A phase I, open-label, randomized, three-way cross-over study to determine the relative bioavailability of an oral capsule formulation, given both in the fasted state and after a high fat meal, compared to an oral suspension of PSN821 in healthy male volunteers.

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Primary:- to determine the relative bioavailability of a solid formulation (capsule) of PSN821 compared with an oral suspension of the drug.Secondary :- to determine the effect of food on to determine the effect of a high fat meal or light breakfast...

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

Summary

ID

NL-OMON34811

Source
ToetsingOnline

Brief title
PSN821 3-way cross-over relative bioavailability study.

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes Type II

Research involving
Human

Sponsors and support

Primary sponsor: OSI Pharmaceuticals
Source(s) of monetary or material Support: Prosidion;een dochteronderneming van OSI Pharmaceuticals

Intervention

Keyword: G-protein coupled receptor, PSN821, Type 2 diabetes

Outcome measures

Primary outcome

Pharmacokinetics:

Concentrations of PSN821 and its metabolite PSN715297 in plasma will be

determined; PK parameters of PSN821 and metabolite PSN715297 will be calculated.

Safety:

Safety will be monitored by AEs, clinical laboratory (haematology, chemistry

and urinalysis), vital signs (supine and standing systolic and diastolic blood

pressure, pulse rate) and ECG.

Secondary outcome

n/a

Study description

Background summary

The study drug to be given, PSN821, is a new experimental drug (study drug) that could potentially be a beneficial treatment for type 2 Diabetes. Type 2 Diabetes is a disease characterized by the presence of a high level of sugar

(glucose) in the blood (hyperglycaemia). Type 2 Diabetes patients have an increased risk of, for example, blindness, kidney (renal) dysfunction and heart or blood vessel (cardiovascular) complications. The prevalence of type 2 Diabetes is high and is growing at an alarming rate. The number of adults with Diabetes in the world is expected to reach 300 million by the year 2025, with more than 90% having type 2 Diabetes. PSN821 interacts with a protein called GPR119 that occurs naturally in the body. GPR119 is a member of the G-protein coupled receptor family, and is found mainly in the gut (gastrointestinal tract) and pancreas. It is involved in the secretion of hormones such as GLP-1 and insulin, and may therefore affect blood glucose levels and body weight. In laboratory experiments, results have been obtained that suggest that PSN821 may possibly lower blood glucose levels, food intake, and body weight, which could be of importance in the treatment of type 2 Diabetes. In addition PSN821 can also be administered through the mouth (orally). This new drug is still in development and is not registered as a drug.

Study objective

Primary:
- to determine the relative bioavailability of a solid formulation (capsule) of PSN821 compared with an oral suspension of the drug.

Secondary :
- to determine the effect of food on to determine the effect of a high fat meal or light breakfast on exposure and pharmacokinetics of PSN821 and its metabolite PSN715297 when PSN is administered as a capsule
- to further evaluate the safety and tolerability of PSN821 in the fasted state (oral suspension and capsule) and in the fed state (oral capsule)

Study design

Design:
A single centre, open-label, randomized, three-way cross-over study in sixteen lean healthy male subjects. Subjects will each receive 4 doses of PSN821 listed below in a randomized open-label three-way crossover study design. Subjects will be assigned to randomization block ABCD, BCAD or CABD, with 4 subjects per randomization block.

Treatment A: Single oral dose of 375 mg of PSN821 as a suspension in the fasted state
Treatment B: Single oral dose of 375 mg of PSN821 as a capsule in the fasted state
Treatment C: Single oral dose of 375 mg of PSN821 as a capsule after consuming a standard high fat breakfast
Treatment D: Single oral dose of 375 mg of PSN821 as a capsule after consuming a light breakfast

There will be a minimum of 6 days between doses. There will be an ambulant visit on Day 3 of each period.
All subjects will return for a follow-up visit 5 to 10 days after their final dose.

Procedures and assessments
Screening and follow-up:
Clinical laboratory (including clinical chemistry, haematology and urinalysis), physical examination (including body weight and Body Mass Index (BMI) calculation), vital signs (including supine and standing systolic and diastolic blood pressure and pulse rate), 12 lead electrocardiogram (ECG), adverse events (AEs) and previous and concomitant medication
Screening: demographics, height, medical history, drug and alcohol screen, HBsAg, anti-HCV and anti-HIC *.
Drug and alcohol screen and previous and concomitant medication to be repeated upon each admission.

Observation period:
Four periods in clinic each being from 17 hours before to 24 hours after drug administration, with an ambulant visit at 48 hours after drug administration.

Blood sampling:
For pharmacokinetics (PK) of PSN821 and its metabolite PSN715297 in plasma: pre-dose, 15 and 30 minutes, 1, 1.5, 2, 3, 4, 5, 6, 8, 12, 24 and 48 hours post-dose.

Safety assessments:
AEs: throughout the study; vital signs (including supine and standing systolic and diastolic blood pressure, and pulse rate): at screening, at pre-dose (triplicate), at 1, 2, 4 and 24 hours post dose and at follow-up; ECG: at screening, at pre-dose (in-triplicate) and 1, 2, 4 and 24 hours post-dose and at follow up; clinical laboratory (including clinical chemistry, haematology and urinalysis): at screening, pre-dose and at 24 and 48 hours post-dose and follow-up; drug and alcohol screen: at 48 hours post-dose.

Intervention

Study Medication
Active substance: PSN821
Activity: GPR119 agonist
Indication: Type 2 Diabetes mellitus
Strength: 50 mg/g (oral suspension) / 375 mg (oral capsule)
Dosage form: oral suspension/oral capsule

Treatment

Treatment A: Single oral dose of 375 mg of PSN821 as a suspension in the fasted state
Treatment B: Single oral dose of 375 mg of PSN821 as a capsule in the fasted state
Treatment C: Single oral dose of 375 mg of PSN821 as a capsule after consuming a standard high fat breakfast
Treatment D: Single oral dose of 375 mg of PSN821 as a capsule after consuming a light breakfast

Study burden and risks

In a previous study in 41 healthy volunteers, with doses up to 3000 mg, the following adverse effects were reported: nausea, headache and dizziness. These adverse events were all mild and only the minority was considered to be possibly related to the study medication

The insertion of the indwelling canula and the venepuncture may cause some pain, and sometimes lead to a
bruise, but the actual collection of blood will not be painful. Light bleeding and possibly an infection may
occur. However, these complications are rare.

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
* between 18 * 55 years of age
* BMI is between 18 * 25 kg/m2
* at screening the state of health must satisfy the entry requirements

Exclusion criteria

* suffering from severe illness such as hepatitis B, hepatitis C or HIV
* taken part in more than 3 other drug studies in the 10 months prior to the start of this study
* donated blood within the 60 days prior to the start of this study (50 mL or more)
* donated more than 1.5 liters during the 10 months prior to the start of this 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):	13-01-2010
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO Date:	29-12-2009
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-01-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-03-2010
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-03-2010
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	EUCTR2009-016832-11-NL
CCMO	NL30604.056.09