

PROthrombin complex concentrate versus fresh frozen Plasma for bleeding in adults undergoing HEart SurgerY (PROPHESY-2 trial)

Submission date	Recruitment status	<input checked="" type="checkbox"/> Prospectively registered
25/01/2024	Recruiting	<input checked="" type="checkbox"/> Protocol
Registration date	Overall study status	<input type="checkbox"/> Statistical analysis plan
16/04/2024	Ongoing	<input type="checkbox"/> Results
Last Edited	Condition category	<input type="checkbox"/> Individual participant data
19/01/2026	Circulatory System	<input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Every year in the UK, severe bleeding occurs in over 10,000 people having cardiac surgery. Severe bleeding increases the risks of complications like organ failure and infections, or death. Stopping bleeding quickly could reduce these risks and improve outcomes. Currently, severe bleeding is stopped by transfusion of fresh frozen plasma (FFP), part of donated blood that contains essential proteins for blood clotting. This study aims to determine whether a blood product called prothrombin complex concentrate (PCC) is a superior treatment to a blood product called FFP for adult patients who are actively bleeding within 24 hours of cardiac surgery.

Who can participate?

Patients aged 18 years and over who are actively bleeding within 24 hours of cardiac surgery

What does the study involve?

Potentially eligible patients will be consented and screened before their cardiac surgery, and if they go on to develop bleeding during or within 24 hours of surgery, they will be randomised to receive either PCC or FFP. Participants will be followed up for 90 days (+/- 7 days) post-surgery and will complete a series of questionnaires relating to their general health, the specific disease that caused them to undergo heart surgery, and the healthcare costs associated with their recovery

What are the possible benefits and risks of participating?

There is no increased risk for patients in this research: the blood product has been used widely in the UK and Europe to treat bleeding in patients with no major safety concerns. If the patient haemorrhages during or soon after surgery, they will require a transfusion regardless so there is no additional treatment required in this trial. There is a small risk that patients may feel uncomfortable being treated with a product that they are not familiar with, in which case they should decline participation in the research. There is a potential burden with completing questionnaires, but research staff can complete these with the patients to decrease that burden. Some participants may have concerns about their data being used for research. The participant

information sheets clearly outline who is responsible for maintaining the integrity and confidentiality of the data, and who they can contact if they have questions.

Where is the study run from?
Queen Mary University of London (UK)

When is the study starting and how long is it expected to run for?
January 2024 to September 2026

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
Charlie Brown, Prophesy2Trial@nhsbt.nhs.uk

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)

1009308

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

IRAS 1009308

Study information

Scientific Title

PROthrombin complex concentrate versus fresh frozen Plasma for bleeding in adults undergoing HEart SurgerY (PROPHESY-2 trial): a phase III, randomised control trial

Acronym

PROPHESY-2

Study objectives

Primary objective:

To find out whether prothrombin complex concentrate (PCC) is better at treating bleeding within 24 hours of cardiac surgery than the current standard care, fresh frozen plasma (FFP). Both are blood products that are widely used in the UK and Europe.

Secondary objective:

To determine if PCC is a better product than FFP when looking at the bigger picture, including organ failure, death, recovery from surgery, stay in hospital (including in intensive care and need for intubation), general health and safety outcomes.

Ethics approval required

Ethics approval required

Ethics approval(s)

approved 15/04/2024, London Fulham REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8084; fulham.rec@hra.nhs.uk), ref: 24/LO/0133

Study design

Randomized controlled pragmatic non-blinded multi-site trial

Primary study design

Interventional

Study type(s)

Efficacy, Safety

Health condition(s) or problem(s) studied

Haemorrhage within 24 hours of the start of cardiac surgery

Interventions

Cardiac surgery patients who haemorrhage during or within 24 hours of the start of surgery are randomly allocated to receive either the current standard treatment (fresh frozen plasma, FFP, or LG Octaplas), or the IMP, Prothrombin Complex Concentrate (PCC).

FFP and LG Octaplas are plasma products and are the current recommended products for the treatment of severe bleeding in patients undergoing cardiac surgery.

