Haemorrhage alleviation with tranexamic acid - Intestinal system

ASSESSING ELIGIBILITY

Protocol Code: ISRCTN11225767
Assessing eligibility – version 2.1 date 12/04/2018

Eligibility for the HALT-IT trial

- Eligibility for the trial should be considered **as soon as possible** after GI bleeding is suspected or diagnosed.
  - Patients might present to A&E because of GI bleeding and their eligibility should be considered immediately after their arrival.
  - Patient might be hospitalised for another reason and present GI bleeding while in hospital. Also in this case, inclusion in the trial should be considered immediately.

Eligibility Overview

Adult age	The age a person is considered an adult varies from country to country. In the UK patients should be at least 16 years old. In other countries, please see Protocol Appendix 5 for the country's minimum age for a person to be considered as an eligible adult.
Significant gastrointestinal bleeding	The diagnosis of significant bleeding is clinical but significant implies a risk of bleeding to death and may include patients with hypotension, tachycardia, signs of shock, or those needing urgent transfusion, endoscopy or surgery.
Where the responsible clinician is substantially uncertain as to the appropriateness of tranexamic acid in that particular patient	• If there is a clear indication for the use of TXA, the patient should **NOT** be randomised • If there is a clear contraindication to the use of TXA, the patient should **NOT** be randomised • If the clinician is uncertain about the use of TXA in a particular patient, the patient **SHOULD** be randomised

Assessing eligibility for HALT-IT

Adult — NO

YES

Significant gastrointestinal bleeding — NO

YES

Clinician substantially uncertain regarding the use of TXA in this patient — NO

YES

Consent process followed (patient, representative or waiver) — NO

YES

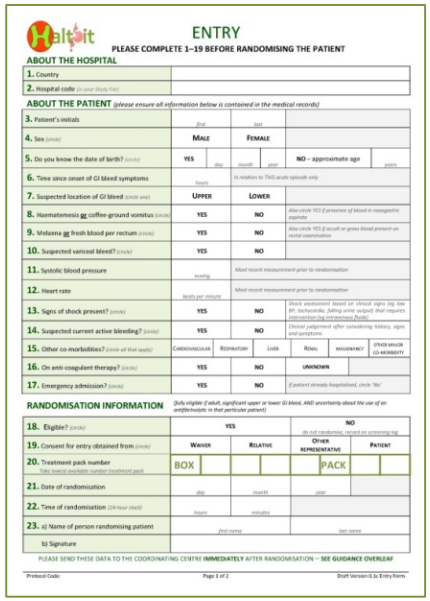
Complete Entry Form

RANDOMISE

DO NOT RANDOMISE

Record on screening log

- Eligibility for the trial should be determined from routine information recorded in patient medical records.
- Use the Entry Form (Questions 1–18) to help guide your assessment of eligibility and to record the information.



ENTRY

PLEASE COMPLETE 1–19 BEFORE RANDOMISING THE PATIENT

ABOUT THE HOSPITAL

1. Country
2. Hospital code

ABOUT THE PATIENT (please ensure all information below is contained in the medical records)

3. Patient's initials
4. Sex — MALE / FEMALE
5. Do you know the date of birth? — YES / NO – approximate age
6. Time since onset of GI bleed symptoms (hours; in relation to THIS acute episode only)
7. Suspected location of GI bleed — UPPER / LOWER
8. Haematemesis or coffee-ground vomitus — YES / NO
9. Melaena or fresh blood per rectum — YES / NO
10. Suspected variceal bleed? — YES / NO
11. Systolic blood pressure (evening; most recent measurement prior to randomisation)
12. Heart rate (beats per minute; most recent measurement prior to randomisation)
13. Signs of shock present? — YES / NO
14. Suspected current active bleeding? — YES / NO
15. Other co-morbidities? — CARDIOVASCULAR / RESPIRATORY / LIVER / RENAL / MALIGNANCY / OTHER MAJOR CO-MORBIDITY
16. On anti-coagulant therapy? — YES / NO / UNKNOWN
17. Emergency admission? — YES / NO

