A Randomized, Placebo- and Active-Controlled, Double-Blind, 4-way Crossover Design, Thorough ECG Study of VX-770 in Healthy Adult Subjects

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Part A:To evaluate the safety and tolerability of increasing doses of VX-770 up to 450 mg (q12h) in healthy male subjects.Part B:To determine if therapeutic or supratherapeutic systemic exposure to multiple doses of VX 770 prolongs the mean…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital and hereditary disorders NEC
Study type	Interventional

Summary

ID

NL-OMON34380

Source
ToetsingOnline

Brief title
Safety, tolerability and QT/QTc study for VX-770

Condition

- Congenital and hereditary disorders NEC

Synonym
Cystic Fibrosis

Research involving
Human

Sponsors and support

Primary sponsor: Vertex Pharmaceuticals

Source(s) of monetary or material Support: Vertex Pharmaceuticals Incorporated

Intervention

Keyword: CFTR, Cystic Fibrosis, VX-770

Outcome measures

Primary outcome

Part A

Safety and tolerability of VX 770 as measured by standard 12 lead electrocardiograms (ECGs), adverse events, physical examinations, vital signs, and clinically significant laboratory assessments.

Part B

Time-matched, baseline-adjusted, placebo-subtracted QTcF interval obtained from continuous 12-lead ECG recording.

Secondary outcome

Part A

- PK parameters of VX 770 and metabolites M1 and M6 in plasma

Part B

- Time-matched, baseline-adjusted, placebo-subtracted QT interval obtained from continuous ECG recording

- Time-matched, baseline-adjusted, placebo-subtracted QTcB interval obtained from continuous ECG recording

- PK parameters of VX 770 and its metabolites in plasma

- Safety of VX 770 as measured by standard 12 lead ECGs, adverse events,

physical examinations, vital signs, and clinically significant laboratory

assessments.

Study description

Background summary

The drug VX-770 to be given is a new, investigational compound that may eventually be used for the treatment of cystic fibrosis.

Cystic Fibrosis is a genetic disorder known to be an inherited disease of the secretory glands, including the glands that produce mucus and sweat. The gene known as CFTR is responsible for aiding in the regulation of salt and water absorption and secretion in various tissues. This function is defective in people with Cystic Fibrosis and supports the theory that by restoring or improving CFTR function that the symptoms of Cystic Fibrosis would be reduced. VX-770 may be effective in the restoration of CFTR and it is therefore possible that it could reduce the symptoms experienced by sufferers of Cystic Fibrosis.

Study objective

Part A:
To evaluate the safety and tolerability of increasing doses of VX-770 up to 450 mg (q12h) in healthy male subjects.

Part B:
To determine if therapeutic or supratherapeutic systemic exposure to multiple doses of VX 770 prolongs the mean Fridericia-corrected QT (QTcF) interval by more than 5 msec (based on an upper bound of 1 sided 95% confidence interval of 10 msec) in healthy male and female subjects, as compared with placebo dosing and baseline.

Study design

Part A will be a double-blind, randomized, placebo-controlled, single-center dose-escalation study investigating oral VX 770 in increasing doses up to 450 mg q12h in healthy male subjects. The safety and tolerability of this dose will be used to confirm the supratherapeutic dose of VX 770 to be used in Part B.

Part B will be a double-blind, randomized, placebo-, and active-controlled, single-center, 4 period crossover study of the effect of VX 770 on QT/QTc

intervals in healthy male and female subjects.

Intervention

Part A
An oral dose of 250 mg VX-770 or placebo twice daily on Day 1, an oral dose of 300 mg VX-770 or placebo twice daily on Day 2, an oral dose of 350 mg VX-770 or placebo twice daily on Day 3, an oral dose of 400 mg VX-770 or placebo twice daily on Day 4 and an oral dose of 450 mg VX-770 or placebo twice daily on Days 5-9

Part B
Therapeutic dose: an oral dose of 150 mg VX-770 twice daily on Days 1-4 and an oral dose of 150 mg VX-770 on Day 5
Supratherapeutic dose: an oral dose of 450 mg VX-770 twice daily on Days 1-4 and an oral dose of 450 mg VX-770 on Day 5
Placebo control: an oral dose of placebo twice daily on Days 1-4 and an oral dose of placebo on Day 5
Positive control: an oral dose of placebo twice daily on Days 1-4 and an oral dose of 400 mg moxifloxacin on Day 5

Study burden and risks

Procedures:
Pain, light bleeding, heamatoma and possibly an infection.

Contacts

Public
Vertex Pharmaceuticals

130 Waverly St
Cambridge, Massachusetts, 02139-4242
US
Scientific
Vertex Pharmaceuticals

130 Waverly St
Cambridge, Massachusetts, 02139-4242
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Part A
Male
Age 18-45
Non-smoking;Part B
Male and females
Age 18-45
Non-smoking

Exclusion criteria

Suffering from: hepatitis B, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of the study. In case of donating any blood or significant loss of blood within 60 days of the start of drug dosing.

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):	11-05-2010
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	29-04-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-05-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-06-2010
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-06-2010
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-06-2010
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	EUCTR2010-019580-11-NL
CCMO	NL32243.056.10