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Testing glenzocimab to treat heart attack and understand how it works

Submission date
27/01/2023

Recruitment status
Stopped

Registration date
25/08/2023

Overall study status
Stopped

Last Edited
14/04/2025

Condition category
Circulatory System

[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
Glenzocimab is a medication that blocks thrombosis, which is an abnormal type of blood clotting that occurs during heart attacks and strokes. Unlike existing anti-blood clotting medications, glenzocimab is thought to have minimal effect on normal types of blood clotting that prevent bleeding. The aim of this trial is to determine if glenzocimab reduces the damage caused by a heart attack in patients presenting with a big heart attack also known as ST-segment elevation myocardial infarction (STEMI). The aim of the study is to determine whether glenzocimab is a safe and effective treatment for large heart attacks. We will assess its effectiveness by determining whether it reduces heart damage, by measuring this using a heart scan called a cardiac MRI after 3 months. Glencozimab (previously known as ACT017) is a Fab fragment of a monoclonal antibody, which inhibits the platelet glycoprotein VI (GPVI) receptor. GPVI has a major role in thrombosis triggered by atherosclerotic plaque (such as during a heart attack or stroke) but appears to have a minimal role in haemostasis. In a phase I clinical trial, glenzocimab did not have a significant effect on bleeding. In preliminary results, glenzocimab was not associated with an increased risk of bleeding in phase 2 studies of patients with stroke or COVID. Although we are not expecting an increased risk of bleeding, we will closely monitor for bleeding. The GPVI receptor is only present on platelets and monoclonal antibodies have highly specific effects on the receptor that they target. Off-target effects are therefore not expected, thereby reducing the risk of adverse reactions.

Who can participate?
Patients with STEMI

What does the study involve?
Over 15 months, patients will be recruited from two centres in the UK (Birmingham and Sheffield). Patients will be randomised to receive either glenzocimab or placebo as soon as they arrive in the hospital. Patients will otherwise receive standard care, including percutaneous coronary intervention, which is the emergency procedure that is used to unblock the blood vessels around the heart (coronary arteries). Patients will be closely monitored for any side effects and their condition will be monitored.

What are the possible benefits and risks of participating?
Patients will be monitored closely in the catheter laboratory during the procedure (after the infusion has started) for any acute adverse effects followed by close monitoring in the Coronary Care Unit (CCU) where the patient will stay for 24 hours as per routine care. They will also have further monitoring on the wards until their discharge. The patient will be given safety net advice prior to discharge and also contact details of the research team if they have any concerns after their discharge. We do not anticipate any long-term effects of the medication due to the short half-life of glencozimab.

At 90 days the patient will have cardiac magnetic resonance imaging (CMR), which is a form of non-invasive imaging that does not involve ionising radiation. All patients have a safety questionnaire form filled out routinely prior to CMR to ensure their eligibility. CMR is safe and routinely performed on patients with heart conditions including heart attacks with heart failure. The patient will be informed of having CMR prior to discharge and will be allowed to ask any questions.

Where is the study run from?
Queen Elizabeth Hospital, Birmingham (UK)

When is the study starting and how long is it expected to run for?
January 2023 to April 2025

Who is funding the study?
Acticor Biotech (France)

Who is the main contact?
LIBERATE Trials Office, Liberate@trials.bham.ac.uk

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-001054-32

Integrated Research Application System (IRAS)
1005400

Protocol serial number
RG_22-013

Study information

Scientific Title
A phase II, randomised, double-bLInd, placeBo-controllEd tRiAl To invEstigate the efficacy and safety of glenzocimab and the mechanism of inhibiting platelet GPVI as a treatment for ST-elevation myocardial infarction (LIBERATE)

Acronym
LIBERATE

Study objectives
Primary objective:
To assess whether glenzocimab reduces myocardial infarct size in patients with ST-elevation myocardial infarction.

Secondary objectives:
1. To assess the effect of glenzocimab on the improvement in indices of microvascular obstruction
2. To assess the effect of glenzocimab on the improvement in indices of myocardial damage
3. To assess the effect of glenzocimab on the reduction in platelet activity
4. To assess the effect of glenzocimab on the reduction of systemic inflammation
5. To assess the safety profile of glenzocimab by reporting deaths, serious adverse events (SAE), Suspected Unexpected Serious Adverse Reactions (SUSARs) and bleeding-related events

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 22/08/2023, East Midlands - Derby Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8236; derby.rec@hra.nhs.uk), ref: 23/EM/0045

Primary study design
Interventional

Study design
Randomized double-blind placebo-controlled study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
ST-elevation myocardial infarction

Interventions
The LIBERATE trial is a double-blind trial for participants who have had an ST-elevation Myocardial Infarction (STEMI).

Participants will be randomised using an online bespoke database on a 1:1 basis and receive either glenzocimab (humanized monoclonal antibody fragment (fab) directed against the human platelet glycoprotein VI (GPVI), and a novel antithrombotic drug, the investigational medicinal product (IMP)) or a matched placebo.

1g of IMP or placebo will be given intravenously during the emergency Primary Percutaneous Coronary Intervention procedure and last 6 hours in total.

