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A study to see how [14C]-S-033188 is taken up, broken down and removed from the body

Submission date
29/09/2016

Recruitment status
No longer recruiting

Registration date
05/10/2016

Overall study status
Completed

Last Edited
06/12/2019

Condition category
Respiratory

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Influenza, known as the flu, is a common viral infection that can cause symptoms such as high fevers, chills, tiredness, muscle aches, headache and cough. Most otherwise healthy people make a full recovery from a flu infection. However, people with certain health problems such as severe asthma, or very young or elderly people may develop life-threatening complications from the flu. There are many different types of flu virus and the virus changes frequently. Therefore vaccination cannot guarantee protection against all types of flu. Current treatments for flu that can be bought from a pharmacy may alleviate only some of the symptoms. Treatments that can be prescribed by a doctor must be taken over several days and may slightly shorten the duration of the flu but do not work for all types of flu. The aim of this study is to look at how radiolabelled S-033188 (the study drug) is taken up, broken down and removed from the body when taken by mouth as an oral suspension (a drink). 'Radiolabelled' means that the test drug has a radioactive component, a tag, which helps us to track where the drug goes as it moves through and out of the body. It is hoped that the study drug will provide information about a treatment for flu that can be taken as a one-off dose and will decrease the duration and complications of flu infection.

Who can participate?
Healthy male volunteers aged between 30 and 65

What does the study involve?
The study involves a screening visit, a study visit and a follow-up visit. The screening visit involves a discussion about medical history; a breath test for smoking and alcohol; a urine test for drugs of abuse; weight and height measurements; blood and urine tests for safety; an electrocardiogram (ECG) (heart test); blood pressure, pulse rate, breathing rate and mouth temperature measurements; and a physical examination. The study visit involves receiving the study drug on Day 1. The same tests are carried out as at the screening visit, along with collection of blood, urine and faecal samples to measure the amount of drug and the amount of radioactivity in the blood, urine and faeces. Participants also provide blood samples to see how their genes affect their response to the drug. The follow-up visit is a short visit lasting about 30 minutes to ensure that volunteers' health is in the same condition as before they started the study, which includes blood and urine samples, ECG, vital signs and physical examination.

What are the possible benefits and risks of participating?
Volunteers will not receive any medical benefit from taking part in this study; however, development of a treatment for influenza may benefit the population as a whole. As with any drugs there is a risk that rare or previously unknown side effects will occur.

Where is the study run from?
Quotient Clinical – Phase I Unit (UK)

When is the study starting and how long is it expected to run for?
February to October 2016

Who is funding the study?
Shionogi (Japan)

Who is the main contact?
Mr Jon Wong

Contact information

Type(s)
Public

Contact name
Mr Jon Wong

Contact details
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Additional identifiers

EudraCT/CTIS number
2016-001195-30

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
1532T0817

Study information

Scientific Title
A phase 1 study to investigate the absorption, distribution, metabolism, and excretion of [14C] S 033188 following oral dose administration in healthy adult male subjects

Study objectives
Aim: to investigate the absorption, distribution, metabolism, and excretion of [14C]-S-033188.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wales Research Ethics Committee 2, 13/07/2016, ref: 16/WA/0184

Study design
Open-label single-centre non-randomized single-dose study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
Not available in web format, please use the contact details to request a patient information

Health condition(s) or problem(s) studied
Influenza virus infection

Interventions
Volunteers will receive a single dose of 40 mg [14C]-S-033188 suspension for oral administration (20 mL) containing not more than 3.77 MBq (102 µCi) of 14C on day 1 and then will stay at the clinical unit for up to 17 days after dosing for blood, urine and faecal samples to be collected and safety assessments to be carried out. Volunteers will be able to leave the clinical unit 13 days after dosing if they and every member of the group have reached the required level of radioactive recovery (radioactivity collected in volunteers' urine and faecal samples). If this has not happened volunteers will remain resident for up to 17 days post dose, discharging from the clinical unit on the morning of Day 18. Follow-up will be a short visit of approximately 30 minutes on Day 22 +/- 3 days to ensure that the volunteers' health is in the same condition as before they started the study, which includes blood and urine samples, ECG, vital signs and physical examination.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)

S-033188

Primary outcome measure
1. Mass balance recovery after administration of a single 40-mg dose of carbon 14 labelled S-033188 ([14C] S 033188) as an oral suspension in the fasted state
2. Whole blood and plasma concentrations of total radioactivity
3. Metabolite profiling and structural identification from plasma, urine and faecal samples

Secondary outcome measures
1. Pharmacokinetics (PK) of the drug after administration of a single 40 mg dose of [14C]-S-033188 as an oral suspension in the fasted state
2. Metabolites of S-033188 identified in plasma, urine, and faeces
3. Safety and tolerability of S-033188 and S-033447 after administration of a single 40-mg dose of ([14C]-S-033188)

