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Evaluate the efficacy, safety and dose-response of S-337395

Submission date
18/02/2025

Recruitment status
No longer recruiting

Registration date
17/03/2025

Overall study status
Completed

Last Edited
17/03/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
This research is testing a new experimental drug called S-337395 to see if it can help treat people infected with Respiratory Syncytial Virus (RSV). RSV can cause serious breathing problems like bronchitis, bronchiolitis, and pneumonia, which are especially dangerous for infants, older adults (especially those 65 and older), and people with heart or lung diseases or weakened immune systems.
The study is funded by Shionogi B.V. and will take place in London. The purpose of this research is to test the effects of an experimental drug called S-337395 (the 'study drug') that may be useful in treating patients infected with Respiratory Syncytial Virus (RSV). To test the study drug, we infect healthy participants with the study virus (a common respiratory virus that usually causes mild, cold-like symptoms) in one of our Quarantine residential facilities. After infection with the study virus, we will give the study drug to participants at random. The other participants will be given a 'placebo' (a dummy drug that looks like S-337395 and is given in the same way but contains none of the active ingredients)

Who can participate?
You must be in good health aged 18 to 55 years (inclusive), have a low resistance to the study virus RSV, and meet the study requirements for entry.
There may also be reasons why this study is not suitable for you, or you are excluded from the study despite initial investigations.

What does the study involve?
A total of up to 114 people will participate, divided into 5 groups. Each person will be part of the study for about 4 months, from the initial screening to the final clinic visit.
The study has three main phases:
1. Screening Phase: This phase happens about 2 to 3 months before the study begins. Participants will go through a screening process to make sure they're eligible for the study. If they qualify, they will sign a consent form before any study activities happen.
2. Quarantine Phase: Participants will stay in a special quarantine facility for about 16 days. They will be exposed to the RSV virus on Day 0, and their health will be closely monitored throughout their stay. Participants will be checked to make sure they're still eligible just before being exposed to the virus, and their health will be assessed regularly while they stay in quarantine.

They will leave the quarantine unit around Day 13, though they might need to stay longer if necessary.
3. Follow-up Phase: About 28 days after being exposed to the virus, participants will have a final check-up. Their symptoms will be reviewed, and a full safety exam will be done to ensure their health.

What are the possible benefits and risks of participating?
There are no specific benefits to your taking part in the study. Taking part will not improve your health, although you might develop some resistance to RSV and benefit from a general health check at Screening.
There may be unexpected and unforeseen risks related to the study drug, study virus, and study procedures. Details are listed within the study specific Informed Consent form. Whilst you are in the Quarantine Unit the medical staff will monitor your condition closely, and medical assistance will be available at all times.

Where is the study run from?
hVIVO Services Limited (UK)

When is the study starting and how long is it expected to run for?
January 2024 to October 2024

Who is funding the study?
Shionogi B.V. (Netherlands)

Who is the main contact?
hVIVO: projectadmin@hvivo.com
Shionogi project Lead: calvin.chen@shionogi.eu

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1008735

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
A phase 2a, randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, and dose-response of S-337395 in healthy participants challenged with respiratory syncytial virus (RSV)

Study objectives
Treatment with S-337395 will show an antiviral effect demonstrated by a significant reduction in RSV VL-AUC (measured by qRT-PCR) compared to placebo.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 29/01/2024, London- City & East Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 1048171; cityandeast.rec@hra.nhs.uk), ref: 23/LO/0987

Study design
Interventional double blind randomized parallel group placebo controlled trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Other

Study type(s)
Safety

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

Health condition(s) or problem(s) studied
Respiratory Syncytial Virus (RSV)

Interventions
This is a single-center, randomized, double-blind, placebo-controlled, parallel-group study in healthy adult male and female participants from 18 to 55 years of age, inclusive. The primary goal of this Phase 2a study is to assess the antiviral activity of S-337395 against RSV in the viral challenge model. In addition, safety, tolerability, and PK of S-337395 will be assessed. Approximately 114 participants are planned to be enrolled in this study, divided over 5 treatment groups:

- Group A: 1 mg S-337395, n=10
- Group B: 10 mg S-337395, n=26
- Group C: 30 mg S-337395, n=26
- Group D: 300 mg S-337395, n=26
- Group E: Placebo, n=26

Group A will be used for assessment of dose-response at a subtherapeutic concentration. Groups B, C, D, and E will be used for assessment of the antiviral activity of S-337395.

