ISRCTN90993148 https://doi.org/10.1186/ISRCTN90993148

A study in healthy volunteers designed to investigate how the radiolabelled test medicine ([14C]-S-217622) is taken up, broken down and removed from the body when taken once by mouth

Submission date
16/06/2022

Recruitment status
No longer recruiting

Registration date
24/06/2022

Overall study status
Completed

Last Edited
18/02/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
The Sponsor is developing a new test medicine for the potential treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2 / COVID-19) in patients. The main symptoms of COVID-19 include a high temperature, a new continuous cough, a runny nose, a stuffy nose, sore throat, muscle aches, diarrhoea and a loss or change in your sense of smell and/or taste. Whilst the symptoms are similar to that of the common cold, COVID-19 can lead to more severe symptoms which may require hospitalisation in order to provide the patient with oxygen or mechanical ventilation. This healthy volunteer study is trying 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) which helps us to track where the test medicine is in the body. The safety and tolerability of the test medicine is also being studied.

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

What does the study involve?
The study consists of one part, involving a single cohort of 6 volunteers. Volunteers receive a single oral dose of the radiolabelled test medicine [14C]-S-217622 Oral Suspension in the fasted state. Volunteers enter the clinical unit on Day -1 (the day before their dose) and are discharged on Day 15 (14 days after their dose) at the earliest. The residency could be extended up to Day 22 (21 days after their dose). Volunteers' blood, urine and faeces are taken throughout the study for analysis of the test medicine and for their safety. Volunteers are expected to be involved in this study for approximately 7 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, the development of a treatment for COVID-19 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?
May 2022 to August 2022

Who is funding the study?
Shionogi B.V.

Who is the main contact?
Sol Yates, sol.yates@shionogi.eu

Contact information

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Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-000356-11

Integrated Research Application System (IRAS)
1005650

Protocol serial number
Sponsor code: 2135T1216

Study information

Scientific Title
A single-group, Phase I, open-label study to investigate the absorption, distribution, metabolism and excretion of [14C]-S-217622 following oral dose administration as a suspension 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 dose of 375 mg carbon-14 labelled S-217622 ([14C]-S-217622) Oral Suspension 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-217622 after administration of a single dose of 375 mg [14C]-S-217622 Oral Suspension in the fasted state

Secondary objectives
1. To characterise and identify metabolites of S-217622 in plasma, urine and faeces
2. To determine the routes and rates of elimination of [14C]-S-217622
3. To evaluate the extent of distribution of total radioactivity into blood cells
4. To assess the safety and tolerability of S-217622 following administration of a single dose of 375 mg [14C]-S-217622 Oral Suspension

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 07/07/2022, HSC REC A (Office for Research Ethics Committees in Northern Ireland (ORECNI), Business Services Organisation, Lissue Industrial Estate West, Rathdown Walk, Moira Road, Lisburn, Co. Antrim, BT28 2RF, United Kingdom; +44 (0)28 9536 1400; reca@hscni.net), ref: 22/NI/0104

Primary study design
Interventional

Study design
Absorption metabolism distribution and elimination (ADME) study

Study type(s)
Other

Health condition(s) or problem(s) studied
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection

Interventions
Each participant will receive a single oral dose of 375 mg [14C]-S-217622 Oral Suspension (12.2 mg/g [active pharmaceutical ingredient/total oral suspension]), containing NMT 3.5 MBq on one occasion.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
[14C]-S-217622

Primary outcome(s)
1. Mass balance recovery of total radioactivity in urine, feces and urine and feces combined: Fe and CumFe at multiple timepoints up to 456 h post-dose
2. Whole blood and plasma concentrations of total radioactivity at multiple timepoints up to 456 h post-dose
3. PK parameters for total radioactivity in whole blood and plasma and for S 217622 in plasma including but not limited to: Cmax, Tmax and AUC at multiple timepoints up to 456 h post-dose

