Trial to evaluate tranexamic acid therapy in thrombocytopenia

Submission date	Recruitment status No longer recruiting	[X] Prospectively registered		
25/03/2015		[X] Protocol		
Registration date 25/03/2015	Overall study status Completed	Statistical analysis plan		
		[X] Results		
Last Edited	Condition category	Individual participant data		
01/04/2025	Cancer			

Plain English summary of protocol

http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-tranexamic-acid-for-low-platelet-counts-treatt

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

Clinical Trials Information System (CTIS)

2014-001513-35

ClinicalTrials.gov (NCT)

NCT03136445

Protocol serial number

CPMS 18157

Study information

Scientific Title

A double blind, randomised controlled TRial EvaluAting the safety and efficacy of Tranexamic acid in patients with haematological malignancies with severe Thrombocytopenia

Acronym

TREATT

Study objectives

Patients with cancers of the blood often develop low blood cell counts either as a consequence of the disease or the treatment by chemotherapy or stem cell transplantation. Platelet transfusions are commonly given to raise any low platelet count and reduce the risk of clinical bleeding (prophylaxis) or stop active bleeding (therapy). But recent studies have indicated that many patients continue to experience bleeding, despite the use of platelet transfusions. Tranexamic acid is a type of drug that is called an antifibrinolytic. These drugs act to reduce the breakdown of clots formed in response to bleeding. These drugs have been used widely in both elective and emergency surgery and have been shown to decrease blood loss and the use of red cell transfusions. The purpose of this study is to test whether giving tranexamic acid to patients receiving treatment for blood cancers reduces the risk of bleeding or death, and the need for platelet transfusions. Patients will be randomised to receive tranexamic acid (given intravenously through a drip, or orally) or a placebo. We will measure the rates of bleeding daily using a short structured assessment of bleeding, and we will record the number of transfusions given to patients.

Ethics approval required

Old ethics approval format

Ethics approval(s)

South-Central Oxford C, 16/03/2015, ref: 14/SC/1290

Study design

Randomized; Interventional; Design type: Treatment

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Patients with haematological malignancies receiving intensive chemotherapy and/or stem cell transplantation

Interventions

Prophylactic TXA/Placebo, double-blind, placebo controlled parallel group trial to assess the safety and efficacy of tranexamic acid at reducing bleeding in patients with haematological malignancies and severe thrombocytopenia. Participants will be randomised to receive TXA or placebo. Trial treatment will be started as per randomisation assignment as soon as possible within 24 hours of the first recorded platelet count = 30 x 109/L.

Dose schedule TXA 1g every eight hours IV or 1.5g every eight hours PO.

Follow Up Length: 4 month(s); Study Entry: Single Randomisation only

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Tranexamic acid

Primary outcome(s)

Current primary outcome measure as of 10/12/2018:

Estimated proportion of participants who died or had bleeding of WHO grade 2 or above during the first 30 days of the trial from the first day of trial treatment. A time-to-event analysis will be used to determine this proportion to ensure that all participants are included in the primary outcome analysis, not just those who are followed up for the full 30 days. Any participants lost to follow-up will be included in the analysis and censored at the time that they were lost.

Previous primary outcome measure:

Proportion of patients who died or had bleeding of WHO grade 2 or above during the first 30 days of the trial. Day 1 being the first day the patient's platelet count falls to ≤30x109/L. A time-to-event analysis will be used to determine this proportion to ensure that all patients are included in the primary outcome analysis, not just those who are followed up for the full 30 days. Any patients lost to follow-up will be included in the analysis and censored at the time that they were lost.

Key secondary outcome(s))

Current secondary outcome measures as of 10/12/2018:

1. Secondary Efficacy Outcomes:

All measured during first 30 days of the trial, i.e. from the first day of trial treatment.