The study is divided into the following phases:

Screening Phase
From Day -90 to Day -2/-1 pre-quarantine admission. Historical generic screening data collected through the hVIVO generic screening process may be transferred to this study after the study-specific consent form has been signed by the participant.

Inpatient Phase
Participants will be resident in the quarantine unit for approximately 16 days (from Day -2/-1 to Day 13). Procedures will include:

- Pre-human viral challenge (HVC):
- Admission to quarantine unit on Day -2/-1.
- Signing of study-specific informed consent form (ICF).
- Baseline assessments will be conducted as per Schedule of Events (SoE) up to Day 0, pre-challenge.

- HVC:
- RSV-A Memphis 37b virus inoculation on Day 0.
- Study assessments will be conducted as per SoE on Day 0.

- Post-HVC:
- Randomization to receive S-337395 or matched placebo.
- Administration of IMP (S-337395/placebo). Each participant will receive IMP once daily for 5 consecutive days:
- IMP dosing will start on confirmation of RSV infection, i.e., after a positive result by qualitative integrative cycler polymerase chain reaction (qicPCR). The qicPCR of nasal wash will be performed twice daily on Days 2 to 5 (Day 5 morning only), or until a positive result is received, whichever is sooner. The earliest start of IMP dosing will be in the evening of Day 2 post-HVC (IMP will be initiated 12 hours [± 1 hour] post-nasal wash confirmation of infection), OR
- IMP dosing will start in the evening of Day 5, if no positive result is obtained by qicPCR by the morning of Day 5.
- Day 1 onwards and each day – study assessments will be conducted as per SoE.
- Participants will be discharged from the quarantine unit on Day 13 (or may remain longer at the discretion of the principal investigator [PI]/investigator).

Outpatient Phase
- Final visit: Day 28 (±3 days)

Intervention Type
Drug

Pharmaceutical study type(s)
Dose response

Phase
Phase II

Drug/device/biological/vaccine name(s)
S-337395 powder for oral suspension

Primary outcome measure
Viral load of RSV-A Memphis 37-b infected participants will be determined using qRT-PCR on nasal wash samples from first dose of study drug until discharge. This will be measured twice daily from D2 until discharge

Secondary outcome measures
1. Viral load of RSV-A Memphis 37-b infected participants will be determined by using viral culture measurements on nasal wash samples to determine the maximum viral load from first dose of study drug until discharge. This will be measured twice daily from D2 until discharge.
2. Clinical symptom related scores in healthy adult participants infected with RSV through clinical symptom diary card administration (participant completed) from D-1 until Discharge, three times per day
3. Total amount of mucus produced through tissue number and weight from first dose of study drug until discharge

