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A study in healthy volunteers to look at the safety and tolerability of the test medicine VS-041 and how it is taken up by the body when given as single and multiple doses

Submission date 06/07/2024	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 02/09/2024	**Overall study status** Completed	
Last Edited 27/06/2025	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine, VS-041, as a potential treatment for heart failure with preserved ejection fraction (HFpEF). This is a condition where the heart has increased difficulty to pump blood resulting in typical symptoms such as breathlessness, ankle swelling and fatigue.

In this study, we'll give healthy volunteers single or repeated doses of test medicine or dummy medicine (placebo), to assess the safety and tolerability of the test medicine, and how the body affects it. The effect of food will also be assessed. We'll collect blood and urine samples to complete safety tests and measure the amount of test medicine.

The test medicine hasn't been given to humans before. We'll start with a low dose and test higher doses as the study progresses.

Who can participate?
This study will take place at one non-NHS site in Nottingham and consists of two parts. We plan to enrol approximately 72 healthy men and women who are unable to have a baby, aged 18-55 years old.

What does the study involve?
SAD Cohorts 1, 2, 4 and 5: Each volunteer will receive a single dose of the test medicine or placebo, as tablets by mouth in the fasted state. Volunteers will stay in the clinic for up to 3 nights, attend 1 follow-up visit, receive 1 follow-up call and take approximately 6 weeks to finish the study.

SAD Cohort 3: Each volunteer will receive a single dose of the test medicine or placebo, as tablets by mouth in the fasted state in Period 1 and a singles dose of the test medicine in the fed state in Period 2. Volunteers will stay in the clinic for up to 3 nights and attend 1 follow-up visit in each period, receive 1 follow-up call and take approximately 12 weeks to finish the study.

MAD Cohorts: Volunteers will receive the test medicine or placebo once or twice daily for 7 days, as tablets by mouth in the fasted state. Volunteers will stay in the clinic for up to 9 nights, attend 1 follow-up visit, receive 1 follow-up call and take approximately 8 weeks to finish the study.

What are the possible benefits and risks of participating?
Benefits:
Participants will get no medical benefit from taking part in this study. We hope that the development of a product to improve the treatment of heart failure with preserved ejection fraction (HRpEF) will be of benefit to patients with this condition.
Risks:
Volunteers may experience side effects from the test medicine. The test medicine has never been given to humans before so its side effects are unknown. Full information on possible side effects is in the Participant Information Sheet and Informed Consent Form (PIS-ICF). There is always a risk of unexpected side effects or an allergic reaction. To mitigate the risk, we'll ensure that volunteers meet the entry criteria for the study and monitor volunteers closely throughout the study.

We won't increase the dose unless the study results show that it will be safe to do so, and the highest dose we can give to volunteers is one that gives blood levels of the test medicine no higher than those that caused no harm in animals.

Our screening tests might be of benefit if we find an important medical problem, but they might reveal something that the volunteer would prefer not to know about. If there are medically important findings in our tests at screening, or during the study, we will inform the volunteer's GP.

Volunteers will be confined to the clinic during the study and must make outpatient visits and comply with the lifestyle restrictions described in the PIS-ICF, including periods of fasting from food and drink except water, and short periods during which they'll be allowed no fluids. As the test medicine might make volunteers more sensitive to sunlight, volunteers must comply with restrictions on exposure to sunlight and other sources of UV light.

The test medicine might harm unborn children, so all volunteers must follow the restrictions on donation of sperm or eggs and use acceptable contraception. Were a volunteer, or a partner of a volunteer to become pregnant during the study, we would ask permission to follow up the pregnancy.

Volunteers will undergo many tests and procedures during the study.
*Blood sampling can cause soreness and bruising of the arms but these problems usually clear up within a few days to a few weeks. Susceptible volunteers may faint when we take blood samples; volunteers must lie down when we take blood samples to mitigate that risk.
*ECG stickers may cause local skin irritation.

Where is the study run from?
Quotient Sciences Limited (UK)

When is the study starting and how long is it expected to run for?
July 2024 to June 2025

Who is funding the study?
Vasa Therapeutics Sp. z o. o. (Poland)

Who is the main contact?
recruitment@weneedyou.co.uk

Contact information

Type(s)
Public, Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
1010070

Protocol serial number
VS-041-01

Study information

Scientific Title

A single and multiple dose-escalation first-in-human study evaluating the safety, tolerability, and pharmacokinetics of VS-041 in healthy subjects

Acronym
FIH SAD MAD Study of VS-041 (QSC302189)

Study objectives
Safety: SAD (Part A) and MAD (Part B)
To evaluate the safety and tolerability of single and multiple oral doses of VS-041 in healthy subjects

Pharmacokinetic SAD (Part A) Only
To evaluate the pharmacokinetics (PK) of VS-041 following single dose administration in healthy subjects

Pharmacokinetic MAD (Part B) Only
To evaluate the PK of VS-041 following multiple-dose administration in healthy subjects

