ISRCTN12615820 https://doi.org/10.1186/ISRCTN12615820

A mass balance study of a [14C]S-309309 oral capsule in healthy adult male participants

Submission date 13/02/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 16/02/2023	**Overall study status** Deferred	
Last Edited 06/11/2025	**Condition category** Other	

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine, S-309309, for the potential treatment of obesity. When a person is overweight due to having a high amount of body fat, they are considered obese. Obesity is a complex disorder and can be associated with an increased risk of a person developing other conditions such as: hypertension (high blood pressure), type 2 diabetes, high cholesterol, cardiovascular (heart) disease, gallbladder disease, osteoarthritis (painful and stiff joints), sleep apnoea (where a person stops breathing in their sleep for short periods) and cancer. This single-part healthy volunteer study will try to identify how the test medicine is taken up, broken down and removed from the body. To help investigate this, the test medicine is radiolabelled, which means that the test medicine has a radioactive component (carbon-14; also referred as 14C) which helps us to track where the test medicine is in the body. The safety and tolerability of the test medicine will also be studied.

Who can participate?
Healthy male volunteers aged 30 to 65 years.

What does the study involve?
On Day 1, 6 volunteers will receive a single oral dose of the radiolabelled test medicine in the fasted state (on an empty stomach). Volunteer's blood, urine and faeces will be taken throughout the study for analysis of the test medicine and its breakdown products (metabolites) and for their safety.
Volunteers will remain in the clinical unit until Day 8, however if relevant radioactivity criteria have not been met, volunteers may be required to remain at the clinical unit until Day 15. If relevant criteria have not been met at this point, home collections of urine and/or faeces may be required.
Volunteers are expected to be involved in this study for approximately 6 weeks from screening to discharge.

What are the possible risks and benefits of participating?
Participants get no medical benefit from taking part in the study. However, development of a treatment for obesity may benefit the population as a whole. It is considered that the risk /benefit evaluation in this study supports the use of healthy volunteers. Full information on

possible side effects is provided to volunteers in the Participant Information Sheet and Informed Consent Form. Volunteers are closely monitored during the study and safety assessments are performed regularly.

Where is the study run from?
Shionogi B.V. (The Netherlands)

When is the study starting and how long is it expected to run for?
Apr 2023 to May 2023

Who is funding the study?
Shionogi B.V.

Who is the main contact?
Shionogi B.V. EU Regulatory Affairs
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Contact information

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Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
1007036

Protocol serial number
2204N1112, Quotient Code: QSC207970

Study information

Scientific Title
A single-group, phase 1, open-label study to investigate the absorption, distribution, metabolism and excretion of [14C]S-309309 following oral dose administration as a capsule in healthy adult male participants

Study objectives
The trial will meet the following primary and secondary objectives:
Primary objectives:
1. To determine the mass balance recovery after administration of a single 30-mg dose of [14C]S-309309 as an oral capsule in the fasted state
2. To determine the whole blood and plasma concentrations of total radioactivity
3. To assess the pharmacokinetics (PK) of total radioactivity and S-309309 after administration of a single 30-mg dose of [14C]S-309309 as an oral capsule in the fasted state
Secondary objectives:
1. To characterise and identify the metabolites of S-309309 in plasma, urine, and faeces
2. To determine the routes and rates of elimination of [14C]S-309309
3. To evaluate the extent of distribution of total radioactivity into blood cells
4. To assess the safety and tolerability of S-309309 following administration of a single dose of 30 mg [14C]S-309309 as an oral capsule

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 22/03/2023, London - Surrey Borders (London HRA Centre, 2nd Floor, 2 Redman Place, Stratford, London, E20 1JQ; surreyborders.rec@hra.nhs.uk), ref: 23/LO/0015
2. Approved 22/03/2023, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, UK; +44 (0)20 3080 6000; info@mhra.gov.uk) ref: CTA 50999/0014/001-0001

Primary study design
Interventional

Study design
Absorption metabolism distribution and elimination (ADME) study

Study type(s)
Other

Health condition(s) or problem(s) studied
Obesity

Interventions
Each participant will receive a single oral dose of [14C]S-309309 Oral Capsule, 30 mg containing not more than (NMT) 1.5 megabecquerel (MBq) after an overnight fast of at least 10 hours on one occasion.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
[14C]S-309309

Primary outcome(s)
1. Mass balance recovery of total radioactivity in urine, faeces and urine and faeces combined (Fe and CumFe) is measured by collection of all urine and faeces from participants from Day 1 until mass balance criteria has been met or discharge from the study.
2. Total radioactivity concentrations in whole blood and plasma are measured using collection of whole blood and plasma samples from Day 1 until mass balance criteria has been met or discharge from the study.
3. Pharmacokinetic parameters (Cmax, Tmax and AUC) for total radioactivity in whole blood and plasma and for S-309309 in plasma are measured using whole blood and plasma sample collections taken from Day 1 until discharge from clinical unit.