Overall study start date
29/01/2024

Completion date
07/10/2024

Eligibility

Key inclusion criteria
1. Written study-specific informed consent signed and dated by the participant and the investigator obtained before any study-related assessment is performed.
2. Adult male or female aged between 18 and 55 years, inclusive, on the day prior to signing the study-specific ICF.
3. A total body weight ≥50 kg and body mass index (BMI) ≥18 kg/m² and ≤35 kg/m².
4. In good health with no history, or current evidence, of clinically significant medical conditions, and no clinically significant test abnormalities that will interfere with participant safety, as defined by medical history, physical examination (including vital signs), ECG, and routine laboratory tests as determined by the investigator.
5. Participants will have a documented medical history either prior to entering the study or following medical history review with the study physician at screening.
6. The following criteria apply to male and female participants:
6.1. Contraceptive use by men or women should be consistent with local regulations regarding the use of contraceptive methods for those participating in clinical studies.
6.2. Male participants:
- Male participants are eligible to participate if they agree to the following during the study intervention period and for at least 90 days after the last dose of study intervention:
- Refrain from donating fresh unwashed semen.
- AND
- Be abstinent from heterosexual intercourse and remain abstinent.
- OR
- Must agree to use contraception/barrier as detailed below.
- Agree to use a male condom and should also be advised of the benefit for a female partner to use a highly effective method of contraception (see Appendix 5, Contraceptive and Barrier Guidance, Contraception Guidance) as a condom may break or leak when having sexual intercourse with a woman of childbearing potential who is not currently pregnant.
- Agree to use a male condom when engaging in any activity that allows for passage of ejaculate to another person.
6.3. Female participants:
- A female participant is eligible to participate if she is not pregnant or breastfeeding, and one of the following conditions applies:
- She is a woman of nonchildbearing potential, as defined in Appendix 5, Contraceptive and Barrier Guidance, Definitions.
- OR
- Is a woman of childbearing potential and using a contraceptive method that is highly effective, with low user dependency, as described in Appendix 5, Contraception and Barrier Guidance, during the study intervention period and for at least 28 days after the last dose of study intervention. The PI/investigator should evaluate the potential for contraceptive method failure (e.g., noncompliance, recently initiated) in relationship to the initiation of study intervention.
7. Females of childbearing potential must have a negative serum pregnancy test prior to enrollment.
8. Serosuitable for the challenge agent.

Participant type(s)

Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Both

Target number of participants
114

Total final enrolment
114

Key exclusion criteria
1. History of, or currently active, symptoms or signs suggestive of upper or lower respiratory tract infection within 4 weeks prior to the first study visit.
2. Any history or evidence of any clinically significant or currently active cardiovascular, respiratory, dermatological, gastrointestinal, endocrinological, hematologic, hepatic, immunological (including immunosuppression), metabolic, urological, renal, neurological, or psychiatric disease and/or other major disease that, in the opinion of the Investigator, may interfere with a participant completing the study and necessary investigations. The following conditions apply:
2.1. Participants with a history of resolved depression and/or anxiety may be included at the discretion of the PI. Participants with a history of stress-related illness, which is not ongoing or requiring current therapy, with good evidence of preceding stressors may also be included at the PI's discretion. As required, participants will be assessed prior to enrollment with a Patient Health Questionnaire (PHQ-9) and/or Generalized Anxiety Disorder Questionnaire (GAD-7) which must score less than or equal to 4 on admission.
2.2. Rhinitis (including hay fever) which is clinically active or a history of moderate to severe rhinitis, or history of seasonal allergic rhinitis likely to be active at the time of inclusion into the study and/or requiring regular nasal corticosteroids on an at least weekly basis, within 30 days of admission to quarantine will be excluded. Participants with a history of currently inactive rhinitis (within the last 30 days) or mild rhinitis may be included at the PI's discretion.
2.3. Atopic dermatitis/eczema which is clinically severe and/or requiring moderate to large amounts of daily dermal corticosteroids will be excluded. Participants with mild to moderate atopic dermatitis/eczema, taking small amounts of regular dermal corticosteroids may be included at the PI's discretion.
2.4. Any concurrent serious illness, including history of malignancy, that may interfere with a participant completing the study. Basal cell carcinoma within 5 years of initial diagnosis or with evidence of recurrence is also an exclusion.
2.5. Participants reporting physician-diagnosed migraine can be included provided there are no associated neurological symptoms such as hemiplegia or visual loss. Cluster headache/migraine or prophylactic treatment for migraine is an exclusion.
2.6. Participants with physician-diagnosed mild irritable bowel syndrome not requiring regular