PCC dosage is calculated according to the patient's weight following the current national guidelines.

Both FFP/LG Octaplas and PCC are administered by injection.

Once the clinical decision has been made that a patient requires a blood transfusion during or within 24 hours of the start of cardiac surgery, the transfusion lab will be instructed to perform the randomisation via Sealed Envelope. The issued product is then administered to the patient. Patients in the IMP arm will receive a maximum of two doses of PCC. If continued treatment is required, any further doses will be FFP or LG Octaplas, according to the hospital's policy.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Prothrombin Complex Concentrate [Human coagulation factor II, Human coagulation factor VII, Human coagulation factor IX, Human coagulation factor X, Protein C, Protein S]

Primary outcome(s)

A composite of any of the following new events from 24 hours post-surgery up to 90 days post-surgery:

1. All-cause mortality according to clinical diagnosis
2. Acute respiratory failure according to clinical diagnosis
3. Acute myocardial injury according to clinical diagnosis
4. Acute renal failure requiring renal replacement therapy (excluding dialysis during cardiopulmonary bypass) according to clinical diagnosis
5. Acute liver injury according to clinical diagnosis
6. Acute intestinal injury according to clinical diagnosis
7. Focal neurological deficit according to clinical diagnosis
8. Infection according to clinical diagnosis

Key secondary outcome(s)

1. Individual components of the primary outcome up to 90 days or death, whichever occurs first:
 - 1.1. All-cause mortality according to clinical diagnosis
 - 1.2. Acute respiratory failure according to clinical diagnosis
 - 1.3. Acute myocardial injury according to clinical diagnosis
 - 1.4. Acute renal failure requiring renal replacement therapy (excluding dialysis during cardiopulmonary bypass) according to clinical diagnosis
 - 1.5. Acute liver injury according to clinical diagnosis
 - 1.6. Acute intestinal injury according to clinical diagnosis
 - 1.7. Focal neurological deficit according to clinical diagnosis
 - 1.8. Infection according to clinical diagnosis
2. Clinical evidence of haemostasis defined as:
 - 2.1. Amount of blood loss (in ml) collected in chest drains at 6 hours and 24 hours post end of

surgery, taken from clinical notes

2.2. Amount of total allogeneic (in units) blood transfusion (red blood cells, fresh frozen plasma, cryoprecipitate, platelets), total dose of haemostatic factor concentrates (PCC, fibrinogen concentrate, activated recombinant factor VIIa, or any other blood product concentrate) at 24 hours and 7 days from randomisation, taken from clinical notes

2.3. Whether re-exploration for bleeding up to 7 days post end of surgery was required, and whether a surgical point of bleeding was identified, taken from clinical notes

3. Length of stay in hospital, measured in days, up to and including 90 days from randomisation or hospital discharge or death whichever occurs first – i.e. time to discharge from acute care after index hospitalisation; this includes time to discharge from satellite acute care units; taken from clinical notes

4. Duration of mechanical ventilation (in days) during index hospitalisation up to 90 days from randomisation or hospital discharge or death, whichever occurs first, taken from clinical notes

5. Number of hospital re-admissions up to and including 90 days from randomisation, taken from medical records

6. Safety measured through:

6.1. Transfusion adverse events up to 7 days or hospital discharge or death, whichever is first, taken from clinical notes.

These will be defined as per UK Serious Hazard of transfusion (<https://www.shotuk.org/reporting>) definitions and will include:

6.1.1. Acute transfusion reactions, that could result in shock or cardiac arrest, taken from clinical notes

6.1.2. Haemolytic transfusion reactions (acute or delayed), taken from clinical notes

6.1.3. Post-transfusion purpura, taken from clinical notes

6.1.4. Transfusion-associated graft versus host disease, taken from clinical notes

6.1.5. Transfusion-associated circulatory overload, taken from clinical notes

6.1.6. Transfusion-associated dyspnoea, taken from clinical notes

6.1.7. Transfusion-related acute lung injury, taken from clinical notes

6.2. Thrombotic events (arterial and venous) confirmed by radiological imaging, autopsy, or through surgical means, up to 90 days or death, whichever occurs first, taken from clinical notes