- 1.1. Proportion of days with bleeding (WHO grade 2 or above)
- 1.2. Time to first episode of bleeding of WHO grade 2 or greater
- 1.3. Highest grade of bleeding a participant experiences
- 1.4. Number of platelet transfusions/participant
- 1.5. Number of red cell transfusions/participant
- 1.6. Proportion of participants surviving up to 30 days without a platelet transfusion
- 1.7. Proportion of participants surviving up to 30 days without a red cell transfusion
- 1.8. Quality of life, measured using EQ-5D-5L and FACT-TH18 (V4) at Day of Randomisation, Day 12, Day 30 and Day 120
- 2. Secondary Safety Outcomes:
- 2.1. Number of thrombotic events from first administration of trial treatment up to and including 120 days after the first dose of trial treatment is administered, per day at risk
- 2.2. Number of participants developing Veno-occlusive Disease (VOD; Sinusoidal obstructive

syndrome, SOS) within 60 days of first administration of trial treatment

- 2.3. All-cause mortality during the first 30 days and the first 120 days after the first dose of trial treatment is administered
- 2.4. Death due to thrombosis during the first 120 days after the first dose of trial treatment is administered
- 2.5. Death due to bleeding during the first 30 days after the first dose of trial treatment is administered
- 2.6. Number of serious adverse events from first administration of trial treatment until 60 days after the first dose of trial treatment is administered
- 3. Other outcomes:

All measured during first 30 days of the trial, i.e. from the first dose of trial treatment

- 3.1. Proportion of days with thrombocytopenia ($\leq 10x109/L$, $\leq 30x109/L$, $\leq 50x109/L$)
- 3.2. Proportion of days with fever (highest daily temperature \geq 38.1°C) of days spent in hospital, up to study day 30
- 3.3. Reasons for platelet and red cell transfusions

Previous secondary outcome measures:

1. Secondary Efficacy Outcomes:

All measured during first 30 days of the trial. Day 1 being the first day the patient's platelet count falls to $\leq 30 \times 109/L$.)

- 1.1. Proportion of days with bleeding (WHO grade 2 or above)
- 1.2. Time to first episode of bleeding of WHO grade 2 or greater for those patients who bled
- 1.3. Highest grade of bleeding a patient experiences
- 1.4. Number of platelet transfusions/patient
- 1.5. Number of red cell transfusions/patient
- 1.6. Proportion of patients surviving at least 30 days without a platelet transfusion
- 1.7. Proportion of patients surviving at least 30 days without a red cell transfusion
- 2. Secondary Safety Outcomes:
- 2.1. Number of thrombotic events from first administration of trial treatment up to and including 120 days after the first dose of trial treatment is administered, per day at risk
- 2.2. Number of patients developing Veno-occlusive Disease (VOD; Sinusoidal obstructive syndrome, SOS) within 60 days of first administration of trial treatment
- 2.3. All-cause mortality during the first 30 days and the first 120 days after the first dose of trial treatment is administered
- 2.4. Death due to thrombosis during the first 120 days after the first dose of trial treatment is administered
- 2.5. Death due to bleeding during the first 30 days after the first dose of trial treatment is administered
- 2.6. Number of serious adverse events from first administration of trial treatment until 60 days after the first dose of trial treatment is administered
- 3. Other outcomes:

All measured during first 30 days of the trial. Day 1 being the first day the patient's platelet count falls to $\leq 30 \times 109/L$.)

- 3.1. Number of days with thrombocytopenia ($\leq 10x109/L$, $\leq 30x109/L$, $\leq 50x109/L$)
- 3.2. Reasons for platelet and red cell transfusions

Completion date

18/06/2022

Eligibility

Key inclusion criteria

- 1. At least 18 years of age
- 2. Confirmed diagnosis of a haematological malignancy
- 3. Undergoing chemotherapy or haematopoietic stem cell transplantation
- 4. Anticipated to have a hypoproliferative thrombocytopenia resulting in a platelet count of $\leq 10x10$ to the power of 9/L for ≥ 5 days
- 5. Able to comply with treatment and monitoring

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Total final enrolment

616

Key exclusion criteria

Current exclusion criteria as of 10/12/2018:

- 1. Patients with a past history or current diagnosis of arterial or venous thromboembolic disease including myocardial infarction, peripheral vascular disease and retinal arterial or venous thrombosis
- 2. Diagnosis of acute promyelocytic leukaemia (APML) and undergoing induction chemotherapy
- 3. Patients with a diagnosis/previous history of veno-occlusive disease (also called sinusoidal obstruction syndrome)
- 4. Patients with known inherited or acquired prothrombotic disorders e.g.
- 4.1. Lupus anticoagulant
- 4.2. Positive antiphospholipids
- 5. Patients receiving any pro-coagulant agents (e.g. DDAVP, recombinant Factor VIIa or Prothrombin Complex Concentrates (PCC) within 48 hours of enrolment, or with known hypercoagulable state
- 6. Patients receiving L-asparaginase as part of their current cycle of treatment
- 7. History of immune thrombocytopenia (ITP), thrombotic thrombocytopenic purpura (TTP) or haemolytic uraemic syndrome (HUS)
- 8. Patients with overt DIC (See Appendix 3 in the protocol for definition)
- 9. Patients requiring a platelet transfusion threshold >10x109/L at time of randomisation (This refers to patients who require their platelet count to be maintained at a certain specified level on an ongoing basis, and excludes a transient rise in the threshold due to sepsis)
- 10. Patients with a known inherited or acquired bleeding disorder e.g.
- 10.1. Acquired storage pool deficiency
- 10.2. Paraproteinaemia with platelet inhibition
- 11. Patients receiving anticoagulant therapy or anti-platelet therapy

