A Phase I randomized, open-label, single dose, 3-period crossover trial in healthy subjects to evaluate the relative oral bioavailability of the 25 mg and 100 mg tablets of TMC125.

Published: 26-10-2006
Last updated: 09-05-2024

The objective of this study is to evaluate the concentrations in blood after a single administration of 100 mg TMC125. The various administration formulations will be compared to demonstrate that the formulations can be exchanged. The administration...

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

Summary

ID

NL-OMON30258

Source
ToetsingOnline

Brief title
Trial to evaluate the relative bioavailability of TMC125.

Condition

- Viral infectious disorders

Synonym
AIDS, HIV

Research involving
Human

Sponsors and support

Primary sponsor: TIBOTEC Pharmaceuticals Ltd., Little Island, Co. Cork; Ireland in Nederland vertegenwoordigd door Janssen-Cilag BV
Source(s) of monetary or material Support: Sponsor

Intervention

Keyword: bioavailability, healthy subjects, HIV, TMC125

Outcome measures

Primary outcome

Pharmacokinetic analysis, blood and urine examination, side-effects (adverse

events), laboratory results, blood pressure, pulse rate, ECG, alcohol breath

test.

Secondary outcome

not applicable

Study description

Background summary

TMC125 is a new investigational product that is in process to be used for the treatment of HIV-1, the virus that causes AIDS. It slows down the replication of HIV and belongs to the class of NNRTIs (the so called Non-Nucleoside Reverse Transcriptase Inhibiters). TIBOTEC Pharmaceuticals developed a 25 mg tablet for pediatric purposes. The dose that will be investigated in this trial is 100 mg (treatment A: 1 tablet of 100 mg; treatment B: 4 tablets of 25 mg; and treatment C: 1 tablet of 100 mg dissolved in 100 mL water).
TMC125 is not yet marketed as drug, but it has already been administered to humans in previous studies.
TIBOTEC Pharmaceuticals Ltd. intends to marketing this drug.

Study objective

The objective of this study is to evaluate the concentrations in blood after a single administration of 100 mg TMC125. The various administration formulations will be compared to demonstrate that the formulations can be exchanged. The

administration of 1 tablet of 100 mg will be compared to the administration of 4 tablets of 25 mg; and the administration of 1 tablet of 100 mg will be compared to the administration of 1 tablet of 100 mg dissolved in 100 mL water. Furthermore, the safety and tolerability will be evaluated.

Study design

A medical screening preceeds participation in the study. The study consists of 3 periods of 5 consecutive days. The three single intakes will be separated by a period of at least 14 days, the washout period.
The study is ended by two follow-up visits.
The subject is treated once with the reference formulation (treatment A) and twice with a test formulation (treatments B and C). The sequence of the different treatments is determined bij chance.

Treatment:
A: 100 mg TMC125, 1 tablet of 100 mg (tablet F060)
B: 100 mg TMC125, 4 tablets of 25 mg (tablet F066)
C: 100 mg TMC125, 1 tablet of 100 mg (tablet F060), dissolved in 100 mL water.

The concentrations of TMC125 in blood will be determined. Therefore, in every period on Day 1, blood samples will be collected before and until 96 hours after intake of the trial medication.

Intervention

One dose per period.

Study burden and risks

Preceding participation, subjects will be screened including drawing a blood sample for laboratory tests. Afterwards, 3 periods will follow. A single dose of trial medication will be administered each period. Blood will be collected 16 times each period to evaluate the absorption on the blood and excretion of TMC125. Between 2 consecutive periods is a washout of 2 weeks. During the study blood is collected 10 times for laboratory tests.

TMC125 has been studied in both healthy subjects and in HIV-1 patients. As of June 2006, about 900 healthy subjects and approximately 500 HIV-1 patients have already received TMC125.
In healthy subjects who received more than one dose of TMC125, the most common side effects were headache, diarrhea, flatulence, abdominal pain and pruritus. There was one death in a healthy volunteer but the trial doctor did not think the death was related to TMC125. Other medically important events that were reported were also not related to TMC125.
In HIV-1 patients, the most common side effects that have been reported and

were sometimes considered by the trial doctor related to TMC125 were: diarrhea, feeling tired (fatigue), rash, fever, headache, pain in the abdomen, vomiting, and nausea. Most of these side effects were mild to moderate in nature and went away on their own without treatment.
Some healthy subjects developed rash with mouth ulcers (sores) or vesicles (blister-like) after treatment with TMC125. This side effect can be serious and therefore need immediate medical attention. If a subject develops any skin changes with any one of these symptoms: fever, nausea, vomiting, diarrhea, abdominal pain, extreme tiredness, aches, generally ill feelings, sore throat, shortness of breath or cough, he or she has to inform the trial doctor immediately and make an appointment for a detailed evaluation.
Some rare serious side effects which occurred in HIV-1 infected subjects and were considered possibly related to TMC125 are decrease in blood cells, pain and swelling in the pancreas (pancreatitis), chest pain, stroke due to decreased blood supply to brain, seizure due to fever, dehydration, excess of lactic acid in blood (chemical byproduct of body cells that can cause dysfunction of body organs) and heart attack leading to decrease in heart function. The patient whose heart function decreased due to the heart attack died. The patient had risk factors for development of cardiac problems but a possible relation to TMC125 could not be excluded.
In both the healthy subjects and HIV-1 patients, there were no significant changes in vital signs (pulse, breathing rate and blood pressure), heart rhythm or laboratory test results.

Contacts

Public
TIBOTEC Pharmaceuticals Ltd., Little Island, Co. Cork; Ireland in Nederland vertegenwoordigd door Janssen-Cilag BV

dr. Paul Janssenweg 150
5026RH Tilburg
Nederland
Scientific
TIBOTEC Pharmaceuticals Ltd., Little Island, Co. Cork; Ireland in Nederland vertegenwoordigd door Janssen-Cilag BV

dr. Paul Janssenweg 150
5026RH Tilburg
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Participants may not have smoked for the last 3 months preceding the start of the trial. Participants have to be healthy on base of physical examination, medical history, ECG, laboratory tests and blood pressure and pulse rate.

Exclusion criteria

Participants may not have (had) relevant skin diseases or use medicines. The participants may not have participated in more than 1 study with TMC125, TMC120 and/or TMC278 (previously R278474) or having developed rash while participating in a trial with any of these compounds. Females may not be fertile anymore.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	30-10-2006
Enrollment:	36
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	TMC125
Generic name:	etravirine

Ethics review

Approved WMO Date:	26-10-2006
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	03-11-2006
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)

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	EUCTR2006-005134-20-NL
CCMO	NL14772.072.06