RANDOMISATION INFORMATION

18. Eligible? — YES / NO
19. Consent for entry obtained from — WAIVER / RELATIVE / OTHER REPRESENTATIVE / PATIENT
20. Treatment pack number — BOX / PACK
21. Date of randomisation (day / month / year)
22. Time of randomisation (24-hour clock) (hours / minutes)
23. a) Name of person randomising patient (first name / last name)
    b) Signature

PLEASE SEND THESE DATA TO THE COORDINATING CENTRE IMMEDIATELY AFTER RANDOMISATION — SEE GUIDANCE OVERLEAF

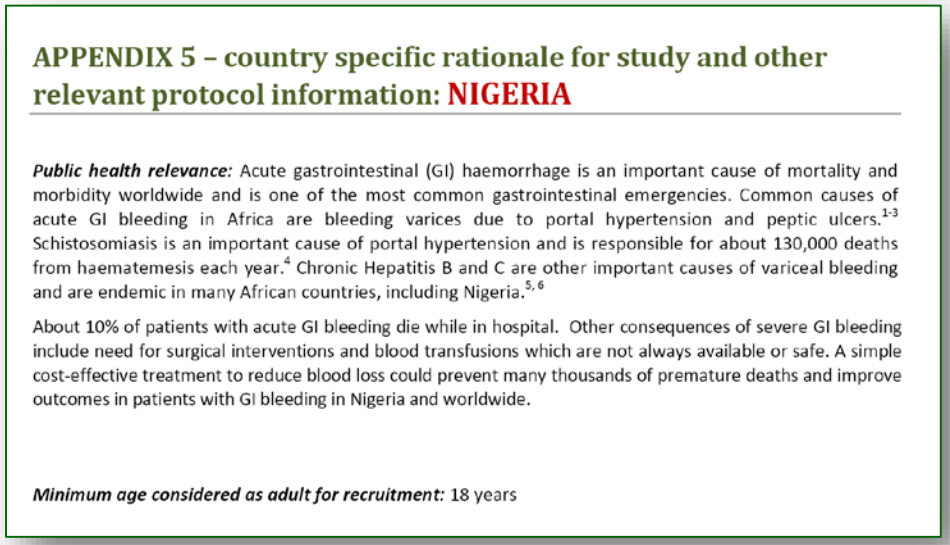
Protocol Code: Page 1 of 2 Draft Version 0.1c Entry Form

Assessing eligibility – Adult

- In this trial, an **adult** will be defined by the relevant Ethics Committee, but in the UK patients should be at least 16 years old.

- The primary reason for limiting the trial to 'adults' is that the trial uses a fixed dose which would not be suitable for children. Dosage for children needs to be adjusted based on their body mass.

- For other countries, Appendix 5 provides the country's minimum age for a person to be considered as an eligible adult.



APPENDIX 5 – country specific rationale for study and other relevant protocol information: NIGERIA

Public health relevance: Acute gastrointestinal (GI) haemorrhage is an important cause of mortality and morbidity worldwide and is one of the most common gastrointestinal emergencies. Common causes of acute GI bleeding in Africa are bleeding varices due to portal hypertension and peptic ulcers.[1-3] Schistosomiasis is an important cause of portal hypertension and is responsible for about 130,000 deaths from haematemesis each year.[4] Chronic Hepatitis B and C are other important causes of variceal bleeding and are endemic in many African countries, including Nigeria.[5, 6]

About 10% of patients with acute GI bleeding die while in hospital. Other consequences of severe GI bleeding include need for surgical interventions and blood transfusions which are not always available or safe. A simple cost-effective treatment to reduce blood loss could prevent many thousands of premature deaths and improve outcomes in patients with GI bleeding in Nigeria and worldwide.

Minimum age considered as adult for recruitment: 18 years

Assessing eligibility – Significant GI bleeding

- The diagnosis of significant bleeding is clinical

- You might consider:
  - ✓ Clinical history (including age and co-morbidities)
  - ✓ Symptoms and signs on presentation (such as hypotension, tachycardia, etc.)
  - ✓ Need of blood transfusion or urgent endoscopy or surgery

- Patients with a Rockall score of 3 or more would certainly be eligible for inclusion

- Bear in mind that a "normal" blood pressure might indicate the presence of a significant bleed in an older patient who was previously hypertensive

