A Phase 1, Randomized, Placebo- and Active-Controlled, Double-Blind, 4-Period Crossover ECG Study to Evaluate the Effect of VX 509 on QT/QTc Interval in Healthy Adult Subjects

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

Summary

ID

NL-OMON37134

Source
ToetsingOnline

Brief title
VX-509 QTc study

Condition

- Autoimmune disorders

Synonym
autoimmune disorders, Rheumatoid arthritis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: healthy volunteers, Multiple dose, QT/QTc interval

Outcome measures

Primary outcome

Part A:

- To evaluate the safety and tolerability of multiple doses of 750 mg qd of

VX-509 in healthy subjects.

Part B:

- To evaluate the effect of 200 mg qd (therapeutic) and 600 or 750 mg qd

(supratherapeutic dose; to be determined from Part A) of VX-509, versus placebo

on the QT/QTc interval in healthy subjects.

Secondary outcome

Part A:

- To evaluate the pharmacokinetics (PK) in healthy subjects receiving multiple

doses of 750 mg qd of VX-509 for 7 days

Part B:

- To assess the effect of 200 mg qd (therapeutic dose) and 600 or 750 mg qd

(supratherapeutic dose; to be determined from Part A) of VX-509, versus placebo

on non-QT interval electrocardiogram (ECG) parameters (heart rate [HR], RR, PR

and QRS interval) in healthy subjects.

- To assess the effects of a positive control (a single, oral dose of 400 mg of

moxifloxacin) on the QTc interval in healthy subjects, as an indicator of study sensitivity.

- To determine the VX-509 plasma concentration-effect relationship for the QT/QTc interval and the magnitude of the relationship, if any exist.

- To evaluate the PK of VX-509 in healthy subjects.

- To evaluate the safety and tolerability of therapeutic and supratherapeutic systemic exposure of VX-509 in healthy subjects.

Study description

Background summary

VX-509 is a new investigational compound that may eventually be used for the treatment of immune mediated disorders such as rheumatoid arthritis (RA). VX-509 is an inhibitor of an enzyme (JAK-3) that contributes to the development of inflammation in rheumatoid arthritis.

Study objective

The purpose of part A of the study is to investigate how safe the study drug is and how well the study drug is tolerated. The study will also investigate how quickly and to what extent the compound is absorbed and eliminated from the body.
The purpose of part B of the study is to investigate if VX-509 has an effect on the electrical activity of the heart. In addition, the safety of the compound is investigated and how well the study drug is tolerated. The study will also investigate how quickly and to what extent the compound is absorbed and eliminated from the body.

Study design

Part A will be a double-blind, randomized, placebo-controlled study investigating oral VX-509 doses of 750 mg qd in healthy male and female subjects.
Part B of the study will be a double-blind (for VX-509/placebo; open label for moxifloxacin), randomized, placebo- and active-controlled, single-center, 4-period crossover study to evaluate the effect of VX-509 on QT/QTc intervals

in healthy male and female subjects.

Intervention

Part A:
750 mg qd VX-509 or placebo as 15 tablets for 7 days.

Part B: The subjects will receive each one of the described treatments during one of the periods in a random order.
Treatment A (Therapeutic Dose): 200 mg qd of VX-509 (4 × 50-mg tablets) and 8 or 11 placebo tablets each morning on Days 1 to 4, depending on determination of supratherapeutic dose.
Treatment B (Supratherapeutic Dose): 600 or 750 mg qd (to be determined in Part A) of VX-509 (12 or 15 × 50-mg tablets) each morning on Days 1 to 4.
Treatment C (Placebo Control): 12 or 15 placebo tablets each morning on Days 1 to 4, depending on choice of supratherapeutic dose.
Treatment D (Positive Control): a single 400-mg dose of moxifloxacin tablet in the morning of Day 4, and 12 or 15 placebo tablets each morning on Days 1 to 4, depending on determination of supratherapeutic dose.

Study burden and risks

During the study several assessments will be performed that may be perceived as a burden. There will be a number of blood draws and in part B subjects will receive a ECG monitor on 2 days each period (in total 8 days) which will monitor their ECG continuously

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 (part A)
18-45 yrs, inclusive (part B)
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 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):	15-08-2012
Enrollment:	80
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	01-08-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-08-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-10-2012
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	EUCTR2012-003080-22-NL
CCMO	NL41343.056.12