An open-label, single-dose study to evaluate the excretion and metabolism of oral [14C]-ONO-5788, and absolute bioavailability of oral ONO-5788 in healthy adult male subjects

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hypothalamus and pituitary gland disorders
Study type	Interventional

Summary

ID

NL-OMON48245

Source
ToetsingOnline

Brief title
ONO-5788 absolute bioavailability and mass balance study

Condition

- Hypothalamus and pituitary gland disorders

Synonym
acromegaly, extreme growth

Research involving
Human

Sponsors and support

Primary sponsor: Ono Pharma UK Ltd.
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: absorption, elimination, ONO-5788, safety

Outcome measures

Primary outcome

Part 1

Absolute BA of ONO-5788 in plasma.

Part 2

Total recovery of radioactivity in urine and faeces following a single oral dose of [14C]-ONO-5788 (expressed as a percentage of the total radioactive dose administered).

Secondary outcome

Part 1 and 2

PK parameters of total drug-related material (radioactivity, ONO-5788, and ONO-ST1-641) in blood and plasma (Table 4).

Blood/plasma ratio of total drug-related material (radioactivity, ONO-5788, and ONO-ST1-641).

Safety and tolerability parameters including collection of adverse events (AEs), physical examinations, vital signs, 12-lead electrocardiograms (ECGs), and laboratory evaluations.

Part 2

Characterization and identification of [14C]-ONO-5788 metabolites in plasma,

urine and faeces.

PK parameters of total radioactivity in urine.

Study description

Background summary

ONO-5788 is a new compound that may eventually be used for the treatment of acromegaly. Acromegaly is a disorder that results from excess production of growth hormone (GH) by the pituitary gland, a gland near the brain involved in the regulation of several hormones. In acromegaly, excess production of GH is caused by an adenoma (a benign tumor, i.e., not cancer) near the pituitary gland. If this happens before or during puberty, it can result in extreme growth. If this happens after puberty, the growth is restricted to the hands and feet and sometimes the forehead, jaw, nose, arms and legs. Treatments for acromegaly include somatostatin analogues (SSAs), compounds that mimic the hormone somatostatin which blocks production of GH in the body. Though SSAs work well in acromegaly, they require frequent injections which can be painful. ONO-5788 is an SSA which can be administered orally, offering a more convenient solution for patients.

Study objective

The purpose of this study is to investigate how quickly and to what extent ONO-5788 is absorbed and how ONO5788 is eliminated from the body. . ONO-5788 will be labelled with 14-Carbon (14C) and is thus radioactive. In this way ONO-5788 can be traced in blood, urine, and feces to determine how it is eliminated from the body.

Study design

The actual study will consist of 1 period during which the subject will stay in the research center for 12 days (11 nights). In addition, the subject will be called between Day 14 and 16. The subject will then be asked about your wellbeing.
Day 1 is the day of administration of the study compound. The subject is expected at the research center at 14:00 h in the afternoon prior to the day of administration of the study compound. He will leave the research center on Day 11 of the study.

However, if the radioactivity found in the urine and feces is higher than the pre-defined levels on Day 11, the subject will return to the research center for 24-hour collection of urine and feces on Day 14-15, Day 21-22, Day 28-29, and Day 42-43. For these collection intervals, the subject is expected in the research center in the morning of Day 14, 21, 28, and Day 42, and he can leave after the 24-hour collection interval (Day 15, 22, 29, and Day 43). He will only need to return until the radioactivity levels fall below the pre-defined levels.

Intervention

Part 1: ONO-5788 will be given as an oral capsule with 240 milliliters (mL) of water. Two hours and 15 minutes after intake of the capsule, an intravenous infusion of 0.1 mg [14C]-ONO-5788 will start. This infusion will last 15 minutes.

Part 2: [14C]-ONO-5788 will be given as a drink of 50 milliliters (mL). After administration of the study compound, the vial will be rinsed with 50 mL of the vehicle (the solution without the study compound) and 50 mL of water, which the subject will also be required to drink. Thereafter the subject is also required to drink an additional amount of 100 mL of water.
The subject will receive 10 mg ONO-5788 containing 4.1 MBq of radioactivity.

Study burden and risks

See section E.9

Contacts

Public
Ono Pharma UK Ltd.

High Holborn 71
London WC1V 6EA
GB
Scientific
Ono Pharma UK Ltd.

High Holborn 71
London WC1V 6EA
GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. The subject is willing and able to provide written informed consent.
2. Male subjects aged 21 to 65 inclusive at the time of signing the informed consent form.
3. The subject is able to communicate with the Investigator and the site staff.
4. A subject is eligible to participate if he is not trying to father a child, is willing to use one of the contraception methods listed in Section 5.3 and agrees not to donate sperm, from Day 1 of the study until 90 days after dosing.
5. The subject has a body mass index of 18.5 to 30.0 kg/m2, inclusive at screening.

Exclusion criteria

1. The Investigator deems the subject unsuitable for the study as a result of the screening examinations.
2. The subject is an employee of the Sponsor or contract research organization.
3. The subject has, or has a history of, any significant disease or disorder that would increase the risk for the subject if they were enrolled in the study or would affect study procedures or outcomes such as:
a. Gallstones, cholangitis, and/or cholecystitis;
b. Pancreatitis;
c. Hypothyroidism;
d. Known diabetes mellitus type 1 or type 2;
e. Hypocalcaemia or hypokalaemia;
f. Hypoglycaemia or hyperglycaemia or fasting blood glucose outside normal local range;
g. Thrombocytopenia or other clinically significant haematologic abnormalities;
h. Inflammatory bowel disease, irritable bowel syndrome, or abdominal surgery (with the exception of appendectomy);
i. Known vitamin B12 deficiency.
4. The subject has a positive, pre-study, hepatitis B, hepatitis C or human immunodeficiency

virus test.
5. The subject has clinically significant serum electrolyte (sodium, potassium, chloride, bicarbonate) abnormalities at screening or admission, in the estimation and clinical judgment of the Investigator or designee.

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):	31-01-2019
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO Date:	07-01-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	17-01-2019
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	EUCTR2018-004270-94-NL
CCMO	NL68467.056.18