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Tranexamic acid to prevent anastomotic leak after rectal cancer surgery

Submission date
03/08/2024

Recruitment status
Recruiting

Registration date
31/10/2024

Overall study status
Ongoing

Last Edited
04/12/2024

Condition category
Digestive System

[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
Anastomotic leak is a life-threatening surgical complication that occurs when the two ends of bowel at the anastomosis fail to heal, causing spillage of bowel contents into the abdomen. Certain bacteria present within stool (the microbiome) have been shown to increase the risk of anastomotic leak by causing the join in the bowel to break down. This study will test a new treatment called tranexamic acid which may prevent this from happening.

This study aims to provide important information about tranexamic acid and whether it can be used to prevent anastomotic leak. Before this new treatment can be tested on a larger scale, it is important to do a small feasibility study to be sure the treatment is acceptable to patients and healthcare workers.

Who can participate?
Patients aged 18 years or older with a diagnosis of cancer of the rectum or sigmoid colon, suitable for curative resection by high or low anterior resection (open, laparoscopic, robotic) with an anastomosis distance measuring less than or equal to 15cm from the anal verge.

What does the study involve?
Patients will be divided into two groups at random. One group will receive a solution of tranexamic acid into the back passage. This will be done using a small flexible tube (rectal catheter) which is placed into the anus during the operation. The catheter will remain in place for 3 days after surgery. This allows tranexamic acid to be delivered close to the join in the bowel, where it may modify bacteria that cause anastomotic leak. Participants allocated to the other group will receive sterile water through a rectal catheter without tranexamic acid. This will give an indication of whether tranexamic acid can influence bacteria at the anastomosis.

During the study, swabs will be used to take samples of bacteria from the back passage. This will be done before surgery, on the day of surgery, and after the final treatment. This is so that we can do further tests to see if the treatment is working against harmful bacteria. At the end of the study, we will invite patients/healthcare workers to talk to us about their experiences. This will help us to design a larger study to test if treatment with tranexamic acid works.

What are the possible benefits and risks of participating?
Benefits: It is hoped that this new treatment will help to prevent anastomotic leak after rectal cancer surgery. This is not certain and is the reason we are performing this study. Whilst this research may not directly benefit the participants, it will help us to better understand why anastomotic leak occurs and how we can improve treatments for this complication in the future.
Risks: Since participants are receiving an additional treatment, there is a risk of added side-effects, which means we must monitor them more closely.
All participants in this study will have a rectal catheter inserted during the operation by their surgeon. While this is a routine practice following surgery for some, it may cause slight discomfort.
Tranexamic acid is a widely used medication and most patients do not experience any adverse effects. However, all medicines carry potential side-effects. Some people taking tranexamic acid can develop nausea, vomiting or diarrhoea. Another possible side-effect is a rash. There are other less common side-effects which are possible with tranexamic acid, if participants notice anything unusual that they are concerned about, they must speak to a member of the medical team.

Where is the study run from?
University of Leeds (UK)

When is the study starting and how long is it expected to run for?
August 2024 to January 2027

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
Jack Helliwell, J.A.Helliwell@leeds.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1009682

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
2022-CT01, NIHR303267

Study information

Scientific Title
TrAnexamic acid to pRevent anastomotic leak after rectal cancer surGEry: a feasibility sTudy (TARGET)

Acronym
TARGET

Study objectives
Feasibility hypothesis 1: The administration of tranexamic acid via rectal catheter after rectal cancer surgery is feasible, acceptable, and safe.
Feasibility hypothesis 2: A definitive study of tranexamic acid for the prevention of anastomotic leak after rectal cancer surgery can be feasibly delivered in the future.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/10/2024, North West - Liverpool Central (2 Redman Place , Stratford, E20 1JQ, United Kingdom; +44 207 104 8340; liverpoolcentral.rec@hra.nhs.uk), ref: 24/NW/0254

Study design
Phase II randomized controlled unblinded trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Anastomotic leak; rectal cancer surgery

Interventions
Surgery will be performed according to the surgeon's usual technique. At the end of the procedure all participants will have a rectal catheter placed by the operating surgeon.
• Tranexamic Acid Group: Participants will receive tranexamic acid solution (1000mg/50ml) administered via a rectal catheter intra-operatively and on post-operative days 1-3.
• Control Group: Participants will receive sterile water (50ml) via rectal catheter intra-operatively and on post-operative days 1-3.

