

# 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 Objective To determine the safety and tolerability of multiple doses 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...

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruitment stopped
<b>Health condition type</b>	Haemoglobinopathies
<b>Study type</b>	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 multiple doses 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

Pfizer

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US

### Scientific

Pfizer

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Cambridge MA 02139  
US

## 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 protocol 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
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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**

CCMO

Other

**ID**

NL53295.056.15

US IND Number 119,467