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WOrld Maternal ANtifibrinolytic Trial

Submission date 08/12/2008	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [X] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 10/12/2008	**Overall study status** Completed	
Last Edited 11/06/2018	**Condition category** Pregnancy and Childbirth	

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.womantrial.lshtm.ac.uk/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00872469

Secondary identifying numbers

N/A

Study information

Scientific Title
Tranexamic acid for the treatment of postpartum haemorrhage: an international randomised, double blind, placebo controlled trial

Acronym
WOMAN

Study objectives
The WOMAN trial will provide reliable evidence as to whether the antifibrinolytic agent tranexamic acid can reduce mortality, hysterectomy and other morbidities in women with clinician-diagnosed postpartum haemorrhage (PPH).

Added 22/03/2012:
The WOMAN-ETAC is a sub-study which is nested in a cohort of WOMAN trial participants and aims to evaluate the effect of tranexamic acid on markers of coagulation in a sample of WOMAN trial participants. Two hundred participants in the WOMAN Trial at one centre in Nigeria (University College Hospital, Ibadan) will have venous blood taken after randomisation and before trial treatment is administered and again 30 minutes after the trial treatment is administered.

Standard coagulation parameters (platelets, fibrinogen, PT and aPTT time and D-dimer) and ROTEM® parameters measured after in vitro activation with tissue factor (EXTEM) and inhibition with aprotinin (APTEM) will be determined (maximum lysis, maximum strength [Maximal Clot Firmness (MCF)], time from start to when the waveform reaches 2mm above baseline [Clotting Time (CT)], time from 2mm above baseline to 20mm above baseline [Clot Formation Time (CFT)], time to lysis [CLT (10% difference from MCF)], time to Maximum strength [MCF-t], Clot elasticity [MCE]).

The hypothesis is that the administration of tranexamic acid will reduce markers of fibrinolytic activity in women with a clinical diagnosis of postpartum haemorrhage.

Added 08/01/2015:
WOMAN-ETAPLAT is a nested study of 128 participants in the WOMAN trial which aims to assess the effect of tranexamic acid on platelet function and thrombin generation in a sample of participants in the WOMAN trial. The primary outcome will be the effect of TXA on thrombin generation. Secondary outcomes will include effect of TXA on platelet function, fibrinogen, D-Dimer and coagulation factor V, VIII and vWF levels. Levels of all parameters will be assessed on venous blood samples. Samples will be collected at baseline and at between 30–60 minutes after the first dose of study treatment is given.

Ethics approval required
Old ethics approval format

Ethics approval(s)
LSHTM Ethics Committee, ref: 5536
All other centres will seek ethics approval before recruiting participants

Study design
Large pragmatic randomised double-blind placebo-controlled trial

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 the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Postpartum haemorrhage

Interventions
Women eligible for inclusion should be randomised, and the trial treatment started, as soon as possible. Randomisation to either active or placebo is done by telephoning a 24-hour freecall service. If telephone randomisation is not feasible a local pack system will be used where the next consecutively numbered treatment pack is taken from a box of eight packs. A loading dose of the trial treatment of tranexamic acid 1 g or placebo will be administered as soon possible, followed by a maintenance dose of tranexamic acid 1 g or placebo over eight hours. Outcome is collected at death, discharge or 6 weeks after randomisation, whichever occurs first.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Tranexamic acid

Primary outcome measure
1. Death (cause of death will be described)
2. Peripartum hysterectomy

The outcome is collected at death, discharge or 6 weeks after randomisation, whichever occurs first.

Added 08/01/2015:

WOMAN-ETAC (sub-study) primary outcome:
The primary outcome is to evaluate the effect of tranexamic acid on fibrinolysis 30 minutes after

the first dose is given. Fibrinolysis will be measured with D-dimer, fibrinogen level and using ROTEM parameters previously reported to be associated with fibrinolysis (i.e., MCF, CA10, CA15, CLI30, and CLI60). Levels of all parameters will be assessed on venous blood samples.

WOMAN-ETAPlaT (sub-study) primary outcome:
The primary outcome is the effect of tranexamic acid on thrombin generation at 30-60 minutes after the first dose is given. Thrombin Generation Assay [Lag Time (LT, min), peak height or time to peak (nMol) and area under the curve or endogenous thrombin potential (ETP, measured in nmol/L per min)] Levels of all parameters will be assessed on venous blood samples.

