An Open-Label, Single Dose, 4-Period, 4-Way Randomized Crossover Study to Evaluate the Pharmacokinetics of Preliminary Market Formulations of MK-8408 in Healthy Adult Subjects.

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Primary:1. To assess the pharmacokinetic profiles following single dose administration of MK-8408 administered as a PMF1 tablet by means of AUC0-*, AUClast, AUC0-24, Cmax, C24, tmax, and t* under fed conditions, following a high fat meal. 2. To...

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

Summary

ID

NL-OMON40769

Source
ToetsingOnline

Brief title
PN005

Condition

- Viral infectious disorders

Synonym
Hepatitis C infection

Research involving
Human

Sponsors and support

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

Intervention

Keyword: - Healthy volunteers, - Pharmacokinetics, - Safety

Outcome measures

Primary outcome

- Pharmacokinetics

Secondary outcome

- Pharmacokinetics

- Safety

Study description

Background summary

This formulation selection study will evaluate the candidate PMF1 (preliminary market formulation 1) and PMF2 tablet formulations and their associated systemic pharmacokinetics when administered under fed conditions following a high fat meal or under fasted conditions in the absence & presence of a histamine (H2)-receptor antagonist, in order to select a formulation for later stage clinical development.

Study objective

Primary:
1. To assess the pharmacokinetic profiles following single dose administration of MK-8408 administered as a PMF1 tablet by means of AUC0-*, AUClast, AUC0-24, Cmax, C24, tmax, and t* under fed conditions, following a high fat meal.

2. To assess the pharmacokinetic profile following single dose administration of MK-8408 administered as a PMF1 tablet by means of AUC0-*, AUClast, AUC0-24, Cmax, C24, tmax, and t* under fasted conditions, in the absence and presence of famotidine.

3. To assess the pharmacokinetic profiles following single dose administration of MK-8408 administered as a PMF2 tablet by means of AUC0-*, AUClast, AUC0-24, Cmax, C24, tmax, and t* under fed conditions, following a high fat meal.

4. To assess the pharmacokinetic profile following single dose administration of MK-8408 administered as a candidate preliminary market formulation PMF2 tablet by means of AUC0-*, AUClast, AUC0-24, Cmax, C24, tmax, and t* under fasted conditions, in the absence and presence of famotidine.

Study design

Open-Label, Single Dose, 4-Period, 4-Way Randomized Crossover Study 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 willbe performed.

For 4 periods during the study, the subjects will stay in the clinic for 3 days and return to the unit the following 2 days. Between the dosings at least 10 washout days are required. Two weeks after the last dosing, a follow-up will occur. 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 drawn for safety, PK measurements and other standard safety assessment (VS, ECG, lab safety tests,*) can be performed during these days.

Study burden and risks

Single doses of MK-8408 have been generally safe and well-tolerated by the subjects in the first studywith MK-8408. No serious adverse experiences have been reported and no subject has been discontinued by the Investigator. Adverse experiences have been mild to moderate in intensity and transient in duration. Twelve (12) subjects have reported adverse experiences. Since the trial is still blinded, it is not known if these adverse events were experienced by subjects receiving active drug or placebo. The reported adverse experiences are headache (19),photophobia (1), nausea (1), sore throat (1), and ecchymosis at the site of a blood draw (1). There have been no consistent treatment-related changes in laboratory, vital signs, or ECG safety parameters.

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. Be a healthy man or woman, aged 18 to 45 years, (inclusive).
2. Have a body mass index (BMI) 18.0 to 30.0 kg/m2, (inclusive).
3. Have a 12-lead electrocardiogram (ECG) and vital signs within normal range at Screening, judged by the Investigator.
4. Be judged by the investigator to be in good health based on previous medical history, physical examination, vital sign measurements, and laboratory safety tests at Screening and/or on Day -1 of Period 1.
5. Be free of any clinically significant disease and have no history of any infectious disease within 4 weeks of the first dose that would interfere with study evaluations.
6. The male subject must
• use two methods of contraception in combination with their partner, if the female subject or female partner of a male subject is of childbearing potential; this combination of

