

# Tranexamic acid to prevent anastomotic leak after rectal cancer surgery

<b>Submission date</b> 03/08/2024	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 31/10/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 04/12/2024	<b>Condition category</b> Digestive System	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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

### Contact name

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Principal Investigator

### Contact name

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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  $\leq 15$ cm 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

Beckett Street

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## Sponsor information

**Organisation**

University of Leeds

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The Secretariat

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**Sponsor type**

University/education

**Website**

<http://www.leeds.ac.uk/>

**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