# A Study to Evaluate the Comparative Bioavailability of Formulation Batches of MK-3682A Fixed-Dose Combination Tablet (MK-3682/MK-5172/MK-8742, 225 mg/50 mg/25 mg) in Healthy Adult Subjects

Published: 01-06-2015
Last updated: 19-04-2024

Primary ObjectiveTo evaluate and compare the pharmacokinetic (PK) parameters (AUC0-t, AUC0-inf, Cmax, C24hr, Tmax, and apparent t*) of MK-3682 and its circulating metabolites MK-5172, and MK-8742 following administration of three test premarket...

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

## Summary

### ID

NL-OMON42602

**Source**
ToetsingOnline

**Brief title**
MK-3682A/PN022 (MK-3682/MK-5172/MK-8742, 225mg/50mg/25mg)

### 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:** bioavailablility, combination tablet, fixed dose

## Outcome measures

### Primary outcome

Hypothesis (Estimation):

To estimate the comparative bioavailability of each of the three test PMFs of

an FDC of MK-3682A (FDC-F, FDC-G, and FDC-H) relative to the reference PMF of

MK-3682A FDC (FDC-E) following single-dose administration.

### 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 a fixed-dose combination (FDC) to provide an all-oral direct-acting antiviral regimen. The current study will provide relative bioavailability (BA) data to guide premarket formulation (PMF) development of an MK-3682A FDC which will be used in Phases 2 and 3. Tablets with different dissolution profiles will be screened; dissolution profiles will be spaced to result in different F2 (similarity factor) values. The information obtained from this study will be

used to (1) set tablet manufacturing compression targets broadly; (2) validate the existing process window; and (3) inform time points for setting in vitro dissolution method specifications.

## Study objective

Primary Objective

To evaluate and compare the pharmacokinetic (PK) parameters (AUC0-t, AUC0-inf, Cmax, C24hr, Tmax, and apparent t*) of MK-3682 and its circulating metabolites MK-5172, and MK-8742 following administration of three test premarket formulations (PMFs) of a fixed-dose combination (FDC) of MK-3682A (FDC-F, FDC-G, and FDC-H), each manufactured to obtain different dissolution properties versus a reference PMF of MK-3682A FDC (FDC-E). Hypothesis (Estimation): To estimate the comparative bioavailability of each of the three test PMFs of an FDC of MK-3682A (FDC-F, FDC-G, and FDC-H) relative to the reference PMF of MK-3682A FDC (FDC-E) following single-dose administration.

Secondary Objective
To evaluate the safety and tolerability of single oral doses of MK-3682, MK-5172, and MK-8742, administered as an FDC tablet.

## Study design

This is an open-label, single-dose, randomized, four-treatment, four-period, foursequence, crossover study in 16 non-tobacco using, healthy adult male and female subjects.

## Intervention

The subjects will receive the study drugs, under direct observation, on Day 1 of each period according to the four-treatment, four-period, four-sequence randomization schedule. Each treatment will be administered to subjects following an overnight fast of at least 10 hours. All doses will be administered with 240 mL of room temperature water.

Treatment 1 (Reference): 1 x MK-3682A (MK-3682/MK-5172/MK-8742, 225 mg/50 mg/25 mg) FDC-E Tablet

Treatment 2 (Test): 1 x MK-3682A (MK-3682/MK-5172/MK-8742, 225 mg/50 mg/25 mg) FDC-F Tablet

Treatment 3 (Test): 1 x MK-3682A (MK-3682/MK-5172/MK-8742, 225 mg/50 mg/25 mg) FDC-G Tablet

Treatment 4 (Test): 1 x MK-3682A (MK-3682/MK-5172/MK-8742, 225 mg/50 mg/25 mg) FDC-H Tablet

**Study burden and risks**

For MK-3682, possible adverse events include: dizziness, headache, nauseam abdominal discomfort, and abnormal feces
For MK-5172, possible adverse events include: headache, loose stools, abdominal pain, nausea, abdmonial discomfort and fatigue
For MK-8742, possible adverse events include: gastrointestinal disorders, fatique, 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 was unknown.

# Contacts

**Public**
Merck Sharp & Dohme (MSD)

East Lincoln Avenue 126
Rahway NJ 07065
US
**Scientific**
Merck Sharp & Dohme (MSD)

East Lincoln Avenue 126
Rahway NJ 07065
US

# 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 females, 18-55 years of age, inclusive.
2. A body mass index (BMI) of 19-32 kg/m² inclusive as calculated according to QPS Netherlands B.V. Standard Operating Procedures.
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 intend to become pregnant during the study.
2. History of allergy or sensitivity to MK-3682, MK-5172, or MK-8742 or history of any drug hypersensitivity or intolerance which, in the opinion of the Investigator, would compromise the safety of the subject or the integrity of study.
3. Significant history or current evidence of chronic infectious disease, system disorders, organ dysfunction, especially cardiovascular disorders (angina, heart failure, irregular heartbeats, heart attack, hypertension, hypotension), stroke, renal or hepatic disorder, diabetes or bleeding
4. Receipt of any drug as part of a research study within 30 days before initial dosing.

## Study design

### Design

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| 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): | 14-06-2015 |
| Enrollment: | 16 |
| Type: | Actual |

### Medical products/devices used

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

## Ethics review

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| Approved WMO Date: | 01-06-2015 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 12-06-2015 |
| 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 | EUCTR2015-002023-26-NL |
| CCMO | NL53636.056.15 |