contraceptive methods must be used from the start of the study until at least 3 months after the last dose of IMP. At least one of the contraception methods must be a barrier contraception method. Contraceptive methods allowed include the following: condoms; diaphragm in combination with a spermicide; intrauterine device (IUD); contraception implants; *mini pills* (with gestagens only); injectable gestagens; combination hormonal contraceptive methods (tablets, patch, or vaginal ring with both ethinylestradiol and gestagen), OR
• not be sexually active at enrolment in the study and accept using double-barrier contraception should they become sexually active during or within 3 months after the last dose of IMP, OR ;Male subjects with female partners must:
• have been surgically sterilised prior to inclusion,OR
• have a partner who is post-menopausal and has had her last natural menstruation at least 24 months prior to inclusion, OR
• have a partner who has had a hysterectomy prior to inclusion, OR
• have a partner who has been surgically sterilised prior to inclusion, AND
• agree not to donate sperm during participation in the trial and up to 3 months after follow up visit.
7. Female subjects of childbearing potential must demonstrate a serum β-hCG level consistent with the nongravid state at the pretrial(screening) visit and agree to use (and/or have their partner use) two (2) acceptable methods of birth control beginning at the pretrial visit throughout the trial (including washout intervals between treatment periods/panels) and until 2 weeks after the last dose of trial drug in the last treatment period. Acceptable methods of birth control two (2)of the following: intrauterine device (IUD-with or without local hormone release, no other hormonal birth control is allowed), diaphragm, cervical cap, contraceptive sponge, and /or condoms. Abstinence is an alternative life style and subjects practicing abstinence may be included in the trial. ;A female subject of non-childbearing potential is defined as:
• a female who is postmenopausal without menses for at least 1 year and an FSH value in the postmenopausal range upon pretrial (screening) evaluation,
and/or
• a female who is status post hysterectomy, oophorectomy or tubal ligation. Documented hysterectomy or oophorectomy must be confirmed with medical records of the actual procedure or confirmed by an ultrasound. Tubal ligation
must be confirmed with medical records of the actual procedure otherwise the subject will be excluded. Information must be captured appropriately within the site's source documents. A female subject, who doesnot meet the entry criteria for
a female of non-childbearing potential (based on the postmenopausal criteria or medically documented surgical sterilization), may be enrolled following the same criteria as for a female subject of childbearing potential (i.e. she agrees to a pre-trial β-hCG pregnancy test and to use two forms of approved birth control or practice abstinence).
8. Be a non-smoker or has not used nicotine or nicotine-containing products for at least 3 months prior to the screening.
9. Subjects must be willing to give written informed consent for the trial and Future Biomedical Research, understand the study procedures, and be able to adhere to dose and visit schedules and study restrictions.

Exclusion criteria

1. Has a history of human immunodeficiency virus (HIV), Hepatitis B or C, liver injury, clinically significant hepatic abnormalities or disease, history of clinically significant abnormalities in liver function tests, or subject has a history of Gilbert*s Syndrome or has a history of elevated unconjugated bilirubin.
2. Is mentally or legally incapacitated, has significant emotional problems at the time of Screening or expected during the conduct of the study or, in the opinion of the investigator, has a history of a clinically significant psychiatric disorder.
3. Has a history of any illness that, in the opinion of the study investigator, might confound the results of the study or poses an additional risk to the subject by his participation in the study.
4. Has used any prescription medications within 14 days or 5 half-lives of the first dose or any non-prescription/over-the-counter or homeopathic remedies, excluding paracetamol/acetaminophen, within 7 days of the first dose. The investigator may allow participation of the subject who does not fulfill this criterion in case no interaction with the study drug is expected.
5. Has a history of regular alcohol consumption exceeding 21 drinks/week (1 drink = 5 ounces [150 mL] of wine or 12 ounces [360 mL] of beer or 1.5 ounces [45 mL] of hard liquor).
6. Consumes excessive amounts, defined as greater than 6 servings (1 serving is approximately equivalent to 120 mg of caffeine) of coffee, tea, cola, or other caffeinated beverages per day.
7. Has had major surgery within 6 months of the first dose, donated or lost 1 unit of blood (approximately 500 mL) within 8 weeks of the first dose.
8. Has participated in another investigational study within 3 months prior to Day 1 of Period 1.
9. In the opinion of the investigator, has a history of significant multiple and/or severe allergies (including latex allergy), or has had an anaphylactic reaction or significant intolerability to prescription or non-prescription drugs or food.
10. Is currently a regular user (including *recreational use*) of any illicit drugs or has a history of drug (including alcohol) abuse in the past 2 years.
11. Is being considered inappropriate for participation in the study or there is any concern by the investigator regarding the safe participation of the subject in the study.

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):	25-08-2014
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	-
Product type:	Medicine
Brand name:	-
Generic name:	Famotidine
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	11-08-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	25-08-2014
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□002287□32-NL
CCMO	NL50237.056.14