Key secondary outcome(s)
1. Chemical structure of each metabolite accounting for more than 5% of circulating total radioactivity in plasma by AUC and each metabolite in urine and faeces accounting for more than 10% of the administered radioactive dose is identified using all urine and faecal collections taken from participants from Day 1 until mass balance criteria has been met or discharge from the study.
2. Routes and rates of elimination of an oral [14C]S-309309 formulation by Ae, Fe, CumAe and CumFe by interval in urine, faeces, and urine and faeces combined, and appropriate pharmacokinetic parameters of total radioactivity in whole blood and plasma and S-309309 in plasma are measured all urine, faecal, whole blood and plasma samples from participants taken from Day 1 until mass balance criteria has been met or discharge from the study.
3. Ratio of whole blood to plasma total radioactivity concentrations and association of total radioactivity with red blood cells are measured using collection of whole blood and plasma

samples from Day 1 until mass balance criteria has been met or discharge from the study.
4. Adverse events, vital signs, ECGs, physical examinations, and safety laboratory tests in study participants exposed to single administration of S-309309 will be measured using vital signs measures, safety blood samples and symptom focused physical examinations taken from baseline until discharge from the clinical unit.

Completion date
09/05/2023

Eligibility

Key inclusion criteria
1. Participant must be ≥ 30 to ≤ 65 years of age inclusive, at the time of signing the informed consent.
2. Participants who are overtly healthy as determined by medical evaluation including medical history, physical examination, safety laboratory tests, vital sign measurements, and 12-lead electrocardiogram (ECG) at the screening visit or upon admission to the CRU.
3. Participants who have regular bowel movements (ie., average stool production of ≥ 1 and ≤ 3 stools per day).
4. Body weight ≥ 50 kg and BMI within the range ≥ 18.0 to ≤ 32.0 kg/m2 (inclusive) at the screening visit.
5. Male
6. Contraceptive use by the male participants should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.
7. Capable of giving signed informed consent that includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol.
8. Must be willing and able to communicate and participate in the whole study.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
30 Years

Upper age limit
65 Years

Sex
Male

Total final enrolment
6

Key exclusion criteria

1. Clinically significant history or presence of current cardiovascular, respiratory, hepatic, renal, gastrointestinal (GI), endocrinological, hematological, or neurological disorders capable of significantly altering the absorption, metabolism, or elimination of drugs; constituting a risk when taking the study intervention; or interfering with the interpretation of data.
2. History of GI surgery including, but not limited to, gastric resection and/or intestinal resection that may result in a clinically significant abnormality in GI function (except for an appendectomy for noncomplicated appendicitis unless it was performed within the previous 12 months).
3. Acute diarrhea, loose stools, or constipation within 14 days prior to the screening visit or upon admission to the CRU.
4. Systolic blood pressure is outside the range of 90 to 140 mmHg, diastolic blood pressure is outside the range of 50 to 90 mmHg, or pulse rate is outside the range of 40 to 100 beats per minute (bpm) or considered ineligible by the investigator or subinvestigator at the screening visit or upon admission to the CRU.
5. Lymphoma, leukemia, or any malignancy within the past 5 years except for basal cell or squamous epithelial carcinomas of the skin that have been resected with no evidence of metastatic disease for 3 years.
6. Breast cancer within the past 10 years.
7. ALT > the upper limit of normal (ULN) at the screening visit or upon admission to the CRU.
8. AST > the ULN at the screening visit or upon admission to the CRU.
9. Alkaline phosphatase > the ULN at the screening visit or upon admission to the CRU.
10. Bilirubin > the ULN (isolated bilirubin > the ULN is acceptable if bilirubin is fractionated and direct bilirubin < 35%) at the screening visit or upon admission to the CRU.
11. Estimated creatinine clearance (CLcr) < 70 mL/min based on the Cockcroft-Gault equation at the screening visit.
12. Current or chronic history of liver disease or known hepatic or biliary abnormalities (with the exception of asymptomatic gallstones). Note: participants with Gilbert's syndrome excluded from this study.
13. Any other clinically significant abnormal blood chemistry, hematology, coagulation, or urinalysis result as judged by the investigator.
14. QT interval corrected for heart rate according to Fridericia's formula (QTcF) > 450 msec at the screening visit or upon admission to the CRU.
15. Any condition requiring medication and/or other treatment, such as dietary restriction and physical therapy including current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.
16. Evidence of current SARS-CoV-2 infection.
17. Past or intended use of over-the-counter or prescription medication including recreational drugs, herbal medications, Chinese medicines, vitamins, minerals, and/or dietary supplements (other than up to 4 g of paracetamol per day) within 14 days or 5 terminal half-lives (whichever is longer) prior to dosing (Day 1). COVID-19 vaccines are accepted concomitant medications up to 7 days (168 hours) before dosing. Exceptions may apply, as determined by the investigator in consultation with the medical monitor, if each of the following criteria are met: medication with a short half-life if the washout is such that no pharmacodynamic activity is expected by the time of dosing with study intervention; and if the use of medication does not jeopardize the safety of the trial participant; and if the use of medication is not considered to interfere with the objectives of the study.
18. Use of drugs or substances known to be inducers of P-glycoprotein within 28 days prior to dosing (Day 1).
19. Participants who have had a COVID-19 vaccine within 7 days (168 hours) before dosing.
20. Live vaccine(s) within 1 month prior to screening, or plans to receive such vaccines during the study.
21. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood.

