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Feasibility study of lidocaine infusion during bowel cancer surgery for cancer outcome

Submission date
21/01/2022

Recruitment status
No longer recruiting

Registration date
06/04/2022

Overall study status
Completed

Last Edited
20/09/2023

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
In most patients, surgery is the main treatment for large bowel cancer. It can lead to a complete cure. Unfortunately, in some patients, cancer can come back after surgery.
Even before surgery, a small number of cancer cells from the tumour can move around the body. When the surgeon removes the tumour, more cancer cells can be released. The surgeon cannot help this even by being careful. The body can deal with these cells, but if there are lots of them, they can clump together (known as micrometastases), and this can cause cancer to spread.
Around the time of surgery, the body reacts to heal the wound. Sadly, this creates an environment that can encourage cancer cells to grow. Surgery can further reduce the body's defence system to deal with this.
Lidocaine is a local anaesthetic drug. It is safe and widely used, such as at the dentists. Anaesthetists sometimes use it for patients during surgery for other indications such as pain. Scientists have found in laboratory and animal studies that lidocaine may prevent and kill micrometastases.
Researchers want to see if lidocaine can prevent bowel cancer recurrence and improve quality of life after surgery. However, they need a big study to see if lidocaine can do this in bowel cancer patients. Before they do this, though, they need to check that such a study can be done in practice. This is done by running a small study known as a feasibility study such as this study. This study aims to see how the future larger study can be done successfully. The researchers also want to find out if they can understand the science of how lidocaine might work in patients.

Who can participate?
Patients over the age of 18 years with stage 2 or 3 large bowel cancer who will have surgery to remove the cancer

What does the study involve?
The study will involve participants:
1. Being randomly allocated to receive lidocaine or a dummy treatment (placebo) into their bloodstream (an infusion). The researchers plan to give this infusion from the start of surgery until after the surgery for a total duration of 24 hours.
2. Answering questionnaires to measure their quality of life before surgery, at 6 and 12 months after surgery via telephone. This may take around 20 minutes. During the 6 and 12 months

telephone call, the researchers will also ask about their health and wellbeing, such as if they had to see their GP, go back to the hospital, or change their social circumstances because of their cancer.
3. The researchers will look at their medical records to see if cancer comes back after a year.
4. Completing a feedback questionnaire on day 3 while in the hospital to see how they get on with the study processes.
5. Having an extra blood test before and during surgery, after they finish the lidocaine/placebo infusion and on day 3 after their surgery. The researchers will try to take this extra blood during their routine hospital blood test. This additional blood test is to help them understand the science of how lidocaine might work for cancer patients.

What are the possible benefits and risks of participating?
It is hoped that lidocaine may help to reduce bowel cancer recurrence and improve quality of life after cancer surgery. However, there may be no medical benefit from participation in this study. The information collected will help the researchers to set up a larger study to determine if lidocaine can benefit bowel cancer survival.
Any bowel surgery has potential risks. Taking part in this study will not change these risks. The researchers do not anticipate any adverse effects on participants' overall recovery.
There is always a minimal risk of side effects or allergies when taking any medication. The dose and duration the researchers have chosen as recommended by an international expert group are unlikely to produce adverse effects. This risk will be like if people receive a local anaesthetic in any other way. Local anaesthetics such as lidocaine have been used every day in NHS hospitals and dentist practices for decades.
In the rare event of a patient showing a reaction, the infusion will be stopped immediately. The doctor looking after the patients will know and have experience managing this. There are drugs available for treatment. Patients are not expected to have late side effects after the treatment has been stopped.
The rare reactions may include:
1. Allergic reaction (including rash, swelling, and blistering)
2. Tingling of the mouth and/or tongue
3. Ringing in the ear
4. Blurred or double vision
5. Nausea and vomiting
6. Dizziness, light-headedness, confusion, drowsiness
7. Breathlessness

Where is the study run from?
This study is being run by the Imperial College London and takes place in two NHS hospitals in England (UK)

When is the study starting, and how long is it expected to run for?
October 2020 to August 2024

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

Who is the main contact?
Dr Raha West
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Contact information

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Principal investigator

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05250791

Clinical Trials Information System (CTIS)
2021-006185-20

Integrated Research Application System (IRAS)
1004491

Central Portfolio Management System (CPMS)
52546

Protocol serial number

21CX7298

Study information

Scientific Title
A randomised feasibility study evaluating the effect of perioperative intravenous lIdocaine on colorectal cancer outcome after surgery

Acronym
FLICOR

Study objectives
There are strong pre-clinical evidence to suggest that lidocaine, a type of local anaesthetic which is commonly used, could potentially reduce cancer recurrence if given during cancer surgery. This study aims to assess the feasibility of conducting a study comparing intravenous lidocaine infusion versus placebo administration for 24 hours, from the start of general anaesthesia. The specific population will be any stage 2 or 3, colon or rectal cancer patient undergoing elective laparoscopic colorectal cancer surgery to look at postoperative cancer outcomes in the NHS setting. This study will explore the acceptability, facilitators and potential barriers of recruiting cancer patients, with possible anxieties of a new cancer diagnosis about to have major surgery along with other potential feasibility issues. It will also assess if follow-up and outcome data collection can be streamlined with usual care processes as much as possible and to guide the future definitive trial.