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 30/08/2024, London Surrey Borders REC (Equinox House, City Link, Nottingham, NG2 4LA, United Kingdom; +44 (0)207 104 8057; surreyborders.rec@hra.nhs.uk), ref: 24/LO/0437

Primary study design
Interventional

Study design
Interventional double-blind randomized group placebo-controlled trial

Study type(s)
Safety

Health condition(s) or problem(s) studied
Heart failure with preserved ejection fraction (HFpEF)

Interventions
This is a randomised, double-blind, placebo-controlled study assessing single and multiple ascending doses, and the effect of food. Participants will receive the test medicine or placebo as a tablet via the mouth. Participants are expected to be involved in this study for approximately 6, 8 or 12 weeks respectively from screening to end of study remote visit phone call

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
VS-041 Immediate Release Tablets, 30 - 150 mg [VS-041]

Primary outcome(s)
Safety: SAD (Part A) and MAD (Part B)
1. The incidence of treatment-emergent adverse events (TEAEs) over time through end of study (EOS)
2. Incidence of serious adverse events (SAEs)
3. Change from baseline over time through EOS in clinical laboratory values (chemistry, haematology, and urinalysis)
4. Change from baseline over time through EOS in vital signs
5. Change from baseline over time through EOS in physical examination
6. Change from baseline over time through EOS in electrocardiogram (ECG)

Pharmacokinetic
SAD (Part A) Only
Tmax, Cmax, AUC(0-last), AUC(0-inf), T1/2el, CL/F, Vz/F, MRT(0-inf), where possible and appropriate

MAD (Part B) Only
Tmax, Cmax, AUC(0-τ) assessed on Day 1
Tmax, Cmax, Cmin, AUC(0-τ), T1/2el, CL/Fτ, Vz /Fτ, PTF%, Rac Cmax, Rac AUC(0-τ), where possible and appropriate assessed on Day 7

Safety endpoint will be assessed by reviewing AEs, vital signs and ECGs, safety blood tests and safety urine tests from screening to EOS for each cohort.
Pharmacokinetic endpoints will be assessed using blood samples taken from pre-dose to the follow up for each cohort.

Key secondary outcome(s)
There are no secondary outcome measures

Completion date
17/06/2025

Eligibility

Key inclusion criteria
1. Males or females 18 to 55 years of age, inclusive at the time of signing the informed consent.
2. Subjects considered reliable and capable of adhering to the protocol, visit schedule and medication intake according to the judgment of the PI.
3. Subjects with suitable veins for multiple venipuncture/ cannulations as assessed by the PI at Screening.
4. Non-tobacco smoker within the previous 6 months (before Screening), and does not use tobacco-containing, or nicotine-containing products (including, but not limited to, cigarettes, pipes, cigars, chewing tobacco, e-cigarettes, nicotine patch, or nicotine gum).
5. Body weight of at least 50 kg and body mass index (BMI) within the range ≥19 to ≤29.9 kg/m².
6. Males who are sexually active and whose partners are females of childbearing potential must be either surgically sterile or using a highly effective method of contraception for the duration of the study (from the time they sign informed consent form (ICF) through at least 90 days after administration of the last dose of study drug). Contraceptive use by men should be consistent with ICH GCP E6(R2) 2016 and local regulations regarding the methods of contraception for those participating in clinical studies. These contraception requirements are more conservative

than the guidance issued by the CTFG, 2022 related to contraception and pregnancy testing in clinical trials. Males must agree not to donate or bank sperm after they signed consent through 90 days after administration of the last dose of study drug.
7. Female subjects must be of non-childbearing potential, who have undergone a sterilization procedure at least 6 months prior to dosing with official documentation (e.g., hysteroscopic sterilization, bilateral tubal ligation or bilateral salpingectomy, hysterectomy, or bilateral oophorectomy), or are postmenopausal with amenorrhea for at least 1 year prior to dosing and follicle-stimulating hormone (FSH) serum levels consistent with postmenopausal status and serum pregnancy test at Screening and upon admission with a negative result as per PI's judgment. Female subject must agree to not donate eggs after they signed consent through 90 days after administration of the last dose of study drug.
8. Able to understand and willing to sign a written ICF.
9. Willing and able to comply with trial procedures and restrictions listed in the ICF and in the protocol.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Total final enrolment
70

Key exclusion criteria
1. Female study subject who is pregnant or breastfeeding.
2. Any clinically significant disease, active malignancy or history of malignancy (excluding basal cell carcinoma) or disorder (eg, cardiovascular, pulmonary, gastrointestinal, liver, renal, neurological, musculoskeletal fractures, endocrine including adrenal insufficiency, metabolic, psychiatric, major physical impairment) which, in the opinion of the PI, may either put the subject at risk because of participation in the study, or influence the result of the study, or the subject's ability to participate in the study.
3. Any physical or psychological condition which, in the opinion of the PI, would compromise the subject's safety or successful participation in this trial.
4. Subjects with a known hypersensitivity to VS-041 or any of the excipients (mannitol, croscarmellose sodium, silica colloidal anhydrous [Aerosil], sodium dodecyl sulfate, sodium stearyl fumarate) of the product.
5. Current evidence of COVID-19 infection as determined by the PI (following local practice) or hospitalized with COVID-19 infection within the last 3 months prior to Screening.