There are two follow-up visits 30 and 90 days after the intervention.

Intervention Type
Biological/Vaccine

Phase
Phase II

Drug/device/biological/vaccine name(s)
Glenzocimab

Primary outcome(s)
Myocardial infarct size as a percentage of left ventricular (LV) mass measured using delayed gadolinium-enhanced cardiovascular magnetic resonance (CMR) imaging at 90 days (± 21 days) post-myocardial infarction

Key secondary outcome(s)
1. Resolution of ST-elevation measured using serial 12-lead ECGs at days 1, 2 and 3 (if still an inpatient)
2. Restoration of Thrombolysis in Myocardial Infarction (TIMI) 3 flow and myocardial blush grade measured using coronary angiography at the time of the therapeutic procedure
3. Collagen-induced platelet aggregation measured using Multiple Electrode Aggregometry on

day 1
4. Area under the curve of serum troponin and CK-MB levels measured in the hospital laboratory over the 48 hours post-myocardial infarction
5. Inflammation assessed through serial high-sensitivity C-reactive protein (CRP) levels measured in serum using a CRP test at days 1, 2, 3 (if still an inpatient) and 30
6. Safety profile of glenzocimab: deaths, SAEs, SUSARs, bleeding-related events and treatment-emergent adverse events measured using study records throughout the trial until day 90

Completion date
30/04/2025

Reason abandoned (if study stopped)
Lack of funding/sponsorship

Eligibility

Key inclusion criteria
1. Informed consent (including emergency consent)
2. Age ≥ 18 years
3. Confirmation of the diagnosis of ST-elevation myocardial infarction by the clinical team on the basis of history and ECG findings
4. Intention to proceed with primary percutaneous coronary intervention (PCI)
5. Presentation within 6 hours of chest pain

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Inability to provide consent
2. All women of childbearing potential (WOCBP) are excluded from study entry. Women are only classed as non-WOCBP if they meet 1 or more of the following criteria:
2.1. Premenopausal female with documented hysterectomy
2.2. Premenopausal female with documented bilateral salpingectomy or oophorectomy
2.3. Postmenopausal female defined as no menses for 12 months without an alternative medical cause. A high follicle-stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a postmenopausal state in women not using contraception or hormonal replacement therapy (HRT). However, in the absence of 12 months of amenorrhoea, a single FSH measurement is insufficient.

3. Active bleeding
4. Known thrombocytopenia (with platelet count < 100,000/µl in last 12 months)
5. Known renal impairment (with estimated Glomerular Filtration Rate (eGFR) < 30ml/minute in last 12 months)
6. Left bundle branch block on ECG
7. Suspected non-thrombotic cause (e.g. spontaneous coronary artery dissection, vasospasm, Takotsubo cardiomyopathy)
8. Current treatment with oral anticoagulants
9. Cardiogenic shock – indicated by systolic blood pressure less than 80 mmHg or use of inotropes
10. Out of hospital cardiac arrest
11. Known history of MI or prior coronary artery bypass graft (CAGB) surgery
12. Known history of pre-existing cardiomyopathy
13. Known history of any type of intracranial haemorrhage
14. Known history of platelet function or coagulation disorder
15. Known history of any spontaneous major bleeding (indicated by bleeding requiring transfusion)
16. Known intracranial malignancy (any type) or intracranial aneurysm (any type)
17. Known history of major surgery defined as surgery involving opening a major body cavity (such as the abdomen, chest, or skull) or well-vascularised tissues (such as the colon mucosa and prostate tissue) or opening a major artery, within the last month
18. Known history of any type of surgery within the last week
19. Known history of major trauma (defined as serious injury with the potential to result in disability or death) within the last month
20. Contraindication to cardiac MRI (pacemaker, allergy to gadolinium contrast, non-MRI compatible implants or foreign bodies)
21. Known hypersensitivity to investigational medicinal product (glenzocimab)
22. Use of an investigational drug within 30 days prior to screening or 5 half-lives or twice the duration of biological effect of the investigational product (whichever is longer)
23. Known use of GPIIb/IIa inhibitor within the last 2 weeks

Date of first enrolment
15/01/2024

Date of final enrolment
01/02/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Queen Elizabeth Hospital Birmingham
University Hospitals Birmingham NHS Foundation Trust
Mindelsohn Way
Birmingham

United Kingdom
B15 2GW

Study participating centre
Northern General Hospital
Sheffield Teaching Hospitals NHS Foundation Trust
Herries Road
Sheffield
United Kingdom
S5 7AU

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Industry

Funder Name
Acticor Biotech

Results and Publications

Individual participant data (IPD) sharing plan
Access to study data will be in accordance with the University of Birmingham and CRUK clinical trial unit (CRCTU) data-sharing policy: https://www.birmingham.ac.uk/research/crctu/data-sharing-policy.aspx. The CRCTU has a defined procedure in place for data sharing which ensures that the necessary legal and ethical requirements are followed, this policy which is based on guidelines published by the Information Commissioners Office.

IPD sharing plan summary
Available on request