A Phase I, open label, randomized, crossover trial in healthy subjects to investigate the pharmacokinetic interaction between didanosine and TMC114, coadministered with low-dose ritonavir, at steady-state.

Published: 29-05-2006
Last updated: 20-05-2024

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

Summary

ID

NL-OMON29874

Source
ToetsingOnline

Brief title
An interaction study of TMC114 combined with ritonavir with didanosine

Condition

- Immunodeficiency syndromes

Synonym
human immunodeficiency virus (aids)

Research involving

Human

Sponsors and support

Primary sponsor: Tibotec Pharmaceuticals
Source(s) of monetary or material Support: Sponsor

Intervention

Keyword: crossover, HIV, pharmacokinetic interaction, TMC114

Outcome measures

Primary outcome

Farmacokinetic blood-and urine investigation

Secondary outcome

Safety and tolerability

Study description

Background summary

The new investigational drug called TMC114 is in process of development for the treatment of people who are infected with the Human Immunodeficiency Virus-Type 1 (HIV-1). TMC114 belongs to a group of medications called protease inhibitors (PIs) used in the treatment of HIV infection. Ritonavir, another protease inhibitor, is a prescription drug used in the treatment of infected subjects with the HIV-1 virus and is often given at a low dose in combination with other protease inhibitors. The co-administration of ritonavir results in more favorable concentrations of
TMC114 in the blood and better tolerability. Didanosine (ddI) - which can be given in combination with TMC114/ritonavir - is also a prescription drug used in the treatment of patients infected with the HIV-1 virus. ddI is a synthetic purine nucleoside analogue active against HIV-1 virus.

Study objective

The primary objectives are:
* to determine the effect of steady-state concentrations of TMC114 coadministered with a low
dose of ritonavir on the steady-state pharmacokinetics of ddI,

* to determine the effect of steady-state concentrations of ddI on the steady-state
pharmacokinetics of TMC114 coadministered with a low dose of ritonavir.

The secondary objective is
* to evaluate the short-term safety and tolerability of the concomitant use of TMC114, lowdose
ritonavir and ddI.

Study design

This is a Phase I, open label, randomized, 3-way crossover trial in healthy subjects to investigate the pharmacokinetic interaction between ddI and TMC114, in combination with a low dose of ritonavir, at steady-state. The study population will consist of 18 healthy subjects. In 3 sessions, each subject will receive 600/100 mg TMC114/rtv b.i.d. (Treatment A), 400 mg ddI q.d. (Treatment B), and a combination of 600/100 mg TMC114/rtv b.i.d. and 400 mg ddI q.d. (Treatment C).

Treatment A will be administered for 6 days with an additional morning dose on Day 7.
Treatments B and C will be administered for 7 days. Subsequent sessions will be separated by a washout period of at least 7 days. ddI should be taken on an empty stomach, TMC114/rtv should be taken under fed conditions (and 2 hours after ddI intake during the coadministration phase).
Full pharmacokinetic profiles will be determined for one dosing interval after the morning intake on Day 7 of Treatment A and C for TMC114 and ritonavir, and of Treatment B and C for ddI.
The short-term safety and tolerability will also be assessed.

Intervention

Treatment Dose Volume
A --> 2 tablets TMC114 and 1 capsule ritonavir b.i.d.
B --> 1 capsule didanosine q.d.
C --> 2 tablets TMC114, 1 capsule ritonavir b.i.d.
1 capsule didanosine q.d.

Study burden and risks

The risks of participation in this trial is associated with possible adverse events of TMC114, ritonavir and didanosine. The burden for the participant is also associated with the admission to the unit, venapunction and insertion of canule. All subjects will be carefully followed on any adverse events and will

be under the supervision of experienced physicians and study personnel.

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 or female subjects, aged between 18 and 55 years, extremes included.
2. Non-smoking or smoking no more than 10 cigarettes, or 2 cigars, or 2 pipes per day for at least 3 months prior to selection.
3. Normal weight as defined by a Quetelet Index (Body Mass Index: weight in kg divided by the square of height in meters) of 18.0 to 30.0 kg/m2, extremes included17 (and of a minimum weight of 60 kg).
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 reveals the absence of any clinically

relevant abnormality and includes physical examination (including skin examination), medical history, electrocardiogram, vital signs and the results of blood biochemistry, hematology and blood coagulation tests and a urinalysis carried out at screening.

Exclusion criteria

- History or evidence of current use of alcohol
- A positive urine drug test at screening
- Participation in an investigational drug trial within 90 days prior to the first intake of trial medication
- Having previously participated in a multiple-dose trial with TMC114
- Having previously participated in more than one single-dose trial with TMC114
- Blood or plasma drawn or donated within 60 days prior to the screening visit
- A positive HIV-1 or HIV-2 test at study screening
- Hepatitis A, B or C infection
- A positive pregnancy test or breast feeding at screening
- History of significant drug allerby such as, but not limited to, sulfonamides and penicillines
- Use of concomitant medication, including over-the-counter products and dietary supplements. All concomitant medication must have been discontinued at least 14 days prior to the first intake of trial medication, except for paracetamol (acetaminophen), which may be used up to 3 days before the first dose of trial medication
- Not suitable to participate in the trial according to the opinion of the investigator

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):	08-06-2006
Enrollment:	18

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NAP
Generic name:	NAP
Product type:	Medicine
Brand name:	Norvir
Generic name:	ritonavir
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Videx EC
Generic name:	didanosine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	29-05-2006
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-06-2006
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-06-2006
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	EUCTR2006-001592-38-NL
CCMO	NL12610.040.06