A Phase 1, Randomized, Double-Blinded, Placebo-Controlled, Single-Dose Escalation Study Followed by a Multiple-Dose Escalation Study and an Open-Label Relative Bioavailability and Food Effect Study of VX-787 in Healthy Subjects

Published: 19-01-2012
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Primary: Part A:to evaluate the safety and tolerability of single oral ascending doses of VX-787 administered to healthy male and female subjects (of non-childbearing potential)Part C:to evaluate safety and tolerability of multiple oral ascending...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON37724

Source
ToetsingOnline

Brief title
VX-787 SAD/MAD study

Condition

- Viral infectious disorders

Synonym
influenza

Research involving

Human

Sponsors and support

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

Intervention

Keyword: influenza, VX-787

Outcome measures

Primary outcome

Pharmacokinetics: plasma/urine VX-787 concentrations, pharmacokinetic

parameters

Safety: adverse events, vital signs, ECG-parameters, laboratory parameters,

physical examination

Secondary outcome

n/a

Study description

Background summary

VX-787 is a new investigational compound under development by Vertex who is the Sponsor of this study. VX-787 is being investigated to determine if it may be used for the treatment of influenza, a widespread and potentially deadly infectious disease. VX-787 is not registered as a drug which means it is experimental and not approved for commercial use. This is the first study where this compound is being given to humans. The study was already started in the USA, but was put on hold by the authorities in the USA. The authorities in the USA requested additional information on results from ongoing animal studies, before allowing the study to proceed. The authorities in The Netherlands feel that these results are not needed at this drug development stage, and feel that it is safe to proceed with the study in The Netherlands.

Study objective

Primary:
Part A:
to evaluate the safety and tolerability of single oral ascending doses of VX-787 administered to healthy male and female subjects (of non-childbearing potential)

Part C:
to evaluate safety and tolerability of multiple oral ascending doses of VX-787 administered for 10 days to healthy male and female subjects (of non-childbearing potential)

Secondary:
Part A:
to evaluate the pharmacokinetics (PK) of VX-787 and its metabolites (if possible)
after administration of a single oral ascending doses of VX-787 to healthy male and
female subjects (of non-childbearing potential)

Part C:
to evaluate the PK profile of VX-787 and its metabolites (if possible) after administration of multiple oral ascending doses of VX-787 to healthy male and female subjects (of non-childbearing potential)

Study design

This ia a randomized, double-blinded, placebo controlled single ascending dose study with Five cohorts of eight volunteers each receiving a single oral dose of VX-787 or placebo (six active, two placebo), followed by a multiple ascending dose study with two cohorts of eight volunteers each receiving multiple doses of VX-787 or placebo (six active, two placebo)

Procedures and assessments:
Screening and follow-up: demographics, medical history, physical examination, height, weight, BMI, HBsAg, anti HCV, anti-HIV1/2, alcohol and drug screen, vital signs, 12-lead ECG, clinical laboratory (including chemistry, hematology, coagulation and urinalysis), creatine kinase, pregnancy test (females only), adverse events and prior and concomitant medication

Throughout the study: physical examination, alcohol and drug screen, vital signs, 12-lead ECG, clinical laboratory (including chemistry, hematology, coagulation and urinalysis), creatine kinase, pregnancy test (females only), adverse events and prior and concomitant medication

Blood sampling for pharmacokinetics of VX-787
Urine sampling for pharmacokinetics of VX-787

Intervention

Part A:
a single dose of VX-787 or placebo administered as a capsule on Day 1 in the fasted state

Part C:
multiple doses of VX-787 or placebo administered as a capsule; once or twice daily and dietary status (fed or fasted) of subjects at the time of dosing will be based on available data from the PK observed in Parts A and Part B

Study burden and risks

The possible adverse effects of the investigational procedures (e.g. the use of the indwelling canula) are described in section 9 of the information booklet. This si the first study in which the compound will be give to humans. This study has already started in the US and will proceed in The Netherlands. VX-787 was administered in doses of 50mg and 100mg was given previously to humans and no adverse effects related to the drug were seen in people who received the 100mg every day for 10 days. There were two subjects who had mild diarrhea at the 50mg dose but none at the 100mg single dose. The starting dose in groep 3 will be 200 mg. The other doses will be determined based on the results of the preceeding groups.

VX-787 has been studied in animals and was well-tolerated at doses up to 100 mg/kg in rats and 150 mg/kg in monkeys. Currently there is a study at even higher doses in rats and monkeys and those results are still pending.

The occurrence of known or other effects cannot be excluded. All potential drugs cause adverse events to some extent.

Registration af adverse effects: During the entire investigation all adverse effect that are reported will be documented.

Blood draw, indwelling canula: During this study less then 500 ml of blood will be drawn.
Part A: Blood will be drawn until 96 hours after administration of VX 787 or placebo (thus until Day 5). It is anticipated that on Day -1 an indwelling canula will be inserted for most of the blood sampling on Day 1 and 2. On the other days during this study, blood will be drawn by direct puncture of the vein.
Part C: Blood will be drawn until 96 hours after the last administration of VX-787 (thus until Day 14). It is anticipated that on Day -1 and Day 9 an indwelling canula will be inserted for most of the blood sampling on Day 1 and 2, and Day 10 and 11. On the other days during this study, blood will be drawn by direct puncture of the vein.

Collection of urine:
Part A: Urine will be collected until 72 hours after administration of VX 787 (thus until Day 4).
Part C (Group 10 only): Urine may be collected on Day 10 and 11.

Heart trace (ECG*s):
Part A: ECG*s will be made regularly: specifically on Day 1.
Part C: ECG*s will be made regularly: specifically on Day 1 and Day 10.

Blood sample for DNA tests:
During the study, a blood sample will be taken and preserved for a maximum of 15 years for possible analyses on genetic material (DNA), relevant to this study. Taking part in this genetic testing is completely voluntary. If a subject does not wish to participate in this part of the study he/she can state so on the form at the end of the ICF. Refusal to participate will involve no penalty or loss of benefits to which the subject would otherwise be entitled. At this very moment it is not yet exactly known which analyses are going to take place. Moreover, new genetic tests might become available in the future, which may be applied to your blood sample. The results from the above tests will be coded, meaning that it will be ensured that the results cannot be linked to the subjects personal identity. For the DNA test a blood sample of 8.5 mL will be taken. Subjects will not receive an additional reimbursement for the DNA sample.

Meals:
If Part C is conducted under fed conditions, a high-fat, high-calorie breakfast will be served 30 minutes before each dosing on Days 1 to 10. Evening meals will be given 30 minutes before evening dose, if applicable. Subjects are required to eat all of the pre-dose meals provided.
The high-fat, high-calorie breakfast consist of:
2 slices of wheat bread (70 g) with 15 g margarine
2 fried eggs (in 15 g butter/margarine) (approximately 100 g)
1 portion of bacon or brie (40 g)
1 portion of fried potatoes (115 g)
1 glass of high fat milk (240 mL)

Contacts

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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
non-smoking

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 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):	18-02-2012
Enrollment:	56
Type:	Actual

Ethics review

Approved WMO Date:	19-01-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-02-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-04-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-04-2012
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	EUCTR2011-005962-39-NL
CCMO	NL39389.056.12
Other	VX11-787-001