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

Submission date
25/01/2024

Recruitment status
Recruiting

Registration date
16/04/2024

Overall study status
Ongoing

Last Edited
09/06/2025

Condition category
Circulatory System

[X] 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
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

Study website
https://www.nhsbt.nhs.uk/clinical-trials-unit/trials-and-studies/blood-and-transfusion/prophesy-2/

Contact information

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Public

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Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1009308

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

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
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

Pharmaceutical study type(s)
Not Applicable

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 measure
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

Secondary outcome measures

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

Overall study start date
23/01/2024

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
496

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, rivaroxban, 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
England

United Kingdom

Wales

Study participating centre
St. Bartholomew's Hospital
Barts Health NHS Trust, West Smithfield
London
United Kingdom
EC1A 7BE

Study participating centre
Castle Hill Hospital
Castle Road
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Study participating centre
Glenfield Hospital
Groby Road
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LE3 9QP

Study participating centre
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PL6 8DH

Study participating centre
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SO16 6YD

Study participating centre
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BS2 8HW

Study participating centre
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Study participating centre
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Sponsor type
University/education

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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

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Internal report

3. Conference presentation
4. Publication on website

Intention to publish date
30/09/2027

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date