Phase I, open-label, 3-way crossover trial in healthy male subjects to evaluate the pharmacokinetics of TMC114 and TMC41629 after a single oral dose of 2 controlled-release coformulations as compared to an immediate-release coformulation of TMC114/TMC41629

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

Summary

ID

NL-OMON32892

Source
ToetsingOnline

Brief title
Phase 1 open label trial with 3 compositions of TMC114/TMC41629.

Condition

- Immunodeficiency syndromes

Synonym
AIDS, HIV

Research involving
Human

Sponsors and support

Primary sponsor: Tibotec Pharmaceuticals Ltd, 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 LIMITED

Intervention

Keyword: Open Label, Phase 1, TMC114, TMC41629

Outcome measures

Primary outcome

Assessing the impact of controlled-release properties on the plasma

concentration-time profiles and relative bioavailability of TMC114 and TMC41629

of 2 different controlled-release formulations of combinations TMC114/TMC41629

to compare with a coformulation immediate release of TMC114/TMC41629 in healthy

male subjects.

Secondary outcome

- The determination of plasma pharmacokinetics of TMC114 and TMC41629 for 2

different controlled-release formulation

TMC114/TMC41629 and a combination of immediate-release coformulation of

TMC114/TMC41629 in healthy male subjects.

- The short-term assessment of the safety and tolerability of TMC114/TMC41629

followed by 3 administrations of single oral doses (expressed as different

coformulaties of TMC114/TMC41629) in healthy male subjects.

Study description

Background summary

TMC41629 is a new research tool that is currently being developed for the treatment of human immunodeficiency virus type 1 (HIV-1). HIV infection can cause the disease AIDS. TMC41629 is not approved for use, either by the U.S. Food and Drug Administration (FDA), nor by regulatory authorities within the European Union (EU). Therefore, the plea may only be used in scientific research. TMC41629 belongs to a group of medicines called protease inhibitors. This means slowing or stopping the development of an HIV infection to AIDS.

TMC114 is a new generation of HIV protease inhibitor (protease is an enzyme) under the name PREZISTA on the market and is used worldwide for patients with HIV-1 infection to treat. In previous clinical trials are already more than three thousand HIV-1 infected patients treated with TMC114. Many patients who participated in these clinical studies were at least a year with TMC114 treated. In addition, about 1300 healthy volunteers for 1 day up to 2 weeks with TMC114 examined in the context of a clinical research. The safety of the use of TMC114 and the possible undesirable side effects are summarized below.

Study objective

This is a scientific research with the aim to investigate the bioavailability of a combination of the drugs TMC114 and TMC41629 . The three dosage forms, each only once ingested. In addition, even in this study the safety of the use and possible side effects of TMC114 and TMC41629 established and in what concentrations the two funds occur in your blood after a single intake after a period of time.

Study design

The study consists of three sessions, which are separated by a so-called "wash out period" (a period without treatment so that all medication from the body for the beginning of a new treatment) of at least seven days. During the three sessions you will follow treatment A, B treatment and treatment C, where you administer each one of the three different dosage forms of the combination of TMC114 and TMC41629 . By means of drawing lots is determined in what order the three treatments are.

In each of the three treatments (A, B and C) you must take four capsules. Each capsule is equivalent to a TMC114 dose of 200 mg and TMC41629 mg 23.67. The

total dose TMC114 is thus 800 (4 x 200) mg per session and the total dose TMC41629 94.68 (4 x 23.67) mg per session. All medicines are taken by mouth and fasted.

In each of the three sessions, the pharmacokinetic profiles of TMC114 and TMC41629 are established for up to 72 hours after taking the drug. The safety and tolerability of TMC114 and TMC41629 during the entire study period will be evaluated.

Intervention

In Treatment A, a single oral dose equivalent to 800 mg TMC114 and 94,64 mg TMC41629 of the immediate-release coformulation (4 capsules) will be administered.

In Treatment B, a single oral dose equivalent to 800 mg TMC114 and 94,64 mg TMC41629 of the following combination will be administered: 25% immediate-release (1 capsule), 50 % enteric-coated (2 capsules) and 25 % colon-targeted (1 capsule).

In Treatment C, a single oral dose equivalent to 800 mg TMC114 and 94,64 mg TMC41629 of the following combination will be administered: 50% enteric-coated (2 capsules) and 50 % colon-targeted (2 capsules). In all treatments, an intake of 4 capsules will be required.

Study burden and risks

The risks associated with this research related to the possible side effects of TMC114 and TMC41629. The tax for the volunteer is further along with the recording periods, venapuncties and the insertion of the cannula. All volunteers are closely monitored for possible side effects and supervised by experienced staff and physicians study.

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. Male subjects, aged between 18 and 55 years, extremes included.
2. Non-smoking for at least 3 months prior to selection.
3. Normal weight as defined by a Body Mass Index (BMI, weight in kg divided by the square of height in meters) of 18.0 to 30.0 kg/m2, extremes included.
4. Informed Consent Form (ICF) signed voluntarily before the first trial-related activity.
5. Able to comply with protocol requirements.
6. Healthy on the basis of a medical evaluation that confirms the absence of any clinically relevant abnormality and includes a physical examination, medical history, labresults and an ECG (in triplicate).

Exclusion criteria

1. Past history of heart arrhythmias (extrasystoli, tachycardia at rest).
2. History or evidence of current use of alcohol, barbiturate, amphetamine, recreational or narcotic drug use, which in the investigator*s opinion would compromise subject*s safety and/or compliance with the trial procedures.
3. Hepatitis A, B, or C infection (confirmed by hepatitis A antibody IgM, hepatitis B surface antigen, or hepatitis C virus antibody, respectively), or HIV-1 or HIV-2 infection at screening.
4. A positive urine drug test at screening. Urine will be tested to check the current use of amphetamines, benzodiazepines, cocaine, cannabinoids, and opioids.
5. Currently active or underlying gastrointestinal, cardiovascular, neurologic, psychiatric,

metabolic, endocrinologic, genitourinary, renal, hepatic, respiratory, inflammatory, or infectious disease.
6. Currently significant diarrhea, gastric stasis, or constipation that in the investigator*s opinion could influence drug absorption or bioavailability.
7. Any history of significant skin disease such as, but not limited to, rash or eruptions, drug allergies, food allergy, dermatitis, eczema, psoriasis, folliculitis or urticaria.
8. History of significant allergy to drugs such as, but not limited to, sulfonamides and penicillines.
9. Use of concomitant medication, including over-the-counter products, herbal preparations and dietary supplements. Concomitant medication must have been discontinued at least 14 days before the first dose of trial medication intake except for paracetamol (acetaminophen (see Section 5.3.9).
10. Participation in an investigational drug trial within 90 days prior to the first intake of trial medication.
11. Donation of blood or plasma within 60 days preceding the first intake of trial medication.
12. Having previously participated in a multiple-dose trial with TMC114.
13. Having previously participated in more than 3 single-dose trials with TMC114.
14. Subjects with laboratory abnormalities at screening.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-11-2008
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Prezista
Generic name:	Darunavir
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	TMC41629
Generic name:	TMC41629

Ethics review

Approved WMO Date:	12-11-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-11-2008
Application type:	First submission
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	EUCTR2008-006717-24-NL
CCMO	NL25665.040.08