A Single-Dose, Open-Label, Randomized, 4-Way Crossover Pivotal Study to Assess the Bioequivalence of Canagliflozin when Administered as the Monohydrate form to the Hemihydrate form in Healthy Adult Subjects under Fasted Conditions

Published: 18-08-2015
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The purpose of this studie is to evaluate the bioequivalence of canagliflozin.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON42409

Source
ToetsingOnline

Brief title
A Pharmacokinetic (PK) study of Canagliflozin in Healthy Volunteers

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
glucose-lowering therapy, glycemic control

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Janssen Research and Development

Intervention

Keyword: bioequivalence, safety, single dose, tolerability

Outcome measures

Primary outcome

Bioequivalence

Secondary outcome

Safety

Tolerability

Study description

Background summary

A new polymorph for canagliflozin (canagliflozin monohydrate) was recently discovered. Since this is a new form, there is no information available on its clinical bioavailability. Results from this study and the comparison to the hemihydrate form (used in the currently marketed tablets) will provide an understanding of the bioavailability of the canagliflozin monohydrate form and also provide useful guidance around active pharmaceutical ingredient (API) process control requirements.

Based on physiologic based dissolution testing and in silico modeling using Gastroplus, the 100% monohydrate form is predicted to be bioequivalent to the 100% hemihydrate form. The results from this study will also confirm the predictions based on the Gastroplus modeling.

Study objective

The purpose of this studie is to evaluate the bioequivalence of canagliflozin.

Study design

This is a randomized, open-label, single-center, single-dose, 4-treatment, 4-way crossover study in 44 healthy adult participants. The study onsists of 3 phases: a Screening Phase of approximately 3 weeks (Days -22 to -2), an Open-Label Treatment Phase consisting of 4 single-dose Treatment Periods of 5 days each (Days -1 through 4) separated by a washout of 7 days (1 day) between Day 1 of each Treatment Period, and a Follow-up Phase occurring 5 to 7 days after the last study-related procedure on Day 4 the last Treatment Period.

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 will be performed.

After the subject passes all above mentioned tests,the subject will be enrolled in the study.

During study the subject will enter the clinic. In P1-P4, the subjects will receive 1 medication once on day 1. Subjects will be asked on a regular basis for possible side effects, blood will be drawn for PK/PD (glucose) and the vital signs will be checked during the 4 confinement periods. Finally a follow-up examination will be performed. During this visit the subjects will be asked for possible side effects, blood and urine be collected for safety, the vital signs/ECG will be checked and a physical examination will be conducted.

Study burden and risks

Side effects that have been seen with, or are more likely to occur with, canagliflozin include:

• Dizziness or lightheadedness upon standing
• Increased urination and thirst
• Urinary tract infections
• Allergic reaction including rash or hives
• Constipation
• Nausea
• Changes in laboratory values have been observed in clinical studies with canagliflozin
• Bone fractures may occur in up to 1 in 50 people per year on canagliflozin.
• Diabetic ketoacidosis (increased levels of blood acids called ketones)

For Women:
• Vaginal yeast infections and vaginal itching

For Men:
• Yeast infection at the head of the penis

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Willing to adhere to the prohibitions and restrictions specified in this protocol ;- If a woman must, must be postmenopausal (age >=40 years with no spontaneous menses for at least 2 years and follicle stimulating hormone [FSH] >= 40 micro international units per milliliters [mIU/mL]), surgically sterile (hysterectomy, bilateral ophorectomy, tubal ligation, or otherwise be incapable of;pregnancy), abstinent, or, if sexually active, be practicing an effective method of birth control (example[e.g], prescription oral contraceptives, contraceptive injections, intrauterine device, double-barrier method, contraceptive patch, male partner sterilization) Note: For abstinent and sexually active females who are able to

become pregnant and not using hormonal contraceptives, must use an effective method for birth control for 14 days before dosing and throughout the study. If a woman using a hormonal contraceptive, must be using the same hormonal contraceptive for 3 months before entry, and throughout the study;- If a woman, must have a negative urine pregnancy test at screening and on Day 1 of each Treatment Period.;- Body mass index (BMI; weight [kilogram {kg}]/height^2 [m^2]);between 18 and 30 kg/m^2 (inclusive), and body weight not less than 50 kg;- Blood pressure (an average of 3 measurements done after the subject is sitting for 5 minutes and with 5 minutes interval between measurements) between 90 and 140 per milliliters of mercury level (mm Hg), inclusive, systolic and no higher than 90 mm Hg diastolic at Screening or Day -1 of the first Treatment Period

Exclusion criteria

- History of or current clinically significant medical illness including (but not limited to) cardiac arrhythmias or other cardiac disease, hematologic disease, coagulation disorders (including;any abnormal bleeding or blood dyscrasias), lipid abnormalities, significant pulmonary disease,;including bronchospastic respiratory disease, diabetes mellitus, hepatic or renal insufficiency, thyroid disease, neurologic or psychiatric disease, infection, or any other illness that the investigator considers should exclude the subject or that could interfere with the interpretation of the study results.;- Clinically significant abnormal values for hematology clinical chemistry or urinalysis at screening. These significant abnormal values for hematology, clinical chemistry, or urinalysis at screening. These;laboratory evaluations will not be performed on Day 1 of Period 1 if the Screening assessments were performed within 3 days of Day 1;- Clinically significant abnormal physical examination (Screening;only), 12-lead electrocardiogram (ECG) (Screening only) or vital signs at screening or on Day -1 of the;first Treatment Period as deemed appropriate by the investigator ;- Use of any prescription or nonprescription medication (including vitamins and herbal supplements), except for paracetamol, hormonal contraceptives and hormonal replacement therapy within 14 days before the first dose of the study drug is scheduled.;- History of or a reason to believe, a subject has a history of drug or alcohol abuse within the past 5 years.

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):	23-09-2015
Enrollment:	44
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Canagliflozin
Generic name:	Invokana
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Canagliflozin 10% monohydrate / 90% hemihydrate
Generic name:	-
Product type:	Medicine
Brand name:	Canagliflozin 100% monohydrate
Generic name:	-
Product type:	Medicine
Brand name:	Canagliflozin 50% monohydrate / 50% hemihydrate
Generic name:	-

Ethics review

Approved WMO Date:	18-08-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-08-2015
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	EUCTR2015-003176-79-NL
CCMO	NL54545.056.15