22. Participants who report exposure to more than 3 new chemical entities within 12 months prior to dosing.
23. Participants who have received any investigational study intervention/IMP in a clinical research study within the 90 days prior to the planned dosing date of this study (Day 1), or less than 5 elimination half-lives prior to Day 1, whichever is longer.
24. Presence of hepatitis B surface antigen (HBsAg) at the screening visit or any history of hepatitis B infection.
25. Positive hepatitis C virus antibody (HCV Ab) test result at the screening visit or any history of hepatitis C infection.
26. Positive human immunodeficiency virus (HIV) 1 or 2 antibody test at the screening visit or any history of HIV infection.
27. Confirmed positive prestudy urine drug screen at the screening visit or upon admission to the CRU.
28. A confirmed positive alcohol breath test at the screening visit or upon admission to the CRU.
29. Carbon monoxide breath test result of greater than 10 ppm, indicative of smoking, at the screening visit or upon admission to the CRU or history or regular use of tobacco- or nicotine-containing products within 6 months prior to screening.
30. Considered inappropriate for participation in the study for any reason by the investigator or subinvestigator.
31. 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 Ionising Radiation Regulations 2017, shall participate in the study.
32. Participants who report having been administered investigational study intervention in a 14C ADME study in the last 6 months.
33. Regular alcohol consumption within 3 months prior to the study defined as an average weekly intake of > 21 units.
34. History or regular use of known drugs of abuse and/or alcohol addiction in the past 2 years.
35. Used tobacco- or nicotine-containing products (including cigarette, pipe, cigar, chewing, nicotine patch, nicotine gum, e-cigarettes or other nicotine replacement products) within 6 months prior to admission to the CRU or refuses to refrain from using tobacco- or nicotine-containing products throughout the study.
36. Consumed alcohol or used alcohol-containing products within 24 hours prior to screening or 72 hours prior to admission to the CRU or refuses to refrain from consuming such products throughout the study.
37. Regularly consumed excessive amounts of caffeine, defined as > 6 servings of coffee, tea, cola, or other caffeinated beverages per day.
38. Sensitivity to heparin or heparin-induced thrombocytopenia.
39. Sensitivity to any of the study interventions, or components thereof, or drug or other allergy including food allergy that, in the opinion of the investigator or medical monitor, contraindicates participation in the study (NOTE: Study participants with seasonal allergies may participate unless they have ongoing symptoms).
40. Participants with pregnant or lactating partners.
41. Participants who do not have suitable veins for multiple venipunctures/cannulationas assessed by the investigator or delegate at screening.
42. Participants who are, or are immediate family members of, a study site or sponsor employee.

Date of first enrolment
04/04/2023

Date of final enrolment

09/05/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
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Sponsor information

Organisation
Shionogi B.V.

Funder(s)

Funder type
Industry

Funder Name
Shionogi B.V.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study are not expected to be made available because of their high commercial sensitivity and the negligible benefit to the public of publication of results of nontherapeutic clinical trials.

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			20/09/2023	No	No