Phase I, open-label, randomized, crossover trial in healthy adults to compare the oral bioavailability of 3 concept pediatric formulations of TMC278 (solution, suspension, granules) to that of the adult 25 mg Phase III tablet formulation, and to assess the food effect for each concept formulation.

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This study involves research and the objective of this study is to evaluate how much and how fast TMC278 is absorbed into the body after administration as these concept pediatric formulations compared to when administered as the 25 mg TMC278 tablet...

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

Summary

ID

NL-OMON32773

Source
ToetsingOnline

Brief title
Phase I trial with 3 concept pediatric formulations of TMC278.

Condition

- Viral infectious disorders

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: bioavailability, Healthy subjects, pediatric formulations, TMC278

Outcome measures

Primary outcome

Compare the oral bioavailability of 3 concept pediatric formulations of TMC278 (solution, suspension, granules) to that of the adult 25 mg Phase III tablet formulation. In addition, the absorption of TMC278 into the body will be compared when the pediatric formulations are administered on an empty stomach and after a breakfast.

Secondary outcome

The safety and tolerability of TMC278 different formulations during the study period to be assessed. Finally, the palatability of each concept pediatric formulation under fasted conditions will be evaluated.

Study description

Background summary

This new investigational drug called TMC278 is in process of development for the treatment of Human Immunodeficiency Virus Type 1 (HIV-1) infection, an infection that can lead to AIDS.
TMC278 is not yet approved for use by the US Food and Drug Administration and other Regulatory Authorities in the European Union (EU). Therefore, it can only be used in a research study.
TMC278 belongs to a class of drugs called non-nucleoside reverse transcriptase inhibitors (NNRTIs), which help to slow or stop the progression of HIV infection. The currently available TMC278 formulation for adults is a tablet. Development of an appropriate formulation of TMC278 for use in children is ongoing. A pediatric formulation must allow for flexibility in dosing depending on age and body weight. Currently, 3 concept pediatric formulations have been identified for further evaluation: an oral solution, an oral suspension and granules.

Study objective

This study involves research and the objective of this study is to evaluate how much and how fast TMC278 is absorbed into the body after administration as these concept pediatric formulations compared to when administered as the 25 mg TMC278 tablet for adults. In addition, the absorption of TMC278 into the body will be compared when the pediatric formulations are administered on an empty stomach and after a breakfast. The safety and tolerability of administration of the different TMC278 formulations will be assessed throughout the study. This trial will aid in the selection of a concept pediatric formulation of TMC278 for further development. Finally, the appreciation of the different flavor formulations TMC278 will be examined.

Study design

Open label, randomised, cross-over study.

Intervention

Dosing with 25 mg TMC278 per treatment.

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, taste questionnaires, restrictions in

living habits, standardized meals during admission.
Al 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) Age between 18 and 55 years
2) Non-smoking or smoking no more than 10 cigarettes, or 2 cigars, or 2 pipes a day for at least 3 months prior to selection.
3) BMI 18.0-30.0.
4) Signed ICF
5) Able to comply with protocol requirements

6) Healthy based on the basis of a medical evaluation.

Exclusion criteria

1) Positive HIV and Hepatitis testresults.
2) Female except if they are of non-childbearing potential.
3) History or evidence of alcohol and or drug abuse.
4) Hepatitis A, B en C
5) Positive urine drug test
6) Currently active or underlying gastrointestinal, cardiovascular, neurologic, psychiatric, metabolic, renal, hepatic, respiratory, inflammatory or infectious disease.
7) Currently significant diarrhea, gastric stasis or constipation that in the investigator's opinion could influence drug absorption or bioavailability.
8) Any history of significant skin disease such as but not limited to rash or eruptions, drug allergies, food allergy, dermatitis, eczema, psoriasis or urticaria.
9) Previously demonstrated clinically significant allergy or hypersensitivity to and/or any of the excipients of the investigational medication administered on this trial.
10) Use of concomitant medication, including over-the-counter products and dietary supplements. Systemic over-the-counter medication must have been discontinued at least 7 days prior to the first dose of study medication; prescribed medications must have been discontinued at least 14 days before the first dose of study medication, except for paracetamol and ibuprofen.
11) Participation in an investigational drug trial within 60 days prior to the first intake of trial medication.
12) Donation of blood plasma within the 60 days preceding the first intake of trial medication.
13) Lab abnormalities
14) Having participated in more than 1 trial (single or multiple dose) with TMC125 (etravine), TMC120 (dapirivine) and/or TMC278 (rilpivirine, formerly known as R278474) or having developed rash, erythema or urticaria while participating in a trial with the aforementioned compounds.
15) Significant heart rhythm disturbances.
16) Subjects with ageusia, hypogeusia or dysgeusia
17) Renal impairment: calculated creatinine clearance (CLCr) < 80 mL/min;

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-01-2009
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	TMC278
Generic name:	TMC278

Ethics review

Approved WMO Date:	09-12-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-01-2009
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-01-2009
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	EUCTR2008-007101-36-NL
CCMO	NL25895.040.08