A single dose study to evaluate the microdose pharmacokinetics of candidate HIV integrase strand transfer inhibitors in healthy subjects

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

Summary

ID

NL-OMON42414

Source
ToetsingOnline

Brief title
Integrase Microdose Study

Condition

- Immunodeficiency syndromes
- Viral infectious disorders

Synonym
HIV-1

Research involving
Human

Sponsors and support

Primary sponsor: Merck Sharp & Dohme (MSD)
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: HIV-1, integrase, viral infection

Outcome measures

Primary outcome

To obtain preliminary plasma pharmacokinetic data (including AUC0-*, AUC0-last,

Cmax, Tmax, apparent terminal t*, Cl, Vd) of single intravenous

microdoses of L-1, L-2, and L-3 in healthy subjects.

Secondary outcome

To evaluate the safety and tolerability of single intravenous microdoses of

L-1, L-2, and L-3 in healthy subjects.

Study description

Background summary

L-1, L-2 and L-3 are new investigational compounds that may eventually be used for the treatment of HIV-1 viral infection. These compounds are able to inhibit the retroviral enzyme integrase during the HIV infection process. The retroviral enzyme integrase are proteins required for the HIV-1 virus to be incorporated into the host cell DNA. This is the first time that these compounds will be given to humans.

Study objective

The purpose of the study is to investigate to what extent L-1, L-2 and L-3 are tolerated when administered as micro-dose.
It will also be investigated how quickly and to what extent L-1, L-2 and L-3 are absorbed and eliminated from the body (this is called pharmacokinetics).

Study design

The actual study will consist of 1 period during which, if the volunteer is assigned to treatment group A, he will stay in the clinical research center in Zuidlaren for 6 days (5 nights). If the volunteer participate in group B or C he will stay in the clinical research center in Zuidlaren for 5 days (4 nights).

During the study the volunteer will receive a single 100 *g micro-dose of either one of the following compounds L-1, L-2 or L-3 as an intravenous injection.

Intervention

The study will consist of 1 period during which the volunteer will receive either one of the three study drugs compounds once. The study drug will be given in the form of an intravenous injection.

Group Dosing Day Number of subjects Treatment

A 1 6 L-1 100 *g
B 1 6 L-2 100 *g
C 1 6 L-3 100 *g

Study burden and risks

To date, L-1, L-2 and L-3 have not been given to people. L-1, L-2 and L-3 have been tested in laboratory animals as required prior to testing in humans. Animal studies do not always predict what will happen when the study drug is given to people.
No side effects were seen in rats when L-1, L-2 and L-3 were given at a dose that was many times higher than the dose of drug that you will receive.
Although L-1, L-2 and L-3 have not been given to people, it is similar to approved drugs called raltegravir (ISENTRESS*) and dolutegravir (TIVICAY®) that are available by prescription.

The most common adverse reactions of moderate to severe intensity (*2%) seen in people who take ISENTRESS* are:
* difficulty falling and/or staying asleep
* headache
* dizziness
* nausea
* lack of energy

Other adverse reactions seen in people who take ISENTRESS* are:
* changes in enzyme levels that may indicate muscle and brain damage
* muscle pain and weakness
* abnormal muscle breakdown which can lead to kidney problems

The most common adverse reactions of moderate to severe intensity (*2%) seen in people who take TIVICAY® are:
* difficulty and/or staying asleep
* lack of energy
* headache

With any drug, there is the potential for an allergic reaction. The most commonly reported symptoms associated with allergic reactions are:
* rash
* nausea
* cough
* dizziness
* fainting
* hives
* itching
* facial flushing
* fever
* muscle aches
* chest tightness
* shortness of breath/difficulty breathing

Rarely, a more severe allergic reaction may occur and may result in death. Additional symptoms may include:
* swelling of the face, lips, throat and tongue
* low blood pressure
* loss of consciousness

Procedures:

Registration of adverse effects:
During the entire study all adverse effects from the volunteer report will be documented.

Blood sampling, indwelling cannula:
During this study less than 500 milliliters of blood will be drawn. An indwelling cannula will be used regularly to sample blood on Day 1. Remaining blood samples between pre study screening and post-study screening will be drawn by direct puncture of the vein.

Intravenous (iv) study drug administration:
For the intravenous injection the volunteer will have an indwelling cannula inserted specifically for this purpose in addition to the indwelling cannula used for blood sampling on Day 1. Thus the volunteer will have a cannula inserted in both arms during dosing. The cannula for the intravenous injection will be removed as soon as possible after dosing.

Vital signs:

Respiratory rate, blood pressure, pulse rate and body temperature will be measured regularly, both in supine and standing position.

Heart trace (ECG):
ECGs will be made regularly, most frequently on Day 1.

Contacts

Public
Merck Sharp & Dohme (MSD)

Merck Drive 1
Whitehouse Station 08889-0100
US
Scientific
Merck Sharp & Dohme (MSD)

Merck Drive 1
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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

healthy male volunteers
18 - 45 yrs, inclusive
BMI: 18.5-32 kg/m2, inclusive
non-smoking

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-04-2015
Enrollment:	18
Type:	Actual

Ethics review

Approved WMO Date:	21-04-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-04-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

(Assen)

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	EUCTR2015-000715-41-NL
CCMO	NL53095.056.15