Overall study start date
15/02/2016

Completion date
02/10/2016

Eligibility

Key inclusion criteria
1. Male subjects who are able to understand the study and comply with all study procedures, and willing to provide written informed consent before screening
2. Male subjects aged from 30 years to 65 years inclusive at the time of signing informed consent
3. Male subjects who are considered healthy by the investigator (or subinvestigator) based on a medical evaluation including medical history, physical examination, laboratory tests, vital signs measurements and ECG. If any clinical abnormality is identified and/or a laboratory test value exceeds the site's standard value, subjects will be considered appropriate for the study only if the investigator judges the abnormality to be not clinically significant and not to increase the risk to the subject by participation in the study nor to compromise study endpoints
4. Male subjects whose body weight is ≥ 50 kg and body mass index (BMI) is ≥ 18.0 to ≤ 32.0 kg /m2
5. Male subjects must agree to use appropriate contraception methods from the admission day (Day -1) until 3 months after discharge and agree not to donate sperm during this period

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
6

Key exclusion criteria
1. Subjects who regularly have < 1 bowel movement every 2 days
2. Subjects who have abnormal bowel habits such as diarrhoea, loose stools, or constipation within 2 weeks prior to the screening visit or prior to Day -1
3. Female subjects
4. Radiation exposure, including that from the present study, excluding background radiation but including diagnostic x-rays and other medical exposures, exceeding 5 mSv in the last 12 months or 10 mSv in the last 5 years. No occupationally exposed worker, as defined in the Ionizing Radiation Regulations 1999, shall participate in the study
5. Subjects who do not have suitable veins for multiple venipunctures/cannulation as assessed by the investigator at screening
6. Subjects with a history of any diseases of metabolism, liver, kidney, blood, lung, heart, stomach and intestines, urinary organs, endocrine system, nervous system, and mental illness, who have been judged to be ineligible for participation in this study by the investigator (or subinvestigator)
7. Subjects who need constant medication or have used any medication (including non-prescription drugs, vitamins, and dietary or herbal supplements) within 14 days before admission; exceptions may be permitted on a case by case basis if considered not to interfere with the aims of the study and agreed by the investigator and sponsor's medical advisor
8. Subjects who have received strong CYP inducers (rifampicin, carbamazepine, phenytoin, enzalutamide, mitotane, and St John's wort) and/or P-gp inducers (rifampicin, carbamazepine, phenytoin, tipranavir/ritonavir, and St John's wort) within 28 days before admission
9. Subjects with the following laboratory abnormalities at screening:
9.1. Total bilirubin >1.2 × upper limit of normal (ULN)
9.2. Alanine aminotransferase (ALT) > 1.2 × ULN
9.3. Aspartate aminotransferase (AST) > 1.2 × ULN
9.4. Creatinine clearance < 60 mL/min/1.73m2
10. Subjects who have QTcF interval of > 450 msec at screening
11. Subjects whose resting systolic pressure is outside the range of 90-140 mmHg (aged 30-45 years) or 90-160 mmHg (aged 46 to 65 years), resting diastolic pressure is outside the range of 40-90 mmHg, or a pulse rate is outside the range of 40-90 beats per minute at screening
12. Subjects with a history of surgical resection of the stomach, vagus nerve, intestines, etc (excluding appendectomy)
13. Subjects with a history of clinically significant allergic symptoms, including food allergies (excluding allergic rhinitis presenting no symptoms at the time of screening)
14. Serious adverse reaction or serious hypersensitivity to any drug or the formulation excipients
15. Subjects who have a history or regular use of tobacco- or nicotine-containing products within 6 months before screening
16. Subjects with a history of drug and/or alcohol addiction within the past 2 years before screening or a positive test for drugs or alcohol at screening or admission visit
17. Regular alcohol consumption in males >21 units per week (1 unit = ½ pint beer, 25 mL of 40% spirit or a 125 mL glass of wine)
18. Subjects with a positive result on any of the tests for the serologic detection of HIV antigen /antibody, hepatitis B surface antigen, and hepatitis C antibody
19. Subjects who have donated > 400 mL of blood within 3 months before screening, > 200 mL within 4 weeks before screening, or who donated blood between screening and admission
20. Subjects who have been exposed to an investigational drug within 90 days prior to study drug administration

21. Subjects who have received S-033188 previously
22. Subjects who are study site employees or immediate family members of a study site, or sponsor employees
23. Subjects who are ineligible for the study for any other reason, as judged by the investigator or subinvestigator

Date of first enrolment
30/08/2016

Date of final enrolment
31/08/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Quotient Clinical Phase I Unit
Mere Way
Ruddington
Nottingham
United Kingdom
NG11 6JS

Sponsor information

Organisation
Shionogi Ltd

Sponsor details
33 Kingsway
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London
United Kingdom
WC2B 6UF

Sponsor type
Industry

Website
www.shionogi.eu

ROR
https://ror.org/01v3bqg10

Funder(s)

Funder type
Industry

Funder Name
Shionogi

Alternative Name(s)
Shionogi & Co. Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Japan

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date
02/10/2017

Individual participant data (IPD) sharing plan
This is a non-paediatric Phase I clinical trial in healthy volunteers. Participant level data won't be published in publicly accessible domains on the grounds of commercial sensitivity. If detailed information on this trial was in the public domain now, it could be of advantage to competitors. Data will be stored at sponsor facilities.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No