A Phase 1 Open-Label, Single Dose Study to Evaluate the Pharmacokinetics of Bedtime Dosing of JZP-324 (Extended Release Oxybate) for Oral Suspension in Healthy Subjects

Published: 18-03-2020
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Ethical review	Approved WMO
Status	Completed
Health condition type	Sleep disturbances (incl subtypes)
Study type	Interventional

Summary

ID

NL-OMON50156

Source
ToetsingOnline

Brief title
JZP-324 (Extended Release Oxybate) bedtime dosing study

Condition

- Sleep disturbances (incl subtypes)

Synonym
Narcolepsy, Sleep disorder

Research involving
Human

Sponsors and support

Primary sponsor: Jazz Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: JZP-324, Pharmacokinetics, Safety, Tolerability

Outcome measures

Primary outcome

To evaluate the pharmacokinetics of JZP-324 Formulation B following a single dose, in which the active moiety is equivalent to a 9g dose of sodium oxybate, at bedtime in healthy volunteers.

Secondary outcome

To evaluate the safety and tolerability of JZP-324 Formulation B following a single dose, in which the active moiety is equivalent to a 9g dose of sodium oxybate, at bedtime in healthy volunteers.

Study description

Background summary

JZP-324 is a new formulation and composition of oxybates that is being evaluated for the treatment of narcolepsy. Narcolepsy is a sleeping disorder that involves excessive daytime sleepiness and, in some people, sudden loss of muscle tone usually triggered by strong emotions (cataplexy). One of the current medications for narcolepsy is Xyrem® (sodium oxybate, also known as the sodium salt of gamma-hydroxybutyric acid [GHB]). Xyrem slows down the activity of the central nervous system and therefore has a depressant or sedative effect on people. Volunteer should be aware that it comes with a warning label as breathing difficulties can occur with Xyrem use. Xyrem is a solution that has to be taken twice nightly. JZP-324 is an investigational, extended release formulation that is expected to provide the same therapeutic benefits when taken once a night. In addition, Xyrem contains a high sodium (salt) content

and JZP-324 has a reduced amount of sodium.

Study objective

The purpose of this study is to investigate how quickly and to what extend JZP-324 is absorbed and eliminated from the body (this is called pharmacokinetics). It will also be investigated how safe the new compound JZP-324 is and how well it is tolerated when it is administered to healthy volunteers. JZP-324 has been administered to humans before in a previous clinical trial. The active compound in JZP-324 has also been extensively tested in the laboratory and on animals. JZP-324 will be tested at a fixed dose of 9 grams and will be given at bedtime, 2 hours after eating a high-fat meal.

This study will be performed in approximately 16 healthy male and female volunteers.

Study design

The actual study will consist of 1 period during which the volunteer will stay in the research center for 4 days (3 nights).

The volunteer will be tested for the presence of coronavirus upon admission to the research center. Until the test results are available, the volunteer will be separated from other volunteers and only have very limited contact with study staff. This is to avoid virus spread from potentially infected volunteers to other volunteers or to the study staff because, until the results are available, it is not certain whether the volunteer is infected or not and can thus potentially infect others. The test results will be available within one hour. If the volunteer test positive for coronavirus, volunteer cannot participate in the study.

The coronavirus test will be done on the following days:
• Day -1 (upon admission)
• Day 2

On Day 1 you will be required to fast for 8 hours (no food and drinks, with the exception of water). After this, you will be given a high calorie meal in the evening. This meal must be consumed entirely within 30 minutes.

Two hours after the start of the meal the volunteer will receive 9 grams of JZP-324 as a single dose. JZP-324 will be given as granules in an oral suspension of 50 milliliters (mL) of (tap) water. After administration of the study compound, the dosing cup will be rinsed twice with 60 mL of water, which the volunteer will also be required to drink.

After receiving JZP-324, the volunteer must fast again for 8 hours. However, 1

hour after dosing the volunteer may drink water.

