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A feasibility randomised controlled trial assessing the use of platelet transfusions versus modified dose blood thinners in patients with low platelets and cancer-related blood clots

Submission date
10/06/2024

Recruitment status
Recruiting

Registration date
08/07/2024

Overall study status
Ongoing

Last Edited
28/08/2024

Condition category
Haematological Disorders

[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
People with cancer are at increased risk of blood clots (venous thromboembolism or VTE). People with cancer often have low levels of platelets (blood cells required for blood clot formation) due to the cancer or anti-cancer treatment. Blood clots are treated with anticoagulation (blood thinners), but in people with low platelets there can be an increased risk of bleeding. We do not know the best way to treat people with cancer-related blood clots and low platelets, and we plan to do a future study to compare the two treatments which are commonly used in the UK. Before this, we will do a smaller study (this one) to see if doctors and patients are happy to take part in such a trial.

Who can participate?
Adults aged 18 years and over with active cancer and newly diagnosed blood clots receiving blood thinners and low platelets

What does the study involve?
We are carrying out a randomised controlled trial of two commonly used treatment approaches in people with newly diagnosed cancer-related blood clots and low platelets (platelet count <50):
1. Giving platelet transfusions and low molecular weight heparin injection (LMWH, blood thinning injections)
2. Giving a lower dose of LMWH injections without platelet transfusion
Volunteers with cancer, blood clots and low platelets will be identified and approached by their doctors. The study will be explained and written information given. They will be given adequate time to consider whether they would like to take part in the study. If they agree, they will be given a consent form to sign.
We will use a computer programme to allocate volunteers into the group with platelet transfusion or the group without platelet transfusion. This process is done by a computer so that

the allocation is totally random and not decided by their doctor or the trials team. This is done with the click of a button so it does not slow down their time to receiving treatment. Randomisation will occur within 72 hours of starting blood thinners for the blood clot.

Group without platelet transfusion:
The participant will receive reduced dose LMWH injections based on the first blood test result of the day (checked daily if they are a hospital inpatient or at least 2 times a week if an outpatient), without platelet transfusion:
1. Platelet count 25-50: half dose LMWH injection
2. Platelet count <25: no blood thinner

Group with platelet transfusion:
The participant will be transfused one unit of platelets when the first platelet count of the day falls below 50 (checked daily if they are a hospital inpatient or at least twice weekly in outpatient). They will receive LMWH injections after the platelet transfusion, based on the platelet count before the transfusion (pre-transfusion) as below:
1. Pre-transfusion platelet count 25-50: full dose LMWH injection after platelet transfusion
2. Pre-transfusion platelet count <25: half dose LMWH injection after platelet transfusion

After 2 weeks, all participants will be treated with a reduced dose LMWH without platelet transfusion as the other study group.
The trial will continue until platelets recover >50 or for 1 month from the start date (30 +/- 3 days), whichever occurs first. Once the platelet count reaches 50, participants will be given a full dose of blood thinners which is the usual treatment.
There are no extra blood tests involved. Participants will have the usual blood tests (total of 10 ml of blood) before starting blood thinners, and the same blood test monitoring they would have if they were not on the study (daily if hospital inpatient or at least two times a week in outpatient). Vital signs will be monitored around platelet transfusion, including temperature, heart rate and blood pressure, as is usual practice.

What are the possible benefits and risks of participating?
There will be no direct benefit to participants, but they will help the researchers to understand more about the different treatment options for patients with cancer thrombosis and low platelets. As one in two patients will develop cancer in their lifetime and patients with cancer are more likely to develop clots as well as bleeding complications, this is an important issue that will affect a significant proportion of the population. The more patients involved, the more data can be collected. The information from this study may help us to increase our understanding and aims to improve future treatment for this group.
There is minimal risk associated with taking part in the study as both treatment arms are currently the standard of care (usual treatment), which means if you decide not to go on the trial, these will still be the treatment your doctor would recommend.
Platelets are a blood product. Platelet transfusions are common procedures that can save and improve lives and death due to platelet transfusion is extremely rare. Most patients who receive a platelet transfusion experience no complications or problems. However, there are associated very rare risks, such as blood-borne infections or transfusion reactions. Most patients with cancer and very low platelets will require platelet transfusion as part of their routine care.

