamatinib as compared with placebo in achieving a stable platelet response in subjects with persistent/chronic ITP.

• Secondary objectives include assessment of the incidence of bleeding complications in subjects receiving fostamatinib as compared with placebo, and assessment of the overall safety and tolerability of fostamatinib versus placebo in subjects with persistent/chronic ITP.

Study design

This is a phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel group study of the efficacy of a 24 week treatment with fostamatinib (R788) vs. placebo to achieve a stable thrombocyte response in subjects with persistent/chronic ITP.

Patient participation in this study include approximately 16 study visits over 30 weeks.

During the 24 week treatment period, subjects are expected to visit the clinic

13 times (including visit 3). During each visit, safety assessments and thrombocyte counts are carried out to assess the safety and efficacy of fostamatinib/placebo and to determine if the dose should be adjusted.

From week 4 the initial dose of fostamatinib 100 mg PO twice daily or corresponding placebo should be increased to fostamatinib 150 mg PO twice daily or corresponding placebo based on the thrombocyte count and tolerability. However, the dose can be lowered at any time to a dose as low as fostamatinib 100 mg PO once daily or corresponding placebo if dose-restricting side effects are observed. The thrombocyte count is assessed in a local laboratory.

Before randomizing a subject to the double-blind treatment, all therapeutic agents, other than those allowed as concomitant treatment (glucocorticoids, < 20 mg prednisone/day equivalent or azathioprine or danazol), should be stopped in accordance with the wash-out periods.

Intervention

After qualifying during the screening period of the study, subjects are randomized in a 2:1 ratio to 1 of 2 treatment groups: fostamatinib 100 mg PO twice daily or corresponding placebo. During the 24 week treatment period, subjects will administer the study drug themselves in the morning and in the evening.

Study burden and risks

The associated benefit of treatment with fostamatinib outweighs any potential risks for subjects participating in the study.

Subjects who complete the planned treatment period successfully, will be given the opportunity to receive an open-label fostamatinib treatment in a long-term extension study.

Non-responders, subjects with the thrombocyte count of < 50,000/µl or those who are not able to achieve a thrombocyte increase of at least 20,000/µl (if the thrombocyte count was < 15,000/µl at baseline) can proceed to receiving open-label fostamatinib in the long-term extension study, C935788-049, starting week 12, provided that they have received 150 mg PO twice daily for at least 4 weeks (unless this higher dose was not tolerated well).

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

1.Subject must be willing and able to give written informed consent by signing an IRB approved Informed Consent Form prior to undergoing any study-specific procedures.;2.Subject must have had a diagnosis of ITP for at least 3 months and no known etiology for thrombocytopenia. ;3.Subject*s platelet count averages < 30,000/µL (and none > 35,000 unless as a result of rescue therapy) from at least 3 qualifying counts within the preceding 3 months. At least 2 of the qualifying counts must have been taken during the screening period. ;4.Must have previously received at least 1 typical regimen for the treatment of ITP. The typical regimen can include such approved agents as: a thrombopoietin (romiplostim, eltrombopag), unless contraindicated; corticosteroids with or without splenectomy; intravenous immunoglobulin.;5.Male or female at least 18 years of age.;6.Performance status on Karnofsky performance status scale (KPS) >=70 ;7.Subject*s concurrent treatment for ITP may consist of either glucocorticoids (< 20 mg prednisone equivalent per day), or azathioprine or danazol. The dose of the concurrent medication must have been stable for 14 days prior to baseline and must be expected to remain stable throughout the study. No other concurrent medications for ITP are permitted.;8.Subject*s other therapeutic agents for ITP have been discontinued in accordance with the washout periods;9.Female subject must be either post-menopausal for at least 1 year or surgically sterile; or if female of child-bearing potential, must not be pregnant or lactating and must

agree to use an acceptable method of birth control throughout the duration of the trial and for 30 days following the last dose. Acceptable methods of birth control are defined as: hormonal contraception (pill, injection or implant) used consistently for at least 30 days prior to screening, an intrauterine device (IUD), a double-barrier method (ie, condom and spermicide, or condom and diaphragm), or complete abstinence.;10.In the Investigator*s opinion, the subject has the ability to understand the nature of the study and any hazards of participation and to communicate satisfactorily with the Investigator.

Exclusion criteria

1.Subject with ITP associated with lymphoma, chronic lymphocytic leukemia, viral infection, autoimmune disorders, thyroid disease, human immunodeficiency virus, or hepatitis or induced or alloimmune thrombocytopenia, or thrombocytopenia associated with myeloid dysplasia. ;2.Subject with autoimmune hemolytic anemia.;3.Subject has a history of or active, clinically significant, respiratory, gastrointestinal (pancreatitis), renal, hepatic, neurological, psychiatric, musculoskeletal, genitourinary, dermatological, or other disorders that, in the Investigator*s opinion, could affect the conduct of the study or the absorption, metabolism or excretion of the study drug. ;4.Subject has had any major cardiovascular event within the 6 months prior to randomization, including but not limited to; myocardial infarction, unstable angina, cerebrovascular accident, pulmonary embolism, or New York Heart Association Class III or IV heart failure.;5.Subject has uncontrolled or poorly controlled hypertension, defined as systolic blood pressure >= 140 mm Hg, or diastolic blood pressure >= 90 mm Hg, whether or not the subject is receiving anti-hypertensive treatment. Subjects may be rescreened if the blood pressure is successfully and promptly controlled (within 30 days) using conventional anti-hypertensive therapy to achieve optimal blood pressure control (< 140/90 mmHg).;6.Subject has a history of coagulopathy including prothrombotic conditions such as Factor V Leiden, APC resistance, AT-III deficiency and lupus anticoagulant, or arterial or deep venous thrombosis within 6 months prior to randomization. ;7.In subjects with deep venous thrombosis greater than 6 months prior to randomization, anticoagulants must have been discontinued for at least 30 days and subsequent D dimer must be within normal limits for the site*s local laboratory. ;8.Subject has a bleeding assessment score of Grade 2 at any site by the ITP Bleeding Scale (IBLS).;9.Subject has 1 or more of the following laboratory abnormalities: leukocyte count < 2,500/µL, neutrophil count of < 1,500/µL, lymphocyte count < 750/µL, Hgb < 10 g/L without ongoing transfusion support, or transaminase levels (ALT, AST) > 1.5x ULN, total bilirubin > 2.0 mg/dL, or estimated glomerular filtration rate (eGFR) < 30 mL/min at the time of screening.
10.Subject has a significant infection, or an acute infection such as influenza, or is known to have an active inflammatory process at the time of screening and/or baseline (Day 1). ;11.Subject has acute gastrointestinal symptoms at the time of screening and/or baseline (eg, nausea, vomiting, diarrhea, abdominal pain). ;12.Subject has increased the dose of, or added, prescription drugs within the 2 weeks prior to Day 1, unless agent is agreed to be not clinically relevant by both the Investigator and Sponsor. ;13.Subject has had positive results for HIV, HBV, or HCV by standard serologic tests.;14.Subject has received any blood or blood products within the 2 weeks prior to randomization. (IVIg or anti-rho (D) immunoglobulin (anti-D IgG) are allowed if used for rescue therapy, unless platelet count is > > -30,000/µL at

the time of randomization.);15.Subject is currently enrolled in an investigational drug or device study or has used an investigational drug or device within 30 -days or 5 half-lives (whichever is longer) of Day 1.;16.Subject has a history of alcohol or substance abuse that, in the judgment of the Investigator, may impair or risk the subject*s full participation in the study.;17.Subject has a known allergy and/or sensitivity to the test article or its components.;18. Subject has had major surgery within 28 days prior to randomization or has a surgical wound that is not fully healed.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-03-2015
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Fostamatinib disodium tablets
Generic name:	Fostamatinib

Ethics review

Approved WMO

Date:	27-05-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	03-10-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	19-02-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	24-02-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	08-01-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	12-02-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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	EUCTR2013-005452-15-NL
ClinicalTrials.gov	NCT02076399
CCMO	NL49120.098.14