Assessing eligibility – The uncertainty principle

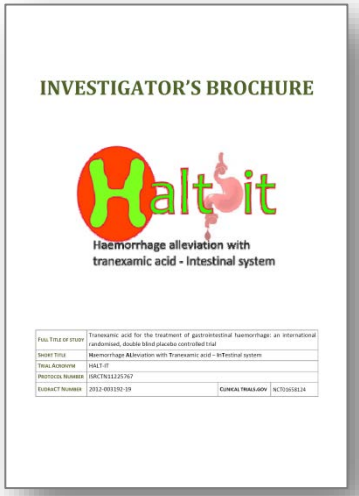
- **Uncertainty principle:** The fundamental eligibility criterion for the trial is the responsible clinician's uncertainty as to whether or not to use TXA in a particular patient with significant GI bleeding. This approach to trial eligibility is well established.
- A patient can be enrolled if, and only if, the responsible clinician is substantially **uncertain** as to which of the trial treatments would be most appropriate for that particular patient.
- A patient **should not** be enrolled if the responsible clinician is for any medical or non-medical reasons reasonably certain that one of the treatments that might be allocated would be inappropriate for this particular individual (in comparison with either no treatment or some other treatment that could be offered to the patient in or outside the trial).
- Using the uncertainty principle should allow the process of this trial to be closer to what is appropriate in normal medical practice.

Assessing eligibility – The uncertainty principle

Information about the available physical, chemical, pharmaceutical, pharmacological, toxicological and clinical information on TXA should allow you to decide whether it is indicated or contraindicated for a particular patient.

Information is provided in the Protocol and more comprehensively in:

1. **Investigator's Brochure** (contained in Study File Folder 1 section 4 – Trial drug guidance and information)
2. **Manufacturer's Summary of Product Characteristics** (contained within the Investigator's Brochure)

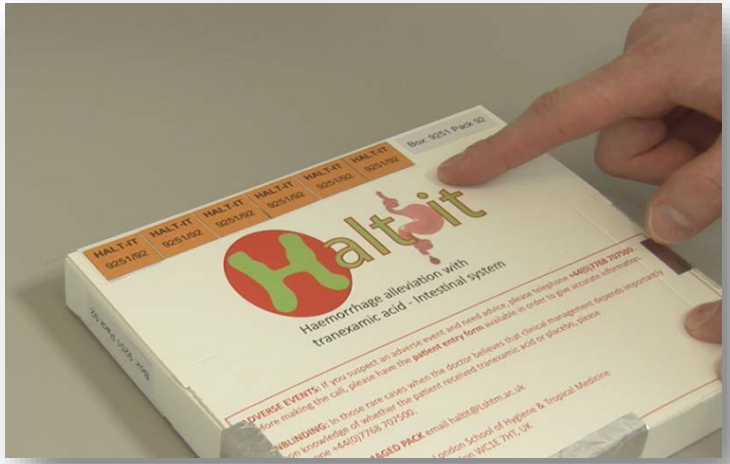


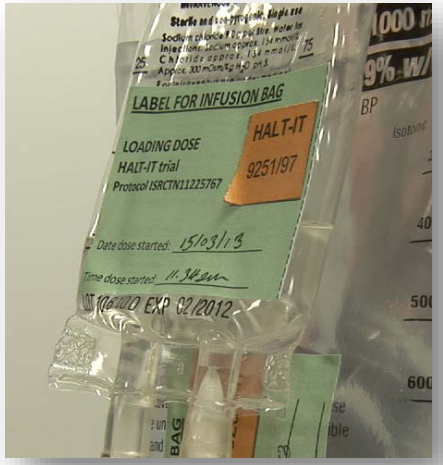
It is important that all trial team members familiarise themselves with these documents.

Clinician certain or clear indication	Do not randomise
Contraindication	Do not randomise
Clinician uncertain	Randomise

Points to remember

- All clinically indicated treatment available **MUST** be given.
- The treatment given in this trial is **ADDITIONAL** to all other treatments and is NOT a substitute for any other clinically indicated treatments.
- **AT THE SAME TIME** as you are starting treatments for GI bleeding, consider inclusion in the trial.
- Aim to give the trial treatment **AS SOON AS POSSIBLE** after significant GI bleeding is suspected and patient has been judged to be eligible.





JOIN THE GLOBAL COLLABORATION

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