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A study in healthy volunteers to assess how safe and effective the test medicine is at reversing anticoagulant medicines

Submission date 23/09/2022	**Recruitment status** Stopped	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 05/10/2022	**Overall study status** Stopped	
Last Edited 08/07/2026	**Condition category** Other	

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine, ciraparantag, for situations when the effects of a commonly prescribed type of oral anticoagulant drug (blood thinner) needs to be reversed quickly.

This healthy volunteer study will evaluate the efficacy and safety of a single intravenous (IV, administered via injection into a vein) dose of the test medicine for reversal of anticoagulation (blood thinning) that has been caused by three different oral anticoagulant drugs.

Who can participate?
Healthy male and non-pregnant, non-lactating female volunteers aged between 18 and 55 years.

What does the study involve?
Three separate groups of volunteers will receive one of the three different oral anticoagulant drugs from Day 1 to Day 4 of the study. The test medicine or placebo (dummy drug) will be given on Day 4 to test whether it reverses the anticoagulant effect. Volunteers will have a 2:1 chance of getting the test medicine versus the placebo. The study is blinded, which means the volunteers and study team will not know which volunteers have received the test medicine and which volunteers have received the placebo. A further 3 groups of volunteers may be given a different dose of the test medicine, depending on the effect seen in the first three groups. Volunteers will be discharged on Day 6 at the earliest, or when the discharge criteria are met, and return for a follow-up visit 3 to 5 days later.

What are the possible benefits and risks of participating?
Healthy volunteers will get no medical benefit from the test medicine; however, the aims of the study can be most efficiently met in volunteers with no concurrent medical conditions and who do not need to take concomitant medication that might interfere with the study objectives or increase the risk of the study. The risk/benefit evaluation in this study supports the use of healthy volunteers.

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

When is the study starting and how long is it expected to run for?
November 2022 to April 2024

Who is funding the study?
Norgine, Ltd (UK)

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

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-002756-39

Integrated Research Application System (IRAS)
1006328

Protocol serial number
Quotient Code: QSC300320

Study information

Scientific Title
A phase I randomized, double-blind, placebo-controlled study to assess the efficacy and safety of ciraparantag for reversal of supratherapeutic doses of anticoagulants in healthy adults

Study objectives
The trial will meet the following primary and secondary objectives:

Primary objectives
- To demonstrate that a single IV administration of ciraparantag is superior to placebo in the reversal of anticoagulation induced by each of the evaluated anticoagulant drugs (edoxaban, apixaban, or rivaroxaban) in healthy adults, as assessed by whole blood clotting time (WBCT) measured at a predefined time point with Perosphere Technologies' Point-of-Care (PoC) Coagulometer.

Secondary objectives
- To further evaluate the efficacy of a single IV administration of ciraparantag compared to placebo in the reversal of anticoagulation induced by each of the evaluated anticoagulant drugs (edoxaban, apixaban, or rivaroxaban) in healthy adults, as assessed by WBCT measured at multiple time points with Perosphere Technologies' PoC Coagulometer.
- To provide additional safety and tolerability information for ciraparantag.
- To evaluate the PK of ciraparantag in healthy adults.
- To evaluate the PK of the evaluated anticoagulant drugs (edoxaban, apixaban, and rivaroxaban) in healthy adults.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 25/10/2022, South Central - Oxford A REC (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, UK; +44 (0)207 104 8290, (0)207 104 8206, (0)207 104 8061; oxforda.rec@hra.nhs.uk); Ref - 22/SC/0294
2. Approved 25/10/2022, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, UK; +44 (0)20 3080 6000; info@mhra.gov.uk), ref: CTA 00322/0315/001-0001

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Efficacy and safety trial in healthy volunteers

Study type(s)
Other

Health condition(s) or problem(s) studied
Anticoagulant reversal therapy

Interventions
This healthy volunteer study will evaluate the efficacy and safety of a single intravenous (IV, administered via injection into a vein) dose of the test medicine for reversal of anticoagulation (blood thinning) that has been caused by three different oral anticoagulant drugs.

This study will take place at 1 non-NHS site, enrolling up to 126 healthy male and non-pregnant, non-lactating female volunteers aged between 18 and 55 years.

Three separate groups of volunteers will receive one of the three different oral anticoagulant drugs from Day 1 to Day 4 of the study. The test medicine or placebo will be given on Day 4 to test whether it reverses the anticoagulant effect. Volunteers will have a 2:1 chance of getting the test medicine versus the placebo. The study is blinded, which means the volunteers and study team will not know which volunteers have received the test medicine and which volunteers have received the placebo. A further 3 groups of volunteers may be given a different dose of the test medicine, depending on the effect seen in the first three groups. Volunteers will be discharged on Day 6 at the earliest, or when the discharge criteria are met, and return for a follow-up visit 3 to 5 days later.