Key secondary outcome(s)
1. Identification of the chemical structure of each metabolite accounting for more than 5% (in plasma) by AUC of circulating total radioactivity and identification of each metabolite in urine and feces that account for more than 10% of the administered radioactive dose at multiple timepoints up to 456 h post-dose
2. Routes and rates of elimination of an oral [14C]-S-217622 formulation by Ae, Fe, CumAe and CumFe by interval in urine, feces, and urine and feces combined, and appropriate PK parameters of total radioactivity in whole blood and plasma and S 217622 in plasma at multiple timepoints

up to 456 h post-dose
3. The ratio of whole blood to plasma total radioactivity concentrations and the association of total radioactivity with red blood cells at multiple timepoints up to 456 h post-dose
4. AEs, vital signs, ECGs, physical examinations and safety laboratory tests in study participants exposed to a single administration of S 217622, from the time of signing the informed consent form up until discharge from the study

Completion date
14/08/2022

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 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 body mass index (BMI) within the range ≥18.0 to ≤32.0 kg/m2 (inclusive) at the screening visit or upon admission to the CRU.
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. Participants should also not donate sperm for the duration of the study and for 100 days after the study intervention administration.
7. Capable of giving signed informed consent that includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in the protocol.
8. Must be willing and able to communicate and participate in the whole study (with the exception of pharmacogenomics (PGx) testing, which is optional).

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. History or presence of/significant history of or 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. Alanine aminotransaminase (ALT) > the upper limit of normal (ULN) at the screening visit or upon admission to the CRU.
8. Aspartate aminotransaminase (AST) > the ULN at the screening visit or upon admission to the CRU.
9. 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.
10. Estimated creatinine clearance (CLcr) < 70 mL/min based on the Cockcroft-Gault equation at the screening visit.
11. Current or chronic history of liver disease or known hepatic or biliary abnormalities (with the exception of Gilbert's syndrome or asymptomatic gallstones).
12. Any other clinically significant abnormal blood chemistry, lipid profile (total cholesterol >7.0 mmol/L), hematology or urinalysis result as judged by the investigator.
13. QT interval corrected for heart rate according to Fridericia’s formula (QTcF) > 450 msec at the screening visit or upon admission to the CRU.
14. Any condition requiring medication and/or other treatment, such as dietary restriction and physical therapy including current SARS-CoV-2 infection.
15. Evidence of current SARS-CoV-2 infection.
16. 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 72 hours before dosing.
17. Participants who have had a COVID-19 vaccine within 72 hours before dosing.
18. Live vaccine(s) within 1 month prior to screening, or plans to receive such vaccines during the study.
19. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood.
20. Participants who report exposure to more than 4 new chemical entities within 12 months prior to dosing.
21. 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.
22. Participants who report current enrollment or past participation in a clinical study of S-217622.
23. Presence of hepatitis B surface antigen (HBsAg) at the screening visit or any history of hepatitis B infection.
24. Positive hepatitis C virus antibody (HCV Ab) test result at the screening visit or any history of hepatitis C infection.
25. Positive human immunodeficiency virus (HIV) 1 or 2 antibody test at the screening visit or any history of HIV infection.
26. Confirmed positive prestudy urine drug screen at the screening visit or upon admission to the CRU.
27. A confirmed positive alcohol breath test at the screening visit or upon admission to the CRU.
28. 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.
29. Considered inappropriate for participation in the study for any reason by the investigator or subinvestigator.
30. 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.
31. Participants who report having been administered investigational study intervention in a 14C ADME study in the last 6 months.
32. Regular alcohol consumption within 3 months prior to the study defined as an average weekly intake of > 21 units.
33. History or regular use of known drugs of abuse and/or alcohol addiction in the past 2 years.
34. 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.
35. 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.
36. Regularly consumes excessive amounts of caffeine, defined as > 6 servings of coffee, tea, cola, or other caffeinated beverages per day.
37. Used caffeine- or other xanthine-containing products/medications within 24 hours prior to admission to the CRU or refuses to refrain from using such products throughout the study.
38. Consumed grapefruit, grapefruit juice, Seville orange juice, orange juice, apple juice, or cranberry within 7 days prior to admission to the CRU or refuses to refrain from consuming such products throughout the study.
39. Sensitivity to heparin or heparin-induced thrombocytopenia.
40. 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.
41. Participants with pregnant or lactating partners.
42. Participants who do not have suitable veins for multiple venipunctures/cannulation as assessed by the investigator or delegate at screening.
43. Participants who are, or are immediate family members of, a study site or sponsor employee.

Date of first enrolment

19/07/2022

Date of final enrolment
14/08/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way
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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			28/06/2023	No	No