A Phase 1, Randomized, Placebo- and Active-Controlled, Double-Blind, Parallel, Electrocardiogram Study to Evaluate the Effect of VX-661 on the QT/QTc Interval in Healthy Subjects

Published: 08-07-2015
Last updated: 19-04-2024

The purpose of Part A is to investigate how safe the study compound is and how well the study compound is tolerated. The study will also investigate how quickly and to what extent the compound is absorbed into and eliminated from the body (this is...

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

Summary

ID

NL-OMON42529

Source
ToetsingOnline

Brief title
VX15-661-010 QTc study

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, QT/QTc interval

Outcome measures

Primary outcome

Part A:

To evaluate the safety and tolerability of multiple ascending doses of VX-661

in healthy subjects.

Part B:

To evaluate the effects of therapeutic and supratherapeutic doses of VX-661

compared with placebo on the QTc interval in healthy subjects

Secondary outcome

Part A:

To evaluate the PK of VX-661 and its metabolites, M1-661 and M2-661, following

multiple ascending doses of VX-661 in healthy subjects

Part B

To evaluate assay sensitivity (i.e., to evaluate the effect of moxifloxacin on

the QTc interval in healthy subjects)

To assess the effects of VX-661 compared with placebo on other

electrocardiogram (ECG) parameters (heart rate [HR], PR, and QRS intervals

and T-wave morphology) in healthy subjects

To determine the VX-661, M1-661, and M2-661 plasma concentration-effect

relationship for the QTc interval and the magnitude of the relationship, if any

exist

To evaluate the PK of VX-661, M1-661, and M2-661 in healthy subjects

To evaluate the safety and tolerability of VX-661 in healthy subjects

Study description

Background summary

VX 661 is a new investigational compound that may eventually be used for the treatment of cystic fibrosis (CF). CF is a genetic disorder that causes the body to produce unusually thick mucus. The thick mucus results in malfunction of organs like the lungs, pancreas and liver.

In the human body, the cystic fibrosis transmembrane conductance regulator (CFTR; this is a protein that can be found on the membrane of cells) plays an important role in the transport of salt and water in and out of cells. In CF, this protein does not work correctly or it is not produced sufficiently. As a result, the transport of salt and water in and out of cells is disturbed and mucus will become unusually thick. VX-661 is thought to improve CFTR functioning by modifying folding of the protein structure.

Study objective

The purpose of Part A is to investigate how safe the study compound is and how well the study compound is tolerated. The study will also investigate how quickly and to what extent the compound is absorbed into and eliminated from the body (this is called pharmacokinetics).

The purpose of Part B is to investigate if VX-661 has an effect on the electrical activity of the heart. In addition, it will be investigate the safety and tolerability of VX-661. The study will also investigate how quickly and to what extent VX-661 is absorbed into and eliminated from the body (this is called pharmacokinetics).

Study design

Part A:
The actual study will consist of 1 period during which you will stay in the clinical research center in Zuidlaren for 12 days (11 nights).
On Days 1 to 7, you will receive VX-661 or inactive formulation (placebo) as oral tablets with 240 milliliters of tap water. On all dosing days, you are not allowed to eat from at least 8 hours prior to study compound administration; on Days 1 and 7, food is also not allowed up to 4 hours after study compound administration. On all dosing days, water will not be allowed from 2 hours before to 2 hours after study compound administration (except for the 240 milliliters of tap water taken with the tablets). On Days 2 to 6, you will receive a breakfast after study compound administration. On all dosing days, at 4 hours after dosing, you will receive a lunch, which you will need to consume entirely within 30 minutes.

Part B:
The actual study will consist of 1 period during which you will stay in the clinical research center in Zuidlaren for 18 days (17 nights).
During the study you will receive VX-661, VX-661-matching placebo, moxifloxacin and/or moxifloxacin matching placebo as oral tablets with 240 milliliters of tap water. Administration will be done according to the schedule given in Section *How much of the study compound will I receive?* On all dosing days, you will have to ingest all tablets within a period of 5 minutes.
On all dosing days, you are not allowed to eat from at least 8 hours prior to study compound administration. On Days -1, 1, 7, 14 and 15 you are also not allowed to eat up to 4 hours after study compound administration. On Days 2 to 6 and Days 8 to 13 you will receive a breakfast after study compound administration. On all dosing days, at 4 hours after dosing, you will receive a lunch, which you will need to consume entirely within 30 minutes.

