A Phase I, Open-label, Single Dose Study to Evaluate the Disposition, Metabolism, and Excretion of Radiolabelled [14C]-BIM23B065 Following Subcutaneous Administration in Healthy Male Subjects

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Endocrine neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON43034

Source
ToetsingOnline

Brief title
[14C]-BIM23B065 mass balance study

Condition

- Endocrine neoplasms malignant and unspecified

Synonym
pituitary adenoma, pituitary tumor

Research involving
Human

Sponsors and support

Primary sponsor: Ipsen Pharmaceuticals
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: [14C]-BIM23B065, mass balance

Outcome measures

Primary outcome

Mass balance recovery of total radioactivity in urine and faeces.

Determination of plasma levels of BIM23B065 and BIM23B133 (main metabolite identified in the nonclinical species),

Determination of total radioactivity in blood and plasma.

Secondary outcome

Metabolite profiling and identification in plasma, urine, and faeces, where possible.

Safety endpoints:

* AEs,

* Physical examination,

* Vital signs including blood pressure and heart rate (in supine and/or standing positions),

* Twelve-lead electrocardiogram (ECG) (in supine and/or standing positions),

* Local tolerance,

* Concomitant administrations (where applicable; no concomitant therapy is

allowed at study entry, but any medication prescribed during the study will be

recorded),

Clinical safety laboratory tests (haematology, coagulation, blood biochemistry,

urinalysis).

Study description

Background summary

BIM23B065 is a new investigational compound that may eventually be used for the treatment of tumors of the pituitary gland.

The pituitary gland is situated in the middle of the head at the base of the brain. The pituitary gland secretes a number of hormones which play an important role in a variety of processes in the body. The gland is about the size of a chickpea (diameter of approximately 1 centimeter). A pituitary tumor is a benign or malignant (cancerous) growth that develops in the pituitary gland. The vast majority of pituitary tumors are benign (in the sense of 'non-cancerous*). This abnormal growth may result in the overproduction of hormones. One of these hormones is the growth hormone, which, when it is overproduced, leads to acromegaly (gigantism).

BIM23B065 binds to 2 types of receptors (proteins) present in the pituitary tumor: the somatostatin receptor 2 and the dopamine receptor 2. It is expected that this will inhibit the overproduction of hormones.

BIM23B065 is in development and is not registered as a drug but has been given to healthy volunteers as a single dose first and then as repeated doses.

Study objective

The purpose of the study is to investigate how quickly and to what extent BIM23B065 is distributed, metabolized (broken down) and excreted from the body, and what the main route of excretion from the body is (urine or feces); this is called pharmacokinetics. BIM23B065 is labeled with 14-Carbon (14C) and is thus radioactive (also called radiolabeled). In this way BIM23B065 and its metabolites can be traced in blood, urine and feces. It will also be

investigated to what extent BIM23B065 is safe and tolerated by the human body.

Study design

Before the study the volunteer will undergo a pre-study screening within 28 days before the day of administration of the study compound (Day 1) during which the volunteer will be subjected to a number of medical examinations. Similar examinations will be performed after the study at the post-study screening.

The actual study will consist of 1 period during which the volunteer will stay in the clinical research center for a minimum of 9 days (8 nights) to a maximum of 16 days (15 nights). Thus, the volunteer will stay from the afternoon of Day -1 (1 day before administration of the study compound; also called admission) until at least Day 8. After administration of the study compound on Day 1, all urine and feces will be collected. The total amount of radioactivity excreted in urine and feces will be measured daily after administration of the study compound. From Day 7 onwards, if the radioactivity levels in urine and feces are below pre-defined levels, the volunteer will be allowed to leave the clinical research center the next day (from Day 8 onwards). The volunteer will leave the clinical research center at the latest on Day 15 (around noon). If the radioactivity levels are still above the pre-defined levels on Day 15, additional short visits will be scheduled for the 24-hour collection of urine and/or feces on Days 22-23 and, if necessary based on the radioactivity levels in urine and feces, on Days 29-30.

Day 1 is the day of administration of study compound. The volunteer is expected at the clinical research center at 14:00 h in the afternoon prior to the day of administration of the study compound. The volunteer will be required not to have consumed any food or drinks during the 4 hours prior to arrival in the clinical research center (with the exception of water).

On the first day of each potential additional short visit, the volunteer is expected at the clinical research center at 9:30 h in the morning and you will leave the clinic the next day in the afternoon after the 24-hour urine and/or feces collection has been completed. There are no food or fluid restrictions prior to arrival for these potential additional short visits.

The post-study screening will be planned within 5 to 9 days after the volunteer left the clinical research center for the last time. The appointment for the post-study screening will be made with as soon as it is known when the study will end for the volunteer.

Participation in the entire study, from pre-study screening until the post-study screening, will be a maximum of 66 days.

The volunteer will receive a single dose of 1.2 mg radiolabeled BIM23B065 as a

subcutaneous injection of 1 milliliter (mL) in the abdominal region. BIM23B065 will be given under fasted conditions. This means that the volunteer is not allowed to eat for at least 4 hours before administration of the study compound. During fasting the volunteer is allowed to drink water. Fasting will continue until 1 hour after administration of the study compound. Then the volunteer will receive a breakfast. During the first 2 hours after administration of BIM23B065 the volunteer will have to lie down (if allowed by the procedures).

Intervention

A single dose of 1.2 milligrams (mg) radiolabeled BIM23B065 as an injection under the skin (subcutaneous).

Study burden and risks

A clinical study with BIM23B065 has been previously conducted where 29 healthy volunteers received a single subcutaneous dose of BIM23B065 at dose levels between 0.1 and 1.5 mg. Common adverse effects observed in that study were skin reactions, such as local redness of the skin, at the site where the subcutaneous injection was given; these effects typically resolved within 2 hours after the injection with BIM23B065 was given. Other common adverse effects were nausea, hypotension (low blood pressure) and orthostatic hypotension (drop in blood pressure on standing from a sitting or lying position that may be accompanied by lightheadedness and/or dizziness); these effects were expected since they are known adverse effects of compounds that bind to dopamine receptors.

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

Provision of written informed consent prior to any study related procedure,
Male subjects aged between 18 and 64 years of age inclusive at the time of giving informed consent,
Body mass index (BMI) between 19 and 30 kg/m²
Good health as determined by a medical and psychiatric history, physical examination, ECG, blood biochemistry, haematology, urinalysis, and serology,
Vital signs (after 5 minutes resting in a supine position) that are within the following ranges (measurements may be repeated at screening at the discretion of the principal Investigator):
(a) Systolic blood pressure: 100 to 145 mm Hg,
(b) Diastolic blood pressure: 60 to 90 mm Hg,
(c) Heart rate: 50 to 100 beats/min

Exclusion criteria

Known hypersensitivity to drugs in general, including comparative drugs to the IMP, or any of the components of the formulation,
Use of any medication, including any prescription, over-the-counter, herbal remedies or other supplements (vitamins and paracetamol excluded), within 14 days prior to dosing,
Any acute or chronic/history of systemic disease or organ disease including, but not limited to gastrointestinal tract, hepatic, renal, endocrine, metabolic or cardiovascular disease or psychiatric disorder,

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):	26-10-2016
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	BIM23B065

Ethics review

Approved WMO Date:	04-10-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	18-10-2016
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	EUCTR2016-002618-31-NL
CCMO	NL59302.056.16