- 12. Patients with visible haematuria at time of randomisation
- 13. Patients with anuria (defined as urine output < 10 mls/hr over 24 hours)
- 14. Patients with severe renal impairment (eGFR ≤30 ml/min/1.73m2)
- 15. Patients with a previous history of epilepsy, convulsions, fits or seizures
- 16. Patients who are pregnant or breastfeeding
- 17. Allergic to tranexamic acid
- 18. Patients enrolled in other trials involving platelet transfusions, anti-fibrinolytics, platelet growth factors or other pro-coagulant agents
- 19. Patients previously randomised into this trial at any stage of their treatment

Previous exclusion criteria:

- 1. Diagnosis of acute promyelocytic leukaemia and undergoing induction chemotherapy
- 2. History of ITP, TTP or HUS
- 3. Patients receiving L-asparginase as part of their current cycle of treatment
- 4. Patients with a past history or current diagnosis of arterial or venous thromboembolic disease including myocardial infarction, peripheral vascular disease and retinal arterial or venous thrombosis
- 5. Patients with a diagnosis/previous history of veno-occlusive disease (also called sinusoidal obstruction syndrome)
- 6. Patients receiving any pro-coagulant agents (e.g. DDAVP, recombinant Factor VIIa or Prothrombin Complex

Concentrates (PCC) within 48 hours of enrolment, or with known hypercoagulable state

- 7. Known inherited or acquired bleeding disorder. E.g. acquired storage pool deficiency; paraproteinaemia with platelet inhibition; known inherited or acquired prothrombotic disorders
- 9. Patients receiving anticoagulant therapy or anti-platelet therapy
- 10. Patients with overt disseminated intravascular coagulation
- 11. Patients with visible haematuria at time of randomisation
- 12. Patients requiring a platelet transfusion threshold >10x10 to the power of 9/L at time of randomisation
- 13. Patients with anuria (defined as urine output < 10mls/hr over 24 hours)
- 14. Patients who are pregnant
- 15. Patients enrolled in other trials involving platelet transfusions, anti-fibrinolytics, platelet growth factors or other pro-coagulant agents
- 16. Allergic to tranexamic acid or epsilon amino caproic acid
- 17. Previously randomised in this study at any stage of their treatment

Date of first enrolment

30/04/2015

Date of final enrolment

18/02/2022

Locations

Countries of recruitment

United Kingdom

England

Australia

Study participating centre John Radcliffe Hospital

National Blood Service – Oxford Centre Headley Way Headington Oxford United Kingdom OX3 9DU

Sponsor information

Organisation

NHS Blood and Transplant (NHSBT)

ROR

https://ror.org/0227qpa16

Funder(s)

Funder type

Hospital/treatment centre

Funder Name

NHS Blood and Transplant

Alternative Name(s)

National Health Service Blood and Transplant, UK National Health Service Blood and Transplant, NHSBT

Funding Body Type

Government organisation

Funding Body Subtype

Local government

Location

United Kingdom

Funder Name

National Health and Medical Research Council

Alternative Name(s)

National Health and Medical Research Council, Australian Government, NHMRC National Health and Medical Research Council, NHMRC

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

Australia

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request from the NHSBT Clinical Trials Unit after de-identification (text, tables, figures and appendices) 9 months after publication and ending 5 years following article publication. Data will be shared with investigators whose use of the data has been assessed and approved by an NHSBT review committee as a methodologically sound proposal.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		03/12/2024	09/01/2025	Yes	No
Protocol article	protocol	15/10/2019	11/02/2020	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results		09/01/2025	09/01/2025	No	Yes
Plain English results			20/02/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes