A Phase 1, Randomized, Double-Blind, Placebo-Controlled, Single- and Multiple-Dose Escalation Study Evaluating Safety and Pharmacokinetics of VX-983 Followed by an Open-Label, Randomized, Crossover Study to Estimate the Effect of Steady State Administration of VX-983 on the Pharmacokinetics of a Single, Oral Dose of Midazolam in Healthy Adult Subjects

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

Summary

ID

NL-OMON37286

Source
ToetsingOnline

Brief title
VX-983 FIH SAD, MAD, Midazolam DDI study in healthy volunteers

Condition

- Respiratory disorders congenital

Synonym
Cystic fibrosis

Research involving
Human

Sponsors and support

Primary sponsor: Vertex Pharmaceuticals
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: Cystic fibrosis, Midazolam, VX 983

Outcome measures

Primary outcome

Safety and tolerability will be based on the assessment of adverse events,

clinically significant laboratory test results, 12-lead lectrocardiograms

(ECGs), and vital signs.

Secondary outcome

Parts A and B: PK parameters will be calculated for VX-983 and its metabolites

(if possible) from plasma and urine samples collected in this

study

Part C: PK parameters will be calculated for midazolam, 1-OHmidazolam, VX-983,

and its metabolites (if possible) from plasma samples collected in this study

Study description

Background summary

VX-983 is a new investigational compound that may eventually be used for the treatment of Cystic Fibrosis. Cystic fibrosis is a genetic disorder that cause the body to produce unusually thick mucus. The thick mucus results in malfunction of organs like the lungs, pancreas and liver.
VX-983 is not registered as a drug and this is the first time that this compound is being given to humans.

Study objective

The study will consist of three parts, part A, B and C. The main purpose of the study is to investigate to what extent VX-983 is safe and tolerated. In addition, it will be investigated how quickly and to what extent VX-983 is absorbed and eliminated from the body (this is called pharmacokinetics). In part A single ascending doses will be investigated and in part B multiple ascending doses will be investigated. In part C the effect of VX-983 on the absorption and elimination of midazolam from the body will be investigated.

Study design

Part A:
The study will consist of 1 period during which you will stay in the clinical research centre in Zuidlaren for 6 days (5 nights).
During the study you will receive VX-983 or inactive formulation (placebo) in an oral suspension after 8 hours of fasting (no food or drinks) with 240 mL of tap water. Six participants will receive VX-983 and 2 participants will receive placebo in each group. Before and after the administration of the study medication a Listerine strip will be administered. This is a small, paper-thin strip that dissolves on the tongue and gives a strong mint taste; which will mask the bitter taste of study medication.
Whether you will receive the active drug or placebo will be determined by chance.

Part B:
The study will consist of 1 period during which you will stay in the clinical research centre in Zuidlaren for 15 days (14 nights).
During the study you will receive VX-983 or inactive formulation (placebo) in an oral suspension after 8 hours of fasting (no food or drinks) with 240 mL of tap water. Six participants will receive VX-983 and 2 participants will receive placebo in each group. Before and after the administration of the study medication a Listerine strip will be administered. This is a small, paper-thin strip that dissolves on the tongue and gives a strong mint taste; which will mask the bitter taste of study medication.
Whether you will receive the active drug or placebo will be determined by chance.

Part C:

The study will consist of 2 periods during which you will stay in the clinical research centre in Zuidlaren for 5 days (4 nights) and 12 days (11 nights). The time interval between the different periods (from discharge first period to admission second period) is 5 days. The time interval between the last dose of study drug of the first period and the first dose of study drug in period 2 will be a minimum of 7 days.
During the study you will receive VX-983 or midazolam in an oral suspension after 8 hours of fasting (no food or drinks) with 240 mL of tap water. Before and after the administration of the study medication a Listerine strip will be administered. This is a small, paper-thin strip that dissolves on the tongue and gives a strong mint taste; which will mask the bitter taste of study medication.

Intervention

Part A: single dose of VX 983 or placebo after 8 hours fasting period in the form of an oral suspension.
Part b: multiple doses of VX 983 or placebo after 8 hours fasting period in the form of an oral suspension.
Part C: treatment A: On Day 1 a single oral dose of 2 mg midazolam will be administered; treatment B: On Day 1 through 9 an oral dose of VX-983 will be administered. On Day 10 VX-983 is administered together with a single oral dose of 2 mg midazolam.

Study burden and risks

Procedures: pain, light bleeding, heamatoma, possibly an infection.

As VX-983 will be administered to men for the first time in this study, so to date adverse effects in men have not been reported. VX-983 has been studied in animals. It was generally well tolerated by animals (rats and dogs). After administration of very high doses, beyond what will be administered in this study, for several weeks the most frequently seen adverse effect was a decrease in food consumption with weight loss, and less frequently diarrhea, vomiting, decreased activity and a lack of voluntary coordination of muscle movements (ataxia).

After the administration of Midazolam® one will probably become very sleepy for the first few hours. The most frequent adverse effects reported are muscle weakness, dizziness, memory loss and gastrointestinal complaints.

Contacts

Public

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

healthy male and female subjects
18-55 yrs, inclusive
BMI: 18.0-31.0 kg/m2, inclusive

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-01-2013
Enrollment:	92
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Midazolam
Generic name:	Midazolam
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	21-12-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-05-2013
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	EUCTR2012-005067-26-NL
CCMO	NL42917.056.12