Where is the study run from?
University College London Hospital (UK)

When is the study starting and how long is it expected to run for?
March 2023 to August 2026

Who is funding the study?
1. Anthos Therapeutics (USA) - unrestricted educational grant
2. Thrombosis UK

Who is the main contact?
Dr Yishi Tan, uclh.cancerthrombosistrials@nhs.net

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Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
334585

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 33458, CPMS 59303

Study information

Scientific Title
A feasibility randomised controlled trial assessing the use of platelet transfusions versus modified dose anticoagulation in patients with thrombocytopaenia and cancer-associated thrombosis receiving anticoagulation (START UK)

Acronym
START UK Pilot Trial

Study objectives
Primary objective:
To determine the feasibility of designing and recruiting to a full randomised controlled trial (RCT) of management in participants with acute cancer-associated thrombosis (developed within 14 days) and thrombocytopaenia.

Secondary objectives:
To determine:
1. Additional feasibility measures, such as recruitment rate, reasons for non-participation in eligible participants and withdrawal rates and participation barriers for the full RCT.
2. The duration of thrombocytopaenia (days of platelet count <25 x10 9/L or 50 x10 9/L) per participant
3. Number of transfused platelets and red cell units per participant
4. Feasibility of follow-up for collection of Health-related quality of life data using the EuroQoL-EQ-5D-5L questionnaire

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/06/2024, Research Ethics Committee/Health Research Authority (Health and Care Research Wales, Castlebridge 5, Cardiff, CF11 9AB, United Kingdom; -; HCRW.approvals@wales.nhs.uk), ref: 24/WA/0111

Study design
Multicenter feasibility randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)

Hospital

Study type(s)
Treatment

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Patients with cancer-associated thrombosis and thrombocytopaenia

Interventions
Randomisation will be by Sealed Envelope, an anonymised online randomisation service.

Study arm without platelet transfusion
Modified dose LMWH
Participants will be given a modified dose LMWH as below based on the first platelet count of the day (checked daily in admitted participants or at least two times a week in outpatients), without platelet transfusion:
1. Platelet count 25-50 x10e9/L: 50% dose LMWH (approximately 50% of the full dose listed below for different LMWH)
2. Platelet count <25 x10e9/L: hold anticoagulation

Study arm with platelet transfusion
Higher dose LMWH with platelet transfusion support
For the first 14 days, participants will be transfused one unit of platelet when the first platelet count of the day falls below 50 x 10e9/L (checked daily in inpatient or at least two times a week in outpatient) and given the higher dose of LMWH after platelet transfusion based on pre-transfusion platelet count as below. As post-transfusion counts may not be readily available and can delay the administration of anticoagulation, it will not be routinely required (but not prohibited):
1. Pre-transfusion platelet count 25-50 x 10e9/L: 100% dose LMWH after platelet transfusion
2. Pre-transfusion platelet count <25 x 10e9/L: 50% dose LMWH after platelet transfusion

Platelet transfusion intervention will be performed until Day 14 after enrolment in the transfusion arm. Starting Day 15, participants will be transitioned to modified dose LMWH without platelet transfusion as the other arm. Participants will continue to be followed for a total of 30 +/-3 days. Both study arms fall within the international guidance from the International Society on Thrombosis and Haemostasis (ISTH) and current UK practice as described in the CAVEAT observational study.

LMWH will be prescribed as standard of care and can include enoxaparin, dalteparin, or tinzaparin. Full (100%) dose LMWH is listed as the following:
1. Enoxaparin - 1 mg/kg subcutaneously twice daily, 1.5 mg/kg once daily
2. Dalteparin - 200 IU/kg subcutaneously daily for the first month of an acute VTE then 150 U/kg subcutaneously daily thereafter
3. Tinzaparin - 175 IU/kg subcutaneously daily
Doses of LMWH will be rounded into the closest dosages available, according to local dose banding guidelines. Doses of LMWH may be split into twice daily dosing.

LMWH was chosen as it is the recommended anticoagulant of choice for participants with cancer-associated thrombosis and thrombocytopaenia by clinical practice guidelines. Both interventions are recognised as SOC in the UK and international practice .

Trial interventions will continue until platelet recovery (defined as the first of two consecutive measured platelet counts on different days that are ≥50 x 10e9/L and increasing in the absence of a platelet transfusion for three consecutive days) or until the end of the planned follow-up period (30 +/- 3 days), whichever occurs first. Once the platelet count reaches ≥50 x 10e9/L, participants will be given full dose anticoagulation as per standard of care. If participants were to have recurrent episodes of thrombocytopaenia, the assigned trial intervention will be applied during each episode until the end of the follow-up. Inferior vena cava (IVC) filter insertion will not be planned (but not prohibited) as all enrolled participants will receive some anticoagulation (consistent with CHEST Guidelines).

