Early Access of TMC125 in combination with other antiretrovirals in treatment-experienced HIV-1 infected subjects with limited treatment options.

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

Summary

ID

NL-OMON30522

Source
ToetsingOnline

Brief title
TMC125-C214

Condition

- Viral infectious disorders

Synonym
HIV-1

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag

Source(s) of monetary or material Support: door de farmaceutische industrie

Intervention

Keyword: early access, HIV-1, limited treatment options, NNRTI

Outcome measures

Primary outcome

The trial is not set up to show a specific statistical hypothesis but to

provide TMC125 to ARV experienced HIV-1 infected subjects with limited

treatment options. Further objective is to gather information on safety and

tolerability aspects of TMC125.

Secondary outcome

Safety of TMC125 will be summarized in terms of

-mortality

-non-HIV related SAE's

-subject's disposition (reasons for discontinuation)

Study description

Background summary

Current options for the treatment of HIV-infected subjects consist of NRTI's, NtRTI's, PI's and fusion-inhibitors.Currently, no single drug or combination drug therapy is able to eradicate HIV-1. A triple drug regimen is considered standard of care and when effective, results in suppression of the virus below the detection limits of the current tests, thereby slowing the progression of the disease and reducing the emergence of viral drug resistance.
There are patients who have failed multiple ARV regimens and have limited treatment options with the currently approved antiretrovirals.

Study objective

The primary objective of this trial is to provide early access to TMC125 for

treatment-experienced HIV-1 infected patients who have failed multiple ARV regimens and have limited treatment options with the currently approved antiretrovirals.
The secondary objective of this trial is to gather information on the safety and tolerability aspects of TMC125 in combination with other antiretrovirals. Available efficacy data will also be collected.

Study design

International, multicenter, phase 3 study.
There is no controlgroup

Intervention

The patient receives two tablets of 100 TMC125 in combination with an investigator-selected background of additional antiretrovirals from the list of allowed medications.

Study burden and risks

The study consists of a screening period, treatment period and follow-up visit (on average 4 to 5 consults per year).
The patient will be asked some questions about his/her medical history, current medical condition and the medication taken.
The interventions are limited to a blood test and urine-sampling.
The venapunction and volume of blood taken are not necessary for the trial bur are done as part of the standard of care in this patientpopulation.
Women are not allowed to become pregnant during and until 4 weeks after the end of the trial. Women and men are asked ,during and until 4 weeks after the trial, to use a good method of birth control. Beside this obligation nothing else is requested and no other behaviour is mandatory.
In this trial patients who have failed multiple ARV regimens and have limited treatment options with the currently approved antiretrovirals are treated. The access to this trial medication in combination with a standard of care treatment might offer new perspectives.

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. Subject or Legal Authorized Representative has voluntarily given informed consent before initiation of trial procedures.
2. Subject has documented HIV-1 infection.
3. Male or female subject (lower age limit 16 or 18 years of age, depending on local regulation)
4. Subject has limited treatment options due to virological failure or intolerance to multiple ARV regimens.
5. Subject is at least 3-class experienced (3 classes of licensed oral ARVs: N[t]RTIs, PIs, NNRTIs).
Note: Subjects with primary NNRTI resistance can be included if they are experienced with at least 2 classes of ARVs (PIs, N[t]RTIs) and meet all the other inclusion criteria.
6. Subject has previously received 1 different PI-based regimens.
7. Subject is unable to use currently approved NNRTIs due to resistance (primary or acquired) and/or intolerance.
8. Subject, if currently receiving an ARV regimen, is not achieving adequate virologic suppression on his/her current regimen (defined as a confirmed detectable plasma VL >or=50 copies/ml on the current treatment). A subject who does achieve adequate virologic suppression is only eligible if
*subject has treatment-limiting toxicity to an agent in his/her ARV regimen that requires substitution of this agent;
or

*subject is at risk of viral rebound and in the opinion of the investigator an intensification of the ARV regimen is appropriate;
or
*subject previously participated in another TMC125 clinical trial or program

