A study to evaluate the relative bioavailability and effect of food on MK-3682B Fixed-Dose Combination Tablet (MK-3682/MK-8408/MK-5172)

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- to evaluate the pharmacokinetic (PK) parameters (AUC0-t, AUC0-*, Cmax, C24, Tmax, and apparent t1/2) of MK-3682 and its circulating metabolites (IDX20664 and IDX23267), MK-5172, and MK-8408 following administration of the fixeddose combination...

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

Summary

ID

NL-OMON41831

Source
ToetsingOnline

Brief title
MK3682-016

Condition

- Viral infectious disorders

Synonym
Hepatitis C

Research involving
Human

Sponsors and support

Primary sponsor: QPS Netherlands B.V.

Source(s) of monetary or material Support: Merck

Intervention

Keyword: bioavailability, combination tablet, fixed dosed, food effect

Outcome measures

Primary outcome

- The pharmacokinetic (PK) parameters (AUC0-t, AUC0-*, Cmax, C24, Tmax, and apparent t1/2) of MK-3682 and its circulating metabolites (IDX20664 and IDX23267), MK-5172, and MK-8408 following administration of the fixeddose combination relative to the individual components when co-administered will be estimated.

Secondary outcome

- The effects of a high fat meal on the pharmacokinetic (PK) parameters (AUC0-t, AUC0-*, Cmax, C24, Tmax, and apparent t1/2) of MK-3682 and its circulating metabolites (IDX20664 and IDX23267), MK-5172, and MK-8408 following administration of the fixed-dose combination relative to the fasted state will be estimated.

Study description

Background summary

MK-3682, MK-5172 and MK-8408 are not registered as medicines. MK-3682 is a drug that is being developed together with MK-5172 and MK-8408 for the treatment of hepatitis C virus (HCV) infection. Early HCV infection is often without symptoms, but chronic infection can lead to serious liver disease. MK-3682, MK-5172 and MK-8408 inhibit certain proteins of the HCV virus that contribute to the multiplication of the virus in the body.

Study objective

- to evaluate the pharmacokinetic (PK) parameters (AUC0-t, AUC0-*, Cmax, C24, Tmax, and apparent t1/2) of MK-3682 and its circulating metabolites (IDX20664 and IDX23267), MK-5172, and MK-8408 following administration of the fixeddose combination relative to the individual components when co-administered.

- to estimate the effects of a high fat meal on the pharmacokinetic (PK) parameters (AUC0-t, AUC0-*, Cmax, C24, Tmax, and apparent t1/2) of MK-3682 and its circulating metabolites (IDX20664 and IDX23267), MK-5172, and MK-8408 following administration of the fixed-dose combination relative to the fasted state.

- To evaluate the safety and tolerability of single oral doses of co-administered MK-3682, MK-5172, and MK-8408.

Study design

This is a single-dose, open-label, randomized, two-period crossover followed by a fixed third period trial in approximately 22 healthy adult subjects to be conducted in conformance with Good Clinical Practices.

Intervention

The study will start with a screening visit. During the screening visit standard medical assessments including safety laboratory tests (blood draw, urine collection), an alcohol breath test, urine drug screen, a physical examination, ECG and a vital signs measurement will be performed. The study has 3 periods. Each period consists of 3 days in clinic (Day -1, Day 1, and Day 2) and 3 ambulant visits (Day 3, Day 4, and Day 6). Between each period at least 10 washout days are required. Period 3 has 5 ambulant visits, next to Day 3, Day 4, and Day 6, also on Day 7 and Day 14 ambulant visits are planned. These are both follow-up visits. During all the (ambulant) visits and during the stays in the unit, subjects will be asked on a regular base for possible side effects, blood will be drawnfor safety, PK and measurements and other standard safety assessment (VS, ECG, lab safety tests,*) can be performed during these days.

Study burden and risks

MK-3682: Potential side effects associated with administration of MK-3682 in single and multiple dose studies in healthy subjects include nausea, upset stomach, vomiting, stomach discomfort/pain, abnormal feces, constipation, diarrhea, runny nose, upper respiratory tract infection, cold sore, skin redness,dry eye, eye itching, drowsiness, lack of energy, dizziness, body and muscle aches, headache, red eye, feeling of rapid or skipped heartbeats, and acne.

MK-5172: Side effects reported when MK-5172 was given in combination with other drugs commonly given to HCV patients (pegylated interferon and ribavirin) included decrease in the blood cells that carry oxygen, decrease in blood cells that fight infection, stomach pain, diarrhea, upset stomach, dry mouth, nausea, vomiting, fever, decreased appetite,back pain, muscle pain, dizziness, metallic taste, headache, trouble falling asleep or staying asleep,feeling irritable, weakness, chills, fatigue, flu-like illness, general pain, cough, shortness of breath, hair loss, dry skin, itchiness, rash, and pain in the joints.

MK-8408: The following side effects were reported by 2 or more people who were in single and multiple-dose studies of MK-8408: headache, eye discomfort in bright light, upset stomach, nausea, vomiting, sore throat, common cold, back pain, blood in the urine,and increased blood pressure.

The blood collection procedure is not dangerous, but may cause discomfort or bruising. Occasionally, fainting or an infection at the blood sampling site can occur.

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. Willing to give written informed consent, including for Future Biomedical Research.
2. Male or female 18 to 45 years of age (inclusive) at the pretrial (screening) visit.
3. Standard liver function tests including ALT, AST, alkaline phosphatase and total bilirubin do not exceed the upper limit of normal for the local laboratory at screening and on Day -1 of Period 1. If total bilirubin is elevated, direct bilirubin will be measured and the subject may be eligible for inclusion if direct bilirubin is within normal limits.

Exclusion criteria

1. A history of liver disease (exception: subjects with remote hepatitis A virus infection with full recovery can be included).
2. Positive results at screening for human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), or hepatitis C virus (HCV).
3. A history of cancer (malignancy).

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):	24-11-2014

Enrollment:	22
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	MK3682
Generic name:	N.A.
Product type:	Medicine
Brand name:	MK5172
Generic name:	N.A.
Product type:	Medicine
Brand name:	MK8408
Generic name:	N.A.

Ethics review

Approved WMO Date:	10-11-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-11-2014
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	EUCTR2014-004743-12-NL
CCMO	NL51384.056.14