A Study to Evaluate the Comparative Bioavailability of One Tablet of 480 mg MK-8228 and Two Tablets of 240 mg MK-8228 Under Fasted Conditions in Healthy Subjects

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- To compare the primary pharmacokinetic parameters AUC0-last, AUC0-*, and Cmax of MK-8228 after single dose administration of one tablet of 480 mg MK-8228 (test) and two tablets of 240 mg MK-8228 (reference) under fasting conditions.- To compare...

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

Summary

ID

NL-OMON40940

Source
ToetsingOnline

Brief title
MK-8228 PN028

Condition

- Viral infectious disorders

Synonym
CMV infection, virus infection

Research involving
Human

Sponsors and support

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

Intervention

Keyword: - Bioavailability, - Healthy volunteers, - Safety, - Tolerability

Outcome measures

Primary outcome

Pharmacokinetics

Secondary outcome

- Pharmacokinetics

- Safety

- Tolerabililty

Study description

Background summary

MK-8228 is currently in phase III. Within the phase III program doses of 480 mg are given. The 480 mg tablet will only be available for the phase III program after initiation. Therefore the Phase III trial will start using 2x240 mg to dose 480 mg. In order to introduce this 480 mg tablet in the ongoing Phase III program, information on the comparative bioavailability of one tablet of 480 mg and two tablets of 240 mg each is desired.

Study objective

- To compare the primary pharmacokinetic parameters AUC0-last, AUC0-*, and Cmax of MK-8228 after single dose administration of one tablet of 480 mg MK-8228 (test) and two tablets of 240 mg MK-8228 (reference) under fasting conditions.

- To compare the pharmacokinetic profiles of MK-8228 following single oral administration of one tablet of 480 mg and two tablets of 240 mg each, under fasted conditions.

- To assess the safety and tolerability of the 480 mg MK-8228 tablet.

Study design

This is a single-center study which consists of 2 periods (period I and period II), sequentially conducted in 14 healthy female subjects. Subjects will participate in both period I and period II.

Intervention

The study will start with a screening. At the screening a physical examination will take place and a few other standard medical assessments will be performed (ECG, vital signs). Furthermore a blood and urine sample will be taken for laboratory tests and an alcohol breath test and drug screen will be done. During the stay in the clinic (P1 and P2) the subject will receive the research medication once. On several time points blood will be taken. The subjects will be asked for possible side effects on regular basis. Furthermore several safety assessments will be done (ECG, vital signs, laboratory tests). Finally, as a follow-up the subjects will receive a phone call.

Study burden and risks

Overall, MK-8228 has been generally well tolerated. The most common non-serious adverse experiences observed with administration of MK-8228 are headache, nausea, dizziness, diarrhea, somnolence, abdominal distension, fatigue and vomiting.

Contacts

Public
Merck Sharp & Dohme (MSD)

MERCK Drive 1
New Jersey 08889-0100
US
Scientific
Merck Sharp & Dohme (MSD)

MERCK Drive 1
New Jersey 08889-0100
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Be a non-pregnant and non-breast feeding female of 18 to 55 years of age (inclusive) at the screening visit, further:;a. [Females of childbearing potential] Demonstrate a serum beta-human chorionic gonadotropin (ß-hCG) level consistent with the non-gravid state at the pre-trial (screening) visit and must agree to abstain from heterosexual intercourse, use a double-barrier local contraception method (e.g., spermicidal gel plus condom), or intra-uterine device (IUD) combined with another allowed contraceptive method, for the entire duration of the trial, until 4 weeks after the last dose of trial drug.;b. [Females of non-childbearing potential] Be postmenopausal without menses for at least 1 year and has an follicle stimulating hormone (FSH) value in the postmenopausal range upon pre-trial (screening) evaluation, and/or is status post hysterectomy, oophorectomy,or tubal ligation, based on the subject's recall of their medical history. Information must be captured appropriately within the clinical site's source documents.
2. Have a Body Mass Index (BMI) between 18.0 and 32.0 kg/m^2 (inclusive) at the screening visit. BMI is calculated according to QPS SOP's.
3. Be judged by the investigator to be in good health based on medical history, physical examination, vital signs measurements, ECG recording and laboratory safety tests performed at the screening visit and/or prior to administration of the initial dose of study drug.
4. Be a nonsmoker or has not used nicotine or nicotine-containing products for at least 3 months prior to screening.
5. Understand the study procedures and agree to participate in the study by giving written informed consent.
6. Is willing to comply with the study restrictions.
7. Subjects provide written informed consent/assent for the trial, including for Future Biomedical Research.

Exclusion criteria

1. Has a history of HIV, hepatitis B/C, liver injury, clinically significant hepatic abnormalities or disease or was confirmed positive by serology test during screening.
2. Has a confirmed positive serum pregnancy test or is reastfeeding.
3. Is mentally or legally incapacitated, has significant emotional problems at the time of the screening visit or expected during the conduct of the study or, in the opinion of the investigator, has a history of a clinically significant psychiatric disorder.
4. 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 their participation in the study.
5. Has a history of clinically significant endocrine, dermatological, neurological, psychiatric, gastrointestinal, cardiovascular, hematological, hepatic, immunological, renal, respiratory, or genitourinary diseases.
6. Has an estimated creatinine clearance (CLCr) of <=80 mL/min at pre-trial (screening) visit based on the Cockcroft-Gault equation; the Cockcroft-Gault equation is as follows:
CLCr = 0.85 x (((140-age [yr])(body weight [kg]))/
((72)(serum creatinine [mg/dL])))
When creatinine is measured in µmole/litre, use the following formula:
CLCr = 0.85 x (((140-age [yr])(body weight [kg]) x constant)/
((72)(serum creatinine [µmole/L])))
An actual CLCr, as determined by a 24-hour urine collection, may be used in place of, or in conjunction with, the Cockcroft-Gault equation
7. Has a history of neoplastic disease.
Exception: Subjects with adequately treated (with at least 5 years of non-relapse recurrence) non-melanomatous skin carcinoma may participate in the study.
8. 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).
9. 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.
10. Has had major surgery within 6 months of first dose, donated or lost 1 unit of blood (approximately 500 mL) within at least 90 days prior to dosing.
11. Has received an investigational study drug within 3 months prior to first dose.
12. 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.
13. Has known sensitivity to the study drug or any excipients used in the tablet composition.
14. Is currently a regular user (including "recreational use") of any illicit drugs or has a history of drug (including alcohol) abuse within approximately 6 months or has a positive urine drug screen or alcohol breath test at the pre-trial (screening) visit or on any admission.
15. 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.
16. Is unable to refrain from or anticipates the use of any medication, including prescription and non-prescription drugs or herbal remedies (such as St. John*s Wort [Hypericum perforatum]). Use of medication that are known to significantly (strong or moderate) inhibit or induce liver enzymes involved in drug metabolism, OATP1B1 or OATP1B3 inducers or inhibitors or Pgp inhibitors within 4 weeks or 5 half-lives prior to dosing, throughout the trial,

until the post-trial visit. There may be certain medications that are permitted (see Section 5.5).

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):	23-06-2014
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Letermovir
Generic name:	MK-8228

Ethics review

Approved WMO

Date:	28-05-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	16-06-2014
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	EUCTR2014-000773-40-NL
CCMO	NL49355.056.14