A Study to Evaluate the Relative Bioavailability and Effect of Food on Two Formulations of the MK-3682A Fixed-Dose Combination Tablets (MK-3682/MK-5172/MK-8742, 300 mg/ 100 mg/50 mg) in Healthy Adult Subjects.

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Primary Objective: - to evaluate the pharmacokinetic (PK) parameters (AUC0-t, AUC0-inf, Cmax, C24hr, Tmax, and apparent t*) of MK-3682 and its circulating metabolites (IDX20664 and IDX23267), MK-5172, and MK-8742 following administration of two...

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

Summary

ID

NL-OMON41736

Source
ToetsingOnline

Brief title
MK-3682A/PN018

Condition

- Viral infectious disorders

Synonym
HCV, Hepatitis C virus

Research involving

Human

Sponsors and support

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

Intervention

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

Outcome measures

Primary outcome

Hypotheses for this study:

- to estimate the pharmacokinetic (PK) parameters (AUC0-t, AUC0-inf, Cmax, C24hr, Tmax, and apparent t*) of MK-3682 and its circulating metabolites (IDX20664 and IDX23267), MK-5172, and MK-8742 following administration of two premarket formulations of a fixed-dose combination of MK-3682A (FDC-A and FDC-B) 300 mg/100 mg/50 mg relative to the individual components when co-administered at a dose of 300 mg/100 mg/50 mg.

- to estimate the effects of a high fat meal on the pharmacokinetic (PK) parameters (AUC0-t, AUC0-inf, Cmax, C24hr, Tmax, and apparent t*) of MK-3682 and its circulating metabolites (IDX20664 and IDX23267), MK-5172, and MK-8742 following administration of two premarket formulations of a fixed-dose combination of MK-3682A (FDC-A and FDC-B) 300 mg/100 mg/50 mg relative to the fasted state.

Secondary outcome

Safety

Study description

Background summary

Merck is developing an all-oral combination regimen consisting of MK-3682 (HCV NS5B nucleoside monophosphate prodrug inhibitor), MK-5172 (HCV NS3A protease inhibitor), and MK-8742 (HCV NS5A inhibitor). MK-3682, MK-5172, and MK-8742, all with potent activity against several HCV genotypes, are being developed as an all-oral direct-acting antiviral regimen. The current study should provide relative bioavailability data to guide pre-market formulation development of an FDC (fixed-dose combination) for these three antiviral agents which will be used in Phase III development.

Study objective

Primary Objective:

- to evaluate the pharmacokinetic (PK) parameters (AUC0-t, AUC0-inf, Cmax, C24hr, Tmax, and apparent t*) of MK-3682 and its circulating metabolites (IDX20664 and IDX23267), MK-5172, and MK-8742 following administration of two premarket formulations of a fixed-dose combination of MK-3682A (FDC-A and FDC-B) relative to the individual components when co-administered at a dose of 300 mg/100 mg/50 mg.

- to evaluate the effects of a high fat meal on the pharmacokinetic (PK) parameters (AUC0-t, AUC0-inf, Cmax, C24hr, Tmax, and apparent t*) of MK-3682 and its circulating metabolites (IDX20664 and IDX23267), MK-5172, and MK-8742 following administration of two premarket formulations of a fixed-dose combination of MK-3682A (FDC-A and FDC-B) relative to the fasted state, when provided at a dose of 300 mg/100 mg/50 mg.

Secondary Objective:

- to evaluate the safety and tolerability of single oral doses of co-administered MK-3682, MK-5172, and MK-8742.

Study design

Open-Label, Single-Dose, Randomized, Three-Period Crossover Study with a Fourth, Fixed-Sequence Fed Period (Five Treatments Administered in Four Periods)

Intervention

Treatment A: Co-administration of 2 x 150 mg MK-3682 tablets, 1 x 100 mg MK-5172 tablet, and 1 x 50 mg MK-8742 tablet
Administered following an overnight fast of at least 10.5 hours.

Treatment B: 1 x MK-3682A (MK-3682/MK-5172/MK-8742, 300 mg/100 mg/50 mg) FDC-A Tablet
Administered following an overnight fast of at least 10.5 hours.

Treatment C: 1 x MK-3682A (MK-3682/MK-5172/MK-8742, 300 mg/100 mg/50 mg) FDC-B Tablet
Administered following an overnight fast of at least 10.5 hours.

Treatment D: 1 x MK-3682A (MK-3682/MK-5172/MK-8742, 300 mg/100 mg/50 mg) FDC-A Tablet

Treatment E: 1 x MK-3682A (MK-3682/MK-5172/MK-8742, 300 mg/100 mg/50 mg) FDC-B Tablet

Study burden and risks

For MK-3682, possible adverse events include: dizziness, headache, nausea, abdominal discomfort, and abnormal feces.
For MK-5172, possible adverse events include: headache, loose stools, abdominal pain, nausea, abdominal discomfort, and fatigue.
For MK-8742, possible adverse events include: included gastrointestinal disorders, fatigue; infections, nervous system disorders, dysguesia, and skin irritation - the most commonly reported adverse event was headache.

The blood collection procedure is not dangerous, but may cause discomfort or bruising. Occasionally, fainting or an infection at the bloodsampling site can occur. The effects of the test medication on an unborn child are unknown

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. Non-tobacco using males and non-pregnant females, 18-55 years of age, inclusive.
2. A body mass index (BMI) of 19-32 kg/m² inclusive.
3. Good health as determined by lack of clinically significant abnormalities in health assessments performed at screening.

Exclusion criteria

1. Females who are pregnant, lactating or likely to become pregnant during the study.
2. Significant history or current evidence of chronic infectious disease, system disorders, organ dysfunction, especially cardiovascular disorders.
3. Receipt of any drug as part of a research study within 30 days before initial dosing.

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):	08-12-2014
Enrollment:	22
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	MK-3682
Generic name:	N.A.
Product type:	Medicine
Brand name:	MK-5172
Generic name:	N.A.
Product type:	Medicine
Brand name:	MK-8742
Generic name:	N.A.

Ethics review

Approved WMO Date:	01-12-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-12-2014
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	EUCTR2014-004907-58-NL
CCMO	NL51532.056.14