During the first 4 hours after administration of the study compound the volunteer must stay in bed (except when indicated as such by one of the investigators). When the 4 hours have passed, the volunteer will be determined for his / her degree of alertness and coordination before he / she can get out of bed again.

Intervention

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Study burden and risks

The active substance in JZP-324 is the same as the active substance in Xyrem (sodium oxybate). The risks associated with JZP-324 are expected to be similar to those associated with Xyrem.

The safety of JZP-324 has been investigated in a single clinical trial before. This study found that JZP-324 is safe, was well tolerated and lead to similar side effects as Xyrem. The most side effects were of mild severity, and none were severe.

The most commonly reported side effects of JZP-324 (in more than 10% of the volunteers) were:
• Sleepiness
• Dizziness
• Headache
• Myoclonus (quick, involuntary muscle jerk)

• Fatigue
• Feeling hot
• Nausea
• Vomiting
• Euphoric mood
• Decreased appetite

Possible discomforts due to procedures:

Drawing blood and/or insertion of the indwelling cannula (tube in an arm vein) may be painful or cause some bruising.

To make a heart tracing, electrodes (small, plastic patches) will be pasted at specific locations on arms, chest and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

A sample for the coronavirus test will be taken from the back of the nose and throat using a swab. Taking the sample only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the throat may cause volunteer to gag. When the sample is taken from the back of the nose, volunteer may experience a stinging sensation and the eyes may become watery.

Contacts

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Scientific
Jazz Pharmaceuticals, Inc.

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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. Healthy male or female subjects aged 18 to 45 years, inclusive.
2. Body mass index (BMI) between 18 and 30 kg/m2, inclusive, with a minimum body weight of
60 kg.
3. Good general health as determined by the investigator through medical history, physical
examination, electrocardiogram (ECG), vital signs, and laboratory tests at Screening and baseline
(Day -1).
4. Negative screens for human immunodeficiency virus antibodies (HIV-Ab), hepatitis B surface
antigens (HBsAg), hepatitis C virus antibodies (HCV-Ab), hepatitis A IgM antibodies (Hep A
IgM - Ab), and no clinical history related to these infections.
5. Negative urine drug and urine alcohol screens and negative serum pregnancy tests (for female
subjects) at Screening and baseline (Day -1).

(For the complete overview of the Main Inclusion Criteria see the protocol)

Exclusion criteria

1. Has a clinically significant unstable medical abnormality, chronic disease, or history or presence
of significant neurological (including seizure and cognitive disorders) or psychiatric disorder (incl. depression suicidality, schizophrenia etc.), hepatic, renal, endocrine, cardiovascular (including hypertension), gastrointestinal, pulmonary, or metabolic disease or any other abnormality that could interfere with the pharmacokinetic evaluation of the study drug.
2. Has a history or the presence of gastrointestinal (including peptic ulcer), hepatic, or renal disease

or other condition known to interfere with the absorption, distribution, metabolism, or excretion of drugs.
3. Is a female subject who is pregnant or plans to become pregnant during the study, nursing, or
lactating.
4. Has any severe drug allergy or a history of allergic or severe adverse reactions (asthma, urticaria)
or intolerance to oxybate products (eg. Xyrem), gamma-hydroxybutyrate (GHB), or any components of the dosage forms.
5. Has a history of substance (drug or alcohol) abuse within the last 2 years, known drug dependence, or positive test for drugs of abuse.

(For the complete overview of the Main Inclusion Criteria see the protocol)

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	15-07-2020
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	na
Generic name:	sodium oxybate mixed salts, immediate release + extended release

Ethics review

Approved WMO Date:	18-03-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-03-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-07-2020
Application type:	Amendment
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	EUCTR2020-000124-19-NL
CCMO	NL73098.056.20

Study results

Date completed:	12-08-2020
Results posted:	20-05-2021

First publication
20-04-2021