A phase 1, open-label, fixed-sequence, drug-drug interaction study between multiple oral doses of Inarigivir Soproxil and a single oral dose of midazolam in healthy subjects

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON46790

Source
ToetsingOnline

Brief title
SB-9200/midazolam DDI

Condition

- Other condition
- Hepatic and hepatobiliary disorders

Synonym
Hepatitis B virus infection

Health condition

Hepatitis B

Research involving
Human

Sponsors and support

Primary sponsor: Spring Bank Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: DDI, Inarigivir, Midazolam

Outcome measures

Primary outcome

To assess the effect of steady-state oral inarigivir on the single dose pharmacokinetics (PK) of oral midazolam in healthy subjects.

Secondary outcome

To evaluate the safety and tolerability of a single oral dose of midazolam, a single oral dose of inarigivir, and multiple oral doses of inarigivir administered without and with a single oral dose of midazolam in healthy subjects.

To assess the PK of inarigivir after single and multiple oral doses in healthy subjects.

Exploratory:

To evaluate the pharmacodynamics (PD) following single and multiple oral doses of inarigivir in healthy subjects.

Study description

Background summary

Inarigivir is a new compound that may eventually be used for the treatment of chronic hepatitis B. Hepatitis B is a worldwide common infection of the liver caused by a virus. If it does not heal spontaneously and evolves into chronic hepatitis, there is no effective treatment. If the infection has not healed spontaneously after 6 months, it is a chronic hepatitis B virus infection. Currently, there is no treatment to cure chronic hepatitis B virus infection. However, the virus can be suppressed with drugs currently available.

Inarigivir is selectively active within cells infected with the hepatitis B virus. Inarigivir binds certain proteins in the cell resulting in the inhibition of replication of the virus and in addition the induction of antiviral defense.

Study objective

The purpose of the study is to investigate the effect of inarigivir on the absorption, distribution and elimination of midazolam in order to assess to what extent inarigivir may possibly change the pharmacokinetics of other drugs when given with inarigivir in the future. In addition, the pharmacokinetics of single and multiple doses of inarigivir will be investigated. It will also be investigated how safe inarigivir is and how well inarigivir is tolerated. Further, the effect of inarigivir on certain blood markers, will be investigated.

Study design

This is an open-label, fixed-sequence, drug-drug interaction study in 16 healthy male or female volunteers.

The actual study will consist of 1 period during which the volunteer will stay in the research center (location UMCG) for 21 days (20 nights).

Day 1 is the first day of administration of the study compound. The volunteer is expected at the research center at 14:00 h in the afternoon prior to the day of first administration of the study compound. The volunteer will leave the research center on Day 20 of the study.

Planned treatments:
Day 1: a single dose of 2 milligrams (mg) midazolam on Day 1 (Day 1 is the first day of administration of the study compound)

Day 3: a single dose of 400 mg inarigivir (4 tablets of 100 mg each) on Day 3

Day 6 to Day 17: a single dose of 400 mg inarigivir (4 tablets of 100 mg each) each day for 12 days (from Day 6 to Day 17)

Day 18: a single dose of 400 mg inarigivir (4 tablets of 100 mg each) will be administered together with a single dose of 2 mg midazolam on Day 18

Intervention

During the study the volunteer will receive a single dose and multiple doses of inarigivir and 2 single doses of midazolam. Inarigivir will be given as oral tablets and midazolam will be given as an oral solution. Inarigivir will be administered with 240 milliliters (mL) of tap water. Midazolam will be administered using a syringe.

Planned treatments:
Day 1: a single dose of 2 milligrams (mg) midazolam on Day 1 (Day 1 is the first day of administration of the study compound)

Day 3: a single dose of 400 mg inarigivir (4 tablets of 100 mg each) on Day 3

Day 6 to Day 17: a single dose of 400 mg inarigivir (4 tablets of 100 mg each) each day for 12 days (from Day 6 to Day 17)

Day 18: a single dose of 400 mg inarigivir (4 tablets of 100 mg each) will be administered together with a single dose of 2 mg midazolam on Day 18

Study burden and risks

One clinical study with inarigivir has been completed and another one is still ongoing. In the completed study, inarigivir was administered as single doses up to 800 mg and multiple doses up to 900 mg for 7 days in patients with hepatitis C virus infection. After both single and multiple doses, inarigivir was well tolerated up to the highest dose level. The most frequently reported side effects following multiple doses of inarigivir were headache, diarrhea, nausea, increased liver enzymes and insomnia. The increased liver enzymes were attributed to the hepatitis C virus infection, not to inarigivir.

The single 2 mg oral dose of midazolam is a standard dose used in drug-drug interaction studies and is less than the usual therapeutic dose of 10 to 20 mg. The dose is expected to be safe and well tolerated even when given together with inarigivir.

Midazolam has a boxed warning from the FDA because it can cause breathing difficulties. Midazolam has been associated with severe breathing

difficulties, including slowed breathing, inability to breathe, airway obstruction and low oxygen most often when used together with other central nervous system depressants (for example, pain medications). A significant decrease in the rate of breathing can cause death if not treated correctly.

Pain, minor bleedings, bruising, possibly an infection.

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

-Healthy male or female subjects
-18-55 years, inclusive, at screening
-BMI 18.0-30.0 kg/m2, inclusive, at screening
-Females must be non-pregnant, non-lactating and of non childbearing potential

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-05-2018
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Inarigivir soproxil
Generic name:	N/A
Product type:	Medicine
Brand name:	Midazolam
Generic name:	n/a
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	13-03-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-04-2018
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	EUCTR2018-000607-16-NL
CCMO	NL65122.056.18