Exclusion criteria

1. Primary HIV infection.
2. Prior or current participation in DUET trials (TMC125-C206 or TMC125-C216).This exclusion criterium was removed according to TMC125-C214-CTPA-GEN-II, dated 10 Oct 07.
3. Any condition (including but not limited to alcohol and drug use), which, in the opinion of the investigator, could compromise the subject*s safety or adherence to the protocol.
4. Use of disallowed concomitant therapy, including disallowed ARVs (See Section 5.3.8.2 protocol).
5. Use of non-ARV investigational medications within the 30 days prior to baseline visit.
6. Use of investigational ARVs, unless stated as an exception in Section 5.3.8.2.2. of the protocol
7. Any active clinically significant disease (e.g., cardiac dysfunction, pancreatitis, acute viral infection) or findings during screening of medical history or physical examination that is not either resolved or stabilized for at least 30 days before the screening phase of the trial.
8. Acute viral hepatitis, including but not restricted to A, B or C.
9. Pregnant or breast-feeding female.
10. Female subject of childbearing potential not using effective non-hormonal birth control methods or not willing to continue practicing these birth control methods from screening until the last trial related activity.
Note: Hormone based contraception may not be reliable when taking TMC125; therefore, to be eligible for this trial, women of childbearing potential who may have vaginal intercourse should either:
(1) Use a double barrier method to prevent pregnancy (i.e., use a condom without spermicide, with either a diaphragm or cervical cap) or
(2) Use hormone based contraceptives in combination with a barrier contraceptive (i.e., male condom without spermicide, diaphragm or cervical cap or female condom) or
(3) Use an intrauterine device (IUD) in combination with a barrier contraceptive (i.e., male condom without spermicide, diaphragm or cervical cap or female condom) or
Note: The use of an IUD has been associated with an increased rate of sexually transmitted diseases.
(4) Be non-heterosexually active, practice sexual abstinence or have a vasectomized partner (confirmed sterile).
Note: Women who are postmenopausal for at least 2 years, women with total hysterectomy and women with tubal ligation are considered of non-childbearing potential.
11. Subjects with the following laboratory abnormalities as defined by a standardized grading scheme based on the Division of AIDS (DAIDS) grading table (updated version from December 2004, see Section 7.2 van het protocol):
- Hemoglobin < 7.4 g/dL (4.5 mmol/L)
- Absolute neutrophil count < 500/mm³ (0.500 x 109/L)

- Platelets <25,000/mm3 (25.000 x 109/L)
- Prothrombin time (PT) >1.50 x upper limit of laboratory normal range (ULN)
Note: Subjects on anticoagulant therapy with elevated PT >1.5 ULN require approval of the sponsor prior to enrollment.
- Alkaline phosphatase >5 x ULN
- Aspartate aminotransferase (AST)/ alanine aminotransferase (ALT) >5 x ULN
- Bilirubin > 5 x ULN
Note: Subjects with elevated bilirubin >5xULN assessed as related to a component of ART therapy may be enrolled with prior approval of the sponsor.
- Lipase >3 x ULN
- Amylase >5 x ULN if lipase >2 x ULN
- Creatinine >1.8 x ULN
12. Subjects with clinical or laboratory evidence of significantly decreased hepatic function or decompensation, irrespective of liver enzyme levels.
Note: Subject can be included with prior approval of the sponsor if the elevated bilirubin (grade 3 or less) is assessed at the time of screening as related to an administered ARV and not to liver disease.
Note: Subjects co-infected with chronic hepatitis B or C will be allowed to enter the trial if their condition is judged to be clinically stable. Subjects diagnosed with acute viral hepatitis at screening will not be allowed in the trial.
13. Previously demonstrated clinically significant allergy or hypersensitivity to any of the excipients of the investigational medication (TMC125).

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-05-2007
Enrollment:	120
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	15-11-2006
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-01-2007
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-07-2007
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-08-2007
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-01-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-01-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2006-002499-16-NL
CCMO	NL14875.078.06