Intervention Type
Drug

Pharmaceutical study type(s)
Prophylaxis, Therapy

Phase
Phase II

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

Primary outcome measure
Measured at the end of the study:
Outcomes to inform progression:
1. Number of eligible patients recruited.
2. Average compliance to the study treatment schedule.
3. Proportion of missing clinical outcome data.
4. Incidence of serious and unexpected serious complications.

Outcomes to explore clinical variability:
1. Anastomotic leak defined and graded using the International Study Group definition.
2. Post-operative complications measured using the Clavien-Dindo scale.

Secondary outcome measures
Exploratory outcomes for the two sub-studies:

Microbiome sub-study:
1. Bacterial 16S rRNA analysis to determine microbiome populations at the following time-

points: i) pre-operative, ii) intra-operative, iii) on post-operative day 3-5.
2. Bacterial collagenase assay to quantify collagenase levels at the following time-points: i) pre-operative, ii) intra-operative, iii) on post-operative day 3-5.

Qualitative sub-study:
1. Patient and healthcare worker experiences of the intervention and the intervention schedule.
2. Enablers and barriers affecting compliance to the intervention.
Individual qualitative interviews will take place after treatment has been completed

Overall study start date
01/08/2024

Completion date
01/01/2027

Eligibility

Key inclusion criteria
1. Aged greater than or equal to 18 years
2. Able to provide written informed consent
3. Biopsy proven adenocarcinoma of the rectum or sigmoid colon
4. The responsible surgeon has determined the patient suitable for curative resection through either high or low anterior resection
5. The responsible surgeon has deemed the patient appropriate for elective open, laparoscopic or robotic surgery.
6. The responsible surgeon has deemed the planned level of distal bowel transection, and thus the level of the colorectal/anal anastomosis, to be ≤15cm from the anal verge
7. American Society of Anesthesiologists grade (ASA) less than or equal to 3
8. Able and willing to comply with the terms of the Protocol, including those related to pregnancy/ contraception

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
45

Key exclusion criteria
1. Patients not undergoing colo-rectal/anal anastomosis e.g., abdominoperineal excision of rectum (APER), Hartmann’s procedure
2. Patients with coexistent colorectal pathology e.g., inflammatory bowel disease

3. Patients for whom the responsible surgeon considers there is a clear contraindication for tranexamic acid e.g. known allergy to tranexamic acid, a prior history of acute venous or arterial thrombosis, a medical history of seizures or convulsions, a medical history of disseminated intravascular coagulation, a medical history of diseases of the retina, a medical history of severe renal impairment.
4. Patients who are breastfeeding, pregnant or likely to become pregnant within 3 months of surgery
5. Concurrent enrolment in another CTIMP
6. Concomitant administration of tranexamic acid for any other indication (tranexamic acid is not part of routine surgical care at LTHT)

Date of first enrolment
10/12/2024

Date of final enrolment
01/10/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St James's University Hospital
Leeds Teaching Hospitals NHS Trust
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Sponsor information

Organisation
University of Leeds

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Sponsor type
University/education

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ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Conference presentation
Other publication
Submission to regulatory authorities

Intention to publish date
01/10/2027

Individual participant data (IPD) sharing plan

Data sharing requests will be considered by the trial management group on written request to the Chief Investigator. Fully anonymised participant data or other prespecified data will be available subject to a written proposal and signed data sharing agreement.

IPD sharing plan summary

Available on request