6. History of drug or alcohol abuse or addiction within 2 years before the start of study medication dosing.
7. Positive test results for alcohol at Screening or admission.
8. Positive drugs of abuse testing at Screening or admission for the drugs listed in the protocol SoA.
9. Use of any medications except for the medications exempted by the PI on a case-by-case basis after they are judged to be unlikely to affect the PK profile of the study medication or subject safety (eg, topical drug products without significant systemic absorption, simple pain killers [eg, acetaminophen/paracetamol up to 2g/24hour]):
9.1. Prescription medications within 14 days prior to the first dosing until follow-up visit
9.2. Over-the-counter products and natural health products (including herbal remedies, homeopathic and traditional medicines, probiotics, food supplements such as vitamins, minerals, amino acids, essential fatty acids, and protein supplements used in sports) within 14 days prior to the first dosing (except for the occasional use of acetaminophen/ paracetamol [up to 2 g daily]) until follow-up visit
9.3. Depot injection or implant of any drug within 3 months prior to the first dosing until follow-up visit
10. Subject has an uncontrolled or serious disease, or any medical or surgical condition, deemed by the PI to be likely to interfere with the participation in the clinical study and/or put the subject at significant risk and or to compromise the interpretation of trial results if she/he participates in the clinical study.
11. Any laboratory values with the following deviations at the Screening; test may be repeated at the discretion of the PI, if abnormal:
11.1. Any positive result on Screening for serum hepatitis B surface antigen (HBsAg), hepatitis B core antibody (HBcAb), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) antibody
11.2. Alanine transaminase (ALT) > 1.1 x upper limit of normal (ULN)
11.3. Aspartate aminotransferase (AST) > 1.1 x ULN
11.4. Total bilirubin (TBL) > ULN
11.5. Platelet count ≤ lower limit of normal (LLN)
11.6. CPK > 2 x ULN
12. Abnormal resting vital signs (after resting supine for 5 minutes) of blood pressure (BP), systolic > 140 mmHg or < 100 mmHg or diastolic > 90 mmHg or < 40 mmHg and heart rate (HR) <50 and >90 bpm.
13. Study subjects have clinically significant ECG abnormality at Screening, in the opinion of the PI. In addition, any study subject with any of the following findings will be excluded:
13.1. Mean QT corrected for HR using Fridericia's formula (QTcF) interval >450 msec for males and females based on the mean of triplicate ECG tracings.
13.2. Bundle branch blocks (complete bundle branch block with, marked right or left axis deviation or second- and third-degree atrioventricular block are excluded). Mild first-degree atrioventricular block (defined as PR interval ≤ 230 ms), incomplete right bundle branch block (QRS ≤ 120 ms) or left anterior hemiblock are acceptable if no underlying disease is suspected by the PI. Entry of any subject with an abnormal but not clinically significant ECG must be approved and documented by signature of the PI or medically qualified sub investigator.
13.3. Irregular rhythms other than sinus arrhythmia or occasional, rare supraventricular or rare ventricular ectopic beats
13.4. T-wave configurations not of sufficient quality for assessing QT interval duration
14. Subject with a history of recurrent unexplained syncope or a family history of sudden death due to long QT syndrome.
15. Significant blood loss or has donated or received 1 or more units (450 mL) of blood within 3 months prior Screening or has donated plasma or platelets within 14 days prior to baseline admission.
16. Vulnerable subject (eg, subjects kept in detention, military, police, adults with legally

authorised representative), employees of the Sponsor or the Contract Research Organisation (CRO) with direct involvement in the proposed study or other studies under the direction of the PI or the CRO, as well as family members of the employees of the Sponsor, CRO, or the PI.
17. Study subjects received an investigational medicinal product or participated in another study within a period 90 days before admission.
18. Received prior treatment with an investigational medical device or participated in a study of an investigational medical device within a period of 90 days before admission.
19. Plans to participate in another medicinal product study or device under investigation during this study period.
20. Any other reason which, in the opinion of the PI, would prevent the subject from participating in the study.
21. Any evidence of a condition, which in the PI's opinion, makes it undesirable for the subject to participate in the study.

Date of first enrolment
02/09/2024

Date of final enrolment
21/05/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
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Sponsor information

Organisation
Vasa Therapeutics Sp. z o. o.

Funder(s)

Funder type
Industry

Funder Name
Vasa Therapeutics Sp. z o. o.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to the fact that a follow-up phase 1 study in patients with heart failure and preserved ejection fraction is planned and only then the comprehensive data will be published and thus will become available.

IPD sharing plan summary
Not expected to be made available