Intervention Type

Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Ciraparantag Solution for Injection, Placebo Solution for Injection (Sodium Chloride Injection), Edoxaban tablets, Apixaban tablets, Rivaroxaban tablets

Primary outcome(s)
1. Results of the formal statistical analysis of the proportion of subjects who achieve a WBCT ≤ the upper limit of normal (295 secs) within 1 h after administration of ciraparantag/placebo, which is subsequently sustained after 1 h through to at least 6 h after ciraparantag/placebo dosing measured using Perosphere Technologies' Point-of-Care (PoC) Coagulometer at Screening until the follow-up visit (up to 6 days post-discharge)

Key secondary outcome(s)
1. Statistical analysis of the proportion of subjects who achieve WBCT ≤ the upper limit of normal (295 secs) within 30 min after administration of ciraparantag/placebo, which is subsequently sustained after 30 min through to at least 6 h after ciraparantag/placebo dosing measured using PoC Coagulometer at Screening until the follow-up visit (up to 6 days post-discharge)

2. Statistical analysis of the proportion of subjects who achieve a WBCT ≤ the upper limit of normal (295 secs) within 15 min after administration of ciraparantag/placebo, which is subsequently sustained after 15 min through to at least 6 h after ciraparantag/placebo dosing, measured using PoC Coagulometer at Screening until the follow-up visit (up to 6 days post-discharge)

3. Statistical analysis of the proportion of subjects who achieve a WBCT ≤ the upper limit of normal (295 secs) at each of the planned WBCT assessment time points: 15 min, 30 min, 1 h, 3 h, 6 h and 24 h after administration of ciraparantag/placebo (relative to the end of infusion) measured using PoC Coagulometer at Screening until the follow-up visit (up to 6 days post-discharge)

4. To provide additional safety and tolerability information for ciraparantag, measured using the incidence of AEs, treatment-emergent AEs and SAEs, changes from baseline in vital signs, electrocardiograms (ECGs), physical examinations and changes from baseline in laboratory safety tests at Day -1 until the follow-up visit (up to 6 days post-discharge)

5. PK parameters for ciraparantag and metabolite (1,4-bis (3- aminopropyl) piperazine [BAP]), including the following: tmax, Cmax, AUC(0-last), AUC(0-inf), λz, t1/2, CL and Vz measured using Serum concentration data at Day 4 until discharge

6. PK parameters for edoxaban, apixaban, and rivaroxaban, including the following: tmax, Cmax, and CL/F measured using Plasma concentration-time data at Day 4 until discharge

Completion date
12/04/2024

Reason abandoned (if study stopped)

Other reason not related to safety

Eligibility

Key inclusion criteria
1. Must provide written informed consent
2. Must be willing and able to communicate and participate in the whole study
3. 18 to 55 years inclusive at the time of signing informed consent
4. Must agree to adhere to the contraception requirements defined in the clinical protocol
5. Healthy males or non-pregnant, non-lactating healthy females of non-childbearing potential (WONCBP) or non-pregnant, non-lactating healthy females on low-user-dependency progesterone-only contraception (e.g., injected, subdermal, intrauterine) who will not be menstruating at the time of study treatment. A woman is considered to be of childbearing potential unless she is permanently sterile (hysterectomy, bilateral salpingectomy, and bilateral oophorectomy) or is postmenopausal (has had no menses for 12 months without an alternative medical cause and a serum follicle-stimulating hormone [FSH] concentration ≥40 IU/L.
6. Have suitable veins for multiple venepunctures/cannulation and IV infusions as assessed by the investigator or delegate at screening
7. Body mass index (BMI) of 18.0 to 32.0 kg/m2 as measured at screening
8. Weight >60 kg at screening
9. WBCT ≤ the upper limit of normal (295 secs) at screening and admission prior to the first NIMP dose

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Total final enrolment
48

Key exclusion criteria
1. Serious adverse reaction or serious hypersensitivity to any drug or formulation excipients
2. Known allergy to edoxaban, apixaban, rivaroxaban or ciraparantag
3. Any contraindication to the use of the anticoagulant drugs (edoxaban, apixaban, or rivaroxaban) as per the Summary of Product Characteristics for each product
4. Presence or history of clinically significant allergy requiring treatment, as judged by the

investigator; hay fever is allowed unless it is active
5. History of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or GI disease, neurological or psychiatric disorder, as judged by the investigator
6. Subjects with a personal or family history of clotting disorder or haematologic abnormality, such as excessive bleeding, joint haematoma, thrombovascular disease, thrombocytopenia, or any chronic condition requiring treatment with transfusions
7. Subjects with a history of a significant head injury in the last 2 years
8. Subjects with a history of venous thromboembolic episodes (including deep vein thrombosis and pulmonary embolism)
9. Subjects with a history of unexplained syncope within 6 months prior to screening
10. Subjects with a history of major bleeding, trauma, surgical procedure of any type, or vaginal delivery within 6 months prior to screening
11. Presence or history of peptic ulcer or GI bleeding (including hematemesis, melena, or rectal bleeding) within 6 months prior to screening.
12. Presence or history of minor bleeding episodes (e.g., epistaxis, unexplained bruising or gingival bleeding) within 6 months prior to screening, or a long-standing history of such bleeding.
13. Dental extraction or surgery in the 4 weeks prior to admission or planned during the study until after the follow-up visit.
14. Female subjects only: history of excessive or dysfunctional uterine bleeding (unless the subject had a subsequent hysterectomy).

Date of first enrolment
16/11/2022

Date of final enrolment
12/04/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way
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NG11 6JS

Sponsor information

Organisation

Norgine (United Kingdom)

ROR
https://ror.org/046zgtw08

Funder(s)

Funder type
Industry

Funder Name
Norgine

Results and Publications

Individual participant data (IPD) sharing plan

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