6.3. Other serious adverse events reported up to 90 days or death whichever occurs first, taken from clinical notes

7. Quality of Life (QoL) measured using the:

7.1. EQ-5D-5L at baseline, 42 days and 90 days after randomisation

7.2. Disease-specific QoL questionnaire, either:

7.2.1. Coronary Revascularization Outcome (CROQ) at baseline and 90 days after randomisation for CABG, or

7.2.2. Kansas City Cardiomyopathy (KCCQ) at baseline and 90 days after randomisation for valve surgery

Both meet the minimum metric properties and have been previously validated in coronary bypass surgery

8. In-patient hospital costs, and separately follow-up health care costs at 90 days as provided in questionnaire responses and according to patient records

Measured at varying time points from 24 hours post-surgery to 90 days post-surgery

Completion date

31/05/2027

Eligibility

Key inclusion criteria

1. Age ≥18 years
2. Undergoing cardiac surgery (Elective and Urgent procedures) not described in the exclusion criteria

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

18 years

Upper age limit

100 years

Sex

All

Total final enrolment

0

Key exclusion criteria

1. Emergency and Salvage procedures (as per definitions in section 6.0)
2. First-time isolated coronary artery bypass graft (CABG) surgery given the low risk of significant bleeding
3. First time isolated aortic valve replacement (excluding active endocarditis)
4. First time isolated mitral valve replacement
5. Surgeries that do not involve cardiopulmonary bypass
6. Heart transplant
7. Use of warfarin within 3 days prior to surgery
8. Use of direct oral anticoagulants (i.e. dabigatran, rivaroxaban, apixaban or edoxaban etc) within 48 hours prior to surgery (or 72 hours if patient has renal impairment – i.e. estimated glomerular filtration rate of <30 ml/min)
9. Any contraindication to PCC or FFP or LG-Octaplas, for example: known or suspected allergy to heparin, Sodium citrate dihydrate, sodium dihydrogenphosphate dihydrate and Glycine, History of Heparin-induced thrombocytopenia, history of blood transfusion reaction due to IgA deficiency with known antibodies against IgA
10. Patients refusing blood transfusion for any reason
11. Inherited bleeding disorder (i.e. any inherited clotting factor deficiencies, or platelet disorders)
12. Pregnancy as PCC is contraindicated
13. Documented thrombophilia defects (antiphospholipid syndrome, severe protein S deficiency, antithrombin deficiency)
14. Documented venous thromboembolism in the last 3 months prior to surgery

15. Patients who are expected to require Extracorporeal Membrane Oxygenation after cardiac surgery
16. Patient previously randomised into this trial and has not reached 90 days post randomisation

Date of first enrolment

06/02/2025

Date of final enrolment

31/05/2027

Locations

Countries of recruitment

United Kingdom

England

Wales

Study participating centre

St. Bartholomew's Hospital

Barts Health NHS Trust, West Smithfield
London
England
EC1A 7BE

Study participating centre

Castle Hill Hospital

Castle Road
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HU16 5JQ

Study participating centre

Glenfield Hospital

Groby Road
Leicester
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LE3 9QP

Study participating centre

Derriford Hospital

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Study participating centre
Southampton General Hospital
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SO16 6YD

Study participating centre
Bristol Royal Infirmary
Marlborough Street
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BS2 8HW

Study participating centre
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Wolverhampton Road, Heath Town
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WV10 0QP

Study participating centre
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Hammersmith Hospital
Du Cane Road
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W12 0HS

Study participating centre
Royal Papworth Hospital
Papworth Road
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CB2 0AY

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Blackshaw Road
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SW17 0QT

Study participating centre
University Hospital of Wales
Heath Park
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Sponsor information

Organisation
Queen Mary University of London

ROR
<https://ror.org/026zzn846>

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan**IPD sharing plan summary**

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		17/01/2026	19/01/2026	Yes	No
Study website		11/11/2025	11/11/2025	No	Yes