Phase I, double-blind, randomized, placebo-controlled trial in healthy volunteers to examine the safety, tolerability and plasma pharmacokinetics of TMC589337 and TMC589354 after increasing single oral doses and in an open-label part after different repeated oral doses in combination with a single oral dose of TMC310911.

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To investigate the safety, tolerability and behavior in the body (absorption and excretion) of oral intake of TMC589337 and TMC589354 after ascending single intakes. In addition, the safety, tolerability and behavior in the body after multipe dose...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immunodeficiency syndromes
Study type	Interventional

Summary

ID

NL-OMON33338

Source
ToetsingOnline

Brief title
A Phase I trial with TMC589337, TMC589354 and TMC310911.

Condition

- Immunodeficiency syndromes

Synonym
AIDS, HIV

Research involving
Human

Sponsors and support

Primary sponsor: Tibotec Pharmaceuticals, EastGate Village, Eastgate, Little Island, CO Cork, Ireland, In Nederland vertegenwoordigd door Janssen-Cilag B.V.
Source(s) of monetary or material Support: Tibotec Pharmaceuticals;EastGate Village;Eastgate;Little Island;CO Cork;Ireland;In Nederland vertegenwoordigd door Janssen-Cilag B.V.

Intervention

Keyword: First-in-Human, HIV, Repeated dose, Single dose

Outcome measures

Primary outcome

The safety, tolerability and behavior in the body (absorption and excretion) of

oral intake of TMC589337 and TMC589354 after ascending single intakes.

The safety, tolerability and behavior in the body after multipe dose intakes of

TMC589337 and/or TMC589354 in combination with a single dose of TMC310911 will

be examined.

Secondary outcome

Not applicable.

Study description

Background summary

TMC589337, TMC589354 and TMC310911 are in process of development for treatment of Human Immunodeficiency Virus-Type 1 (HIV-1). TMC310911 is novel and potent compound and belongs to a medication class called preotease inhibitors (PI). It is being developed because it is assumed to be very active against the HIV-1 virus that causes AIDS, when other treatments will fail. TMC589337 and TMC589354 are novel molecules with no antiviral activity to be used to enhance the levels of TMC310911 in the blood. In this study, TMC589337 and TMC589354 will be administered for the first time to humans.

Study objective

To investigate the safety, tolerability and behavior in the body (absorption and excretion) of oral intake of TMC589337 and TMC589354 after ascending single intakes. In addition, the safety, tolerability and behavior in the body after multipe dose intakes of TMC589337 and/or TMC589354 in combination with a single dose of TMC310911 will be examined.

Study design

The single ascending dose part of the study has a randomized, double-blind, placebo-controlled design, which consists of
The multiple dose part of the study is open label.

Intervention

Single Dose:
The SAD part of the study consists of Panel 1 and 2. In both panels, the subjects will take 4 increasing oral doses of the study drug (active or placebo) in 4 seperate sessions. Each dose will be taken once. In each session, 6 subjects will receive the study drug and 2 subjects will receive placebo. The treatment schedule will be made in such a way that for both panels over 4 sessions each subject will receive the study drug 3 times and placebo once. Each single dosing session will have a staggered approach meaning that first 4 subjects will be dosed and 48 hours later the next 4 subjects will be dosed. A washout period of at least 10 days will be respected between consecutive single oral TMC589337, TMC589354 or placebo dosing within each panel. During the washout period no study drugs will be taken.

Multiple dose:
The MAD part of the study consists of Panel 3 through 7. Panels 3 through 6 will have 1 session in which TMC589337 (panel 3 and 5) or TMC589354 (panel 4 and 6) will be administered twice a day during 7 days. The subjects in panel 7 will have one session in which TMC589337 or TMC589354 will be administered twice or once a day during 7 days. For panel 7 TMC589337 or TMC589354 will be

selected.
In addition, teh subjects Panels 3 through 6 will have an additional session of 3 days in which a single oral dose of 300mg TMC310911 will be administered. Subjects of Panel 7 will receive either 300mg or 600mg of TMC310911.

Study burden and risks

The risks associated with this investigation are linked together with the possible side effects of the investigational product. The burden on the volunteer will continue to work with the recording periods, venapunctions and the introduction of the cannula. All volunteers are closely monitored and supervised by experienced doctors and studystaff for possible side effects.
The following tests will be performed during this trial: physical examination, measuring bloodpressure and hart rate, blood- and urine tests, pregnancy test (women only), drugscreen, alcohol tests, ECGs, restrictions in living habits, standardized meals during admission. 8 Hours telemetry recording on dosing days in the single ascending dose part of the study.
All volunteers will be closely monitored by experienced physicians and staff.

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

1. Subjects aged between 18 and 55 years, extremes included.
2. Non smokers for at least 3 months prior to selection.
3. Body Mass Index (BMI) of 18.0 to 30.0 kg/m2, extremes included.
4. Informed consent signed voluntarily.
5. Able to comply with protocol requirements.
6. Healthy on basis of a pre-trial physical examination, medical history, the results of blood biochemistry and hematology tests, a urinalysis, vital signs and an ECG.

Exclusion criteria

1. Past history of significant heart arrhythmias.
2. Female, except if postmenopausal for more than 2 years, or posthysterectomy or post-surgical sterilization (without reversal operation).
3. History of alcohol or drug abuse.
4. Hepatitis A, B or C infection of HIV-1 or HIV-2 infection at trial screening.
5. A positive urine drug test at screening.
6. Currently active clinically relevant or significant underlying gastro-intestinal-, cardiovascular-, nervous system-, psychiatric-, metabolic-, renal-, hepatic-, respiratory-, inflammatory-, or infectious disease.
7. History of clinically relevent skin disease such as but not limited to dermatitis, eczema, drug allergy, psoriasis, food allergy, urticaria.
8. History of drug allergy such as but not limited to sulfonamides and penicillins or drug allergy witnessed in previous trials with experimental drugs.
9. Use of concomitant medication, except for paracetamol (acetaminophen) and ibuprofen in a period of 14 days before the first trial medication intake.
10. Participation in an investigational drug trial within 90 days (after last intake) prior to the first intake of trial medication.
11. Donation of blood or plasma in the 60 days preceding the first intake if trial medication.
12. Subjects with lababnormalities at screening.

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):	20-05-2009
Enrollment:	46
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	TMC310911
Generic name:	TMC310911
Product type:	Medicine
Brand name:	TMC589337
Generic name:	TMC589337
Product type:	Medicine
Brand name:	TMC589354
Generic name:	TMC589354

Ethics review

Approved WMO

Date:	21-04-2009
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO

Date:	18-05-2009
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-06-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2009-011432-36-NL
CCMO	NL27815.040.09