ISRCTN73545489 https://doi.org/10.1186/ISRCTN73545489

Trial to evaluate tranexamic acid therapy in thrombocytopenia

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

Study website
https://treatt.org

Contact information

Type(s)
Scientific

Contact name
Ms Claire Rourke

ORCID ID
http://orcid.org/0000-0002-7631-9275

Contact details
NHSBT Clinical Trials Unit
Cambridge Blood Donor Centre
Long Road
Cambridge
United Kingdom
CB2 0PT
+44 (0)7385 964361
Claire.Rourke2@nhsbt.nhs.uk

Additional identifiers

EudraCT/CTIS number
2014-001513-35

IRAS number

ClinicalTrials.gov number
NCT03136445

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)

Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a patient information sheet

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 measure
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.

Secondary outcome measures
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 (≤10x109/L, ≤30x109/L, ≤50x109/L)
3.2. Proportion of days with fever (highest daily temperature ≥ 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 ≤30x109/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 ≤30x109/L.)
3.1. Number of days with thrombocytopenia (≤10x109/L, ≤30x109/L, ≤50x109/L)
3.2. Reasons for platelet and red cell transfusions

Overall study start date
30/04/2015

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 ≤10x10 to the power of 9/L for ≥ 5 days
5. Able to comply with treatment and monitoring

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
616

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
Australia

England

United Kingdom

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)

Sponsor details
John Radcliffe Hospital
Headley Way
Oxford
England
United Kingdom
OX3 9DU

Sponsor type
Hospital/treatment centre

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)
NHMRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Australia

Results and Publications

Publication and dissemination plan
Current publication and dissemination plan as of 17/07/2023:
The trialists have published the protocol and will add the final results of the study once ready.

Previous publication and dissemination plan:
The trialists plan to publish the protocol and the final results of the study.

Intention to publish date
31/10/2024

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?
Protocol article	protocol	15/10/2019	11/02/2020	Yes	No
HRA research summary			28/06/2023	No	No
Plain English results		09/01/2025	09/01/2025	No	Yes
Results article		03/12/2024	09/01/2025	Yes	No
Plain English results			20/02/2025	No	Yes