A Phase 1b, Randomized, Double-Blind (Sponsor Open), Placebo-Controlled Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of PF-04447943, Co-Administered with and Without Hydroxyurea, in Subjects with Stable Sickle Cell Disease

Published: 01-06-2015
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Primary ObjectiveTo determine the safety and tolerability of multipledoses of PF-04447943 Secondary ObjectiveTo characterize the PK of PF-04447943 in plasma following oral administrationExploratory ObjectivesTo evaluate biomarkers that may be...

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

Summary

ID

NL-OMON44079

Source
ToetsingOnline

Brief title
PF-04447943 in SCD patients

Condition

- Haemoglobinopathies
- Blood and lymphatic system disorders congenital

- Vascular disorders NEC

Synonym
Sickle cell anemia

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer
Source(s) of monetary or material Support: Pfizer;inc.

Intervention

Keyword: Anemia, endothelium, PDE9 inhibitor, sickle cell disease

Outcome measures

Primary outcome

Safety will be assessed through adverse events, changes in laboratory results,

changes in ECG measurements, and changes in vital sign measurements

Secondary outcome

Pharmacokinetic endpoints will include plasma PF-04447943 AUC(0-12h), C12h,

Cmax, and Tmax on Days 1. C1h and C2h will also be measured on Days 7 to assess

steady-state Cmax.

Pharmacodynamic endpoints will include:

Plasma cGMP

Markers associated with cellular adhesion:

E-selectin, P-selectin

ICAM, VCAM

Platelet-monocyte aggregates, platelet neutrophil aggregates

MAC-1 expression on monocytes and neutrophils

Markers associated with coagulation:

Tissue Factor

Thrombin-Antithrombin Complexes

Prothrombin Fragments F1 + F2

D-dimers;

Circulating endothelial microparticles

Hemoglobin F

Study description

Background summary

This study is the first evaluation of PF-04447943, a selective inhibitor of the cyclic guanosine monophosphate (cGMP) specific phosphodiesterase-9A (PDE9A) enzyme, in subjects with sickle cell disease (SCD). The goal is to assess the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) in subjects with stable sickle cell disease with and without co-administration of hydroxyurea (HU). This study will also aid in
dose selection and evaluation of exploratory biomarkers.
(see page 17)

Study objective

Primary Objective
To determine the safety and tolerability of multipledoses of PF-04447943
Secondary Objective
To characterize the PK of PF-04447943 in plasma following oral administration
Exploratory Objectives
To evaluate biomarkers that may be informative in demonstrating the pharmacologic effect and to characterize the pharmacodynamics of PF-04447943

Study design

A Randomized, Double-Blind (Sponsor Open), Placebo-Controlled multi center Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of PF-04447943 in SCD patients, Co-Administered with and Without Hydroxyurea.

Intervention

Multiple doses of PF-04447943 or placebo.

Study burden and risks

Burden: PF-04447943/placebo administration, measurements, blood sampling, compliance with strict lifestyle restrictions and time investment.
Risks: potential side effects of PF-04447943 and potential complaints caused by being fasted and blood sample collection

Contacts

Public
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US
Scientific
Pfizer

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

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

Inclusion criteria

- Stable SCD patients (Hbss or HbSB-thalasamia)
- Male/female, age 18-65, BMI 17.5-35, incl
(see protool p31)

Exclusion criteria

- Recent Vaso occlusive crisis (<2 months)
- Severe infection (<1 month)
- Recent surgery (<3 months)
-Use of CYP3A4 inhibitors/inducers; use of PDE5 inhibitors; use of QT-prolonging medication/medication lowering seizure threshold
-History of cerebrovascular accident or seizure disorder
(see protocol p32)

Study design

Design

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):	06-01-2016
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	PF-04447943
Generic name:	PF-04447943

Ethics review

Approved WMO Date:	01-06-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-02-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-02-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2014-001677-13-NL

Register	ID
CCMO	NL53295.056.15
Other	US IND Number 119,467