Starting Day 15, all participants will be treated with a modified dose LMWH without platelet transfusion as the other study arm.
At the end of study follow-up, all anticoagulation management will be at the discretion of the treating physician.
For participants who develop platelet refractoriness either due to alloimmunization or non-immune causes, further management will be at the discretion of the attending clinician. Discussion with the principal investigators is welcomed. All participants will be followed until the end of the study, regardless of the treatment decisions.

Intervention Type
Mixed

Primary outcome measure
The primary feasibility outcome is the number of participants recruited from all centres per month over 18 months

Secondary outcome measures
Feasibility:
1. Proportion of eligible participants who provide consent by 18 months
2. Reasons for non-participation in eligible participants by 18 months
3. Proportion of participants who complete study procedures by 18 months
4. Proportion of participants who adhere to the protocol (such as anticoagulation, transfusion, platelet count monitoring according to the protocol) by 18 months
5. Rates of withdrawal, loss to follow-up, or crossover between treatment arms by 18 months

Other:
1. Duration of thrombocytopaenia (days of platelet count <25 or 50 x10e9 /L) per participant by day 30 +/- 3 days
2. Number of transfused packed red cells and platelet units – with one red cell unit being one standard UK adult unit of packed red cells with a volume of 220-340 ml and one platelet unit being one standard UK adult platelet dose with a mean of around 3 × 10e11 platelets by day 30 +/- 3 days
3. Feasibility of collection of health-related quality of life data using EuroQoL-EQ-5D-5L questionnaire (% completed) by day 30 +/- 3 days

Overall study start date
01/03/2023

Completion date
01/08/2026

Eligibility

Key inclusion criteria
1. Adult participants (age ≥18 years) with active malignancy (malignancy diagnosed or treated within the previous 6 months, or progressive/relapsed)
2. Imaging confirmed pulmonary embolism, deep vein thrombosis (proximal or distal, including central venous catheter-related DVT), or unusual site VTE (either symptomatic or incidentally diagnosed) within the last 14 days for which anticoagulation is planned (including VTE in the deep vein system that progressed from a prior superficial vein thrombosis for which anticoagulation is to be started)
3. Platelet count <50 x 10e9/L from cancer therapy or malignancy itself
4. Able to provide written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
99 Years

Sex
Both

Target number of participants
20

Key exclusion criteria
1. Receipt of anticoagulant for index VTE with platelet count <50 x10 9/L for >72 hours
2. Superficial vein thrombosis only
3. Tumour thrombus
4. Life expectancy <1 month (as judged by the treating physicians)
5. Creatinine clearance < 30 ml/min
6. Contraindication to LMWH such as a history of heparin induced thrombocytopaenia
7. Thrombocytopaenia from other causes, such as thrombotic microangiopathy, immune thrombocytopaenia, disseminated intravascular coagulation
8. Previously documented history of refractoriness to platelet transfusion secondary to HLA antibodies
9. Refusal of blood products
10. Anticoagulation at any dose is deemed unsafe (i.e. recent, active bleeding or inherited bleeding disorders)

Date of first enrolment

08/08/2024

Date of final enrolment
01/02/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital
Headley Way
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Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
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Sponsor information

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Sponsor type
University/education

Website
http://www.ucl.ac.uk/

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Industry

Funder Name
Anthos Therapeutics

Alternative Name(s)
Anthos, Anthos Therapeutics Inc, Anthos Therapeutics Inc., Anthos Therapeutics, Inc., Anthos Therapeutics, LLC

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Funder Name
Thrombosis UK

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal and presentation at international conferences.

Intention to publish date
01/07/2027

Individual participant data (IPD) sharing plan
The sharing of datasets generated during and/or analysed during the current study will be limited by the confines of GDPR. Data sharing will be reviewed formally within the study core team. All individuals involved in the study will have access to the full dataset.

Data will be made available after publication within the confines of GDPR and will not be given to third parties. However, if there are any potential new collaborators during the project, they may be granted individual access to data earlier.

If any external users request data, a data-sharing agreement will be drawn up and reviewed by the Joint Research Office at UCLH/UCL. External user responsibilities will encompass maintaining data confidentiality and exclusivity and discussion with PI regarding acknowledgement for any outputs/publications.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	13/05/2024	13/06/2024	No	Yes