Intervention

Part A:
On Days 1 to 7 you will receive VX-661 or placebo once daily as oral tablets. A placebo is a tablet without the active ingredient. Whether you will receive VX-661 or placebo will be determined by chance. In each group, 8 volunteers will receive VX-661 and 2 volunteers will receive placebo. Neither you nor the study doctor will know if VX-661 or placebo will be dosed; we call this *the study is blinded*. However, information on the administration of the study compound will be present in the clinical research center, in sealed envelopes, which can be opened in case of emergency.

Group Day Treatment How often
1 1 to 7 VX-661 200 milligrams or placebo (4 tablets)
Once daily
2 1 to 7 VX-661 300 milligrams or placebo (6 tablets)
Once daily
3 (optional) 1 to 7 VX-661 (dose and number of tablets to be determined) or

placebo Once daily

Part B:
In this study, you will receive either VX-661, VX-661-matching placebo, moxifloxacin and/or moxifloxacin matching placebo; all will be administered as oral tablets. A placebo is a tablet without the active ingredient.
Treatments are planned as follows:

Day(s) Treatment A
-1 VX-661 or matching placebo (2 tablets)
1 VX-661 100 milligrams (2 tablets) and moxifloxacin or matching placebo (1 tablet)
2 to 7 VX-661 100 milligrams (2 tablets) once daily
8 to 14 VX-661 once daily (dose level and number of tablets to be determined based upon Part A results; as soon as the dose level is available, all subjects in Part B will be informed by an amendment to this form)
15 Moxifloxacin or matching placebo (1 tablet)

Day(s) Treatment B
-1 VX-661 or matching placebo (2 tablets)
1 VX-661 or matching placebo (2 tablets) and moxifloxacin 400 milligrams (1 tablet)
2 to 7 VX-661 or matching placebo (2 tablets) once daily
8 to 14 VX-661 or matching placebo once daily (number of tablets same as number of VX-661 tablets for Treatment A)
15 Moxifloxacin or matching placebo (1 tablet)

Day(s) Treatment C
-1 VX-661 or matching placebo (2 tablets)
1 VX-661 or matching placebo (2 tablets) and moxifloxacin or matching placebo (1 tablet)
2 to 7 VX-661 or matching placebo (2 tablets) once daily
8 to 14 VX-661 or matching placebo once daily (number of tablets same as number of VX-661 tablets for Treatment A)
15 Moxifloxacin 400 milligrams (1 tablet)

Study burden and risks

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

Single and multiple doses of VX-661 given alone or in combination with ivacaftor (an approved drug for the treatment of some patients with CF) have been studied in 106 healthy volunteers. Safety results from these studies indicate that VX-661 was generally well tolerated at single doses up to 300 milligrams, at multiple doses up to 200 milligrams once daily for 28 days, and as a fixed dose combination of 50 milligrams VX-661 with 150 milligrams

ivacaftor. Most adverse effects reported by volunteers in these studies were mild or moderate in severity. Adverse effects reported included: elevation of liver enzymes (values had returned to normal within approximately 1 week), constipation, back pain and pain in extremity, headache, diarrhea and contact dermatitis.

Moxifloxacin is known to have the following side effects: temporary changes in the electrical activity of the heart, palpitations, inflammation of the tendons, fainting spells, dizziness or lightheadedness, allergic reactions and convulsions.

Contacts

Public
Vertex Pharmaceuticals

Northern Avenue 50
Boston 02210
US
Scientific
Vertex Pharmaceuticals

Northern Avenue 50
Boston 02210
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

healthy male or female
18-45 y, incl.
BMI 18.0 - 30.0

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:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-07-2015
Enrollment:	130
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Avelox

Ethics review

Approved WMO Date:	08-07-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-07-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-09-2015
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	EUCTR2015-001711-12-NL
CCMO	NL54095.056.15