Secondary outcome measures
1. Surgical interventions used to treat obstetric haemorrhage:
1.1. Hysterectomy
1.2. Any brace suture
1.3. Arterial ligation
1.4. Artery selective embolisation
2. Mortality (outcome added 08/01/2015)
3. Transfusion requirements (blood/components)
4. Thromboembolic events:
4.1. Deep venous thrombosis
4.2. Pulmonary thromboembolism
4.3. Stroke
4.4. Myocardial infarction
5. Length of stay in hospital
6. If an Intensive Care Unit is available, time spent in the ICU
7. Suspected Unexpected Serious Adverse Reactions (SUSAR)
8. Status of baby up to 6 weeks of delivery

The outcome is collected at death, discharge or 6 weeks after randomisation, whichever occurs first.

Added 08/01/2015:

WOMAN-ETAC (sub-study) secondary outcome:
As a secondary outcome we will evaluate the relationship between coagulation parameters and mortality.

WOMAN-ETAPlaT (sub-study) secondary outcome:
Secondary outcomes will include effect of tranexamic acid on platelet function, fibrinogen, D-Dimer and coagulation factor V, VIII and vWF levels.

Overall study start date
01/03/2009

Completion date
30/05/2016

Eligibility

Key inclusion criteria

Immediately after delivery, all usual care should be given for the prevention of PPH. If bleeding continues and a clinician diagnosis of PPH is made, all usual treatments should be given and at the same time assessment for inclusion in the WOMAN Trial should be done. As most women die within 2 - 4 hours of delivery, it is important to consider inclusion as early as possible. Clinician diagnosis of PPH may be based on any of the following:
1. Blood loss after vaginal delivery greater than 500 ml, or
2. Greater than 1000 ml after caesarian section, or
3. Blood loss enough to compromise the haemodynamic status of the woman

Other inclusion criteria:
4. All women who are clinician-diagnosed with postpartum haemorrhage following vaginal delivery or caesarean section
5. Consent has been obtained in line with local procedures

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
20,000

Key exclusion criteria
1. The responsible clinician is uncertain as to whether or not to use an antifibrinolytic agent in a particular woman with postpartum haemorrhage
2. The responsible doctor considers there to be a clear indication for antifibrinolytic therapy
3. Women for whom there is considered to be a clear contraindication to antifibrinolytic therapy

When the responsible clinician is substantially uncertain as to whether or not to use an antifibrinolytic, all these women are eligible for randomisation and should be considered for the trial. There are no other pre-specified exclusion criteria.

Date of first enrolment
01/03/2009

Date of final enrolment
30/05/2016

Locations

Countries of recruitment
Albania

Bangladesh

Burkina Faso

Cameroon

Colombia

Egypt

England

Ethiopia

Ghana

Jamaica

Kenya

Nepal

Nigeria

Pakistan

Sudan

Tanzania

Uganda

United Kingdom

Zambia

Study participating centre
London School of Hygiene and Tropical Medicine
London
United Kingdom
WC1E 7HT

Sponsor information

Organisation
London School of Hygiene and Tropical Medicine (LSHTM) (UK)

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Sponsor type
University/education

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

ROR
https://ror.org/00a0jsq62

Funder(s)

Funder type
University/education

Funder Name
London School of Hygiene and Tropical Medicine

Alternative Name(s)
London School of Hygiene & Tropical Medicine, LSHTM

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Funder Name
Health Innovation Challenge Fund (Department of Health and Wellcome Trust) - award number HICF-0510-007

Funder Name
Bill and Melinda Gates Foundation

Alternative Name(s)
Bill & Melinda Gates Foundation, Gates Foundation, BMGF, B&MGF, GF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	16/04/2010		Yes	No
Statistical Analysis Plan	statistical analysis plan	17/05/2016		No	No
Statistical Analysis Plan	WOMAN-ETAPlaT sub-study statistical analysis plan	15/12/2016		No	No
Protocol article	WOMAN-ETAC sub-study protocol and statistical analysis plan	16/12/2016		Yes	No
Results article	results	01/05/2017		Yes	No
Results article	exploratory subgroup analysis results	07/06/2018		Yes	No