treatment can be included at the discretion of the PI.
3. Any participants who have smoked ≥10 pack years at any time (10 pack years is equivalent to 1 pack of 20 cigarettes a day for 10 years).
4. Females who have been pregnant within 6 months prior to the study.
5. Lifetime history of anaphylaxis and/or a lifetime history of severe allergic reaction. Significant intolerance to any food or drug in the last 12 months, as assessed by the PI.
6. Venous access denied inadequate for the phlebotomy and cannulation demands of the study.
7.
7.1. Any significant abnormality altering the anatomy of the nose in a substantial way or nasopharynx that may interfere with the aims of the study and, in particular, any of the nasal assessments or viral challenge, (historical nasal polyps can be included, but large nasal polyps causing current and significant symptoms and/or requiring regular treatments in the last month will be excluded).
7.2. Any clinically significant history of epistaxis (large nosebleeds) within the last 3 months of the first study visit and/or history of being hospitalized due to epistaxis on any previous occasion.
7.3. Any nasal or sinus surgery within 3 months of the first study visit.
8.
8.1. Evidence of vaccinations within the 4 weeks prior to the planned date of viral challenge.
8.2. Intention to receive any vaccination(s) before the last day of follow-up. (NB. no travel restrictions will apply after the Day 28 follow-up visit).
9. Receipt of blood or blood products, or loss (including blood donations) of ≥550 mL of blood during the 3 months prior to the planned date of viral challenge or planned during the 3 months after the final visit.
10.
10.1. Receipt of any investigational drug within 3 months or 5 half-lives of the IMP used in the other study, whichever is greater, prior to the planned date of viral challenge.
10.2. Receipt of 3 or more investigational drugs within the previous 12 months prior to the planned date of viral challenge.
10.3. Prior inoculation with a virus from the same virus-family as the challenge agent.
10.4. Prior participation in another HVC study with a respiratory virus in the preceding 3 months, taken from the date of viral challenge in the previous study to the date of expected viral challenge in this study.
11. Use or anticipated use during the conduct of the study of concomitant medication (prescription and/or non-prescription), including vitamins or herbal and dietary supplements within the specified windows, unless in the opinion of the study physician/PI, the medication will not interfere with the study procedures or compromise participant safety. Specifically, the following are excluded:
11.1. Herbal supplements within 7 days prior to the planned date of viral challenge.
11.2. Chronically used medication, vitamins, or dietary supplements, including any medication known to be potent inducers or inhibitors of cytochrome P450 (CYP) enzymes, within 21 days prior to the planned date of viral challenge.
11.3. Over-the-counter medication (e.g., paracetamol or ibuprofen) where the dose taken over the preceding 7 days prior to the planned date of viral challenge has exceeded the maximum permissible 24-hour dose (e.g., ≥4 g paracetamol over the preceding week).
11.4. Systemic antiviral administration within 4 weeks of the planned date of viral challenge.
12.
12.1. Confirmed positive test for drugs of misuse and cotinine on first study visit. One repeat test is allowed at PI discretion.
12.2. History or presence of alcohol addiction, or excessive use of alcohol (weekly intake in excess of 28 units alcohol; 1 unit being a half glass of beer, a small glass of wine, or a measure of spirits), or excessive consumption of xanthine-containing substances (e.g., daily intake in excess of 5 cups of caffeinated drinks, e.g., coffee, tea, cola).

13. A forced expiratory volume in 1 second (FEV1) <80%.
14. Positive HIV, hepatitis B virus, or hepatitis C virus test.
15. Presence of fever, defined as participant presenting with a temperature reading of ≥37.9°C on Day -2, Day -1, and/or pre-HVC on Day 0.
16. Those employed, or immediate relatives of those employed, at hVIVO or the sponsor.
17. Any other medical, psychiatric, social, or occupational condition and/or responsibility that, in the opinion of the investigator, would interfere with or serve as a contraindication to protocol adherence or the assessment of safety (including reactogenicity) will deem the participant unsuitable for the study. Any other reason that, in the opinion of the investigator, raises a concern that the subject will not be able to cope with quarantine requirements.

Date of first enrolment
03/04/2024

Date of final enrolment
04/09/2024

Locations

Countries of recruitment
England

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Sponsor type
Other

Funder(s)

Funder type
Industry

Funder Name
Shionogi BV

Results and Publications

Publication and dissemination plan
Internal Report
Publication on website
Other Publication
submission to regulatory authorities

Intention to publish date

Individual participant data (IPD) sharing plan
No plan for individual participant data sharing.

IPD sharing plan summary
Not expected to be made available