1. To collect data on clinical and patient-reported outcomes at 6 and 12 months to inform the definitive trial. This includes cancer recurrence and death from any cause, colorectal cancer-specific quality of life questionnaire and total hospital stay at 12 months.
2. Exploratory outcome to look at the potential clinically relevant mechanism of lidocaine from blood tests during treatment that may suggest how lidocaine could reduce cancer recurrence. Measurement from the blood will include circulating tumour cells (CTCs) quantity (this is not detectable by the conventional test that is usually used for cancer surveillance), a potential by product of cancer cells breakdown called circulating free DNA (cfDNA) and pro-inflammatory cytokines (these are biomarkers released by the body in response to surgery and can influence cancer recurrence). We will also see if these may be suitable markers and if it would be feasible to undertake this work as part of the future definitive trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/03/2022, London - Dulwich Research Ethics Committee (Health Research Authority, 2nd Floor, 2 Redman Place, Stratford, London, E20 1JO, UK; +44 (0)207 104 8241; dulwich.rec@hra.nhs.uk), ref: 22/LO/0114

Primary study design
Interventional

Study design
Randomized controlled double-blind parallel-group trial

Study type(s)

Treatment

Health condition(s) or problem(s) studied
Colorectal cancer patient undergoing surgery for cancer resection

Interventions
The feasibility trial will be a double-blinded, randomised, controlled trial, comparing intravenous lidocaine administration versus placebo. An intravenous bolus of 2% lidocaine or placebo will be administered following the induction of anaesthesia at 1.5 mg/kg ideal body weight over 20 minutes followed by intravenous infusion of 1.5 mg/kg/hour ideal body weight with a maximum rate of 120 mg/hour for 24 hours, in patients undergoing laparoscopic colorectal cancer surgery for stage 2 or stage 3, colon or rectal cancer. The randomisation method will involve a 1:1 parallel allocation ratio to either lidocaine or placebo. All patients will be followed up until 12 months from the date of study drug administration.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Lidocaine hydrochloride 2% for injection

Primary outcome(s)
Feasibility outcomes measured at baseline, hospital discharge, 6- and 12-months follow up post-randomisation:
1. The number of eligible patients and the actual number recruited for colon and rectal cancer with stage 2 or 3, taken from screening and recruitment logs
2. Trial retention measures by the number of participants who consent to participate who remain in the study until the end of follow up at 12 months
3. The feasibility, acceptability and return rates of data collection instruments, including those for the future economic evaluation alongside the definitive trial, measured using:
3.1. The completeness of responses to the health-related quality of life questionnaire, EQ- 5D-5L, collected at baseline, 6- and 12-months follow-up visit, which would be the outcome measure used in an economic evaluation as part of the definitive trial
3.2. The completeness of resource use data collected from an NHS and personal social services perspective using inpatient resource use data collected during the hospital stay from medical notes. A healthcare resource use form will be piloted for the definitive trial. This will be a bespoke patient questionnaire on primary and secondary healthcare and social care resource use following discharge at 6- and 12-months telephone follow up
4. Participants and clinical staff's experiences of the research process will be assessed at the end of the study with a short (10-question) close-ended questionnaire with optional free text relating to informed consent procedures, the information given, the recruitment process and any suggestions for improvement
5. Patients who refuse consent will be asked for their reasons at the point of recruitment only. Clinicians will be asked their reasons for not recruiting patients. Responses will be recorded on the screening log.

Key secondary outcome(s)

Clinical and patient-reported outcomes:
1. Disease-free survival, including cancer recurrence and death from any cause, will be captured from hospital medical records, health care resource use form and GP records at 12 months post-randomisation. Cancer recurrence will be assessed from routine cancer surveillance, including CT scan, colonoscopy, serum carcinoembryonic antigen tests, and histopathology reports. The cause of death will be looked at from the hospital and GP records.
2. Feasibility and completion of the outcome measure cancer-specific quality of life measured using the Functional Assessment of Cancer Therapy-Colorectal cancer (FACT-C) questionnaire at baseline, 6- and 12-months phone follow-up
3. Return to theatre, routine blood results, complications, blood transfusion and total hospital stay including readmission up to 12 months will be recorded from medical notes and healthcare resource use form

Exploratory outcomes
All measured at baseline, during surgery, at 24 hours (following completion of treatment) and on day 3:
1. The quantity of circulating free DNA in patients' blood measured using circulating nucleic acid kit (Qiagen) and quantitative polymerase chain reaction assays and DNA next-generation sequencing panel for whole-genome sequencing on samples.
2. The circulating tumour cells quantity and functional characteristics between the two treatment groups will be measured using the cellular fraction of peripheral blood mononuclear cells through a sorter for non-immune cells. Cells will be cultured in vitro; functional characterisation study with flow method.
3. Pro-inflammatory cytokine levels measured using an enzyme-linked immunosorbent assay

Completion date
15/09/2024

Eligibility

Key inclusion criteria
1. Aged 18 years and above, undergoing laparoscopic surgery with stage 2 or 3 colon cancer
2. Ability and willingness to consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria

1. Stage 1 and stage 4 colon or rectal cancer
2. Palliative surgery with no curative intent
3. Extensive comorbidities, i.e. American Society of Anesthesiologists (ASA) Score IV
4. Patients with known allergy to lidocaine
5. Patients who are pregnant or breastfeeding
6. Patients who are likely to have adverse effects from the accumulation of intravenous lidocaine:
6.1. Known liver disease with liver function outside the normal laboratory range
6.2. Epilepsy
6.3. Cardiac conduction abnormalities based on history and confirmed by electrocardiogram

Date of first enrolment
15/09/2022

Date of final enrolment
30/06/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Charing Cross Hospital
Fulham Palace Road
London
United Kingdom
W6 8RF

Study participating centre
Chelsea & Westminster Hospital
369 Fulham Road
London
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SW10 9NH

Sponsor information

Organisation
Chelsea and Westminster Hospital

ROR

https://ror.org/038zxea36

Funder(s)

Funder type
Government

Funder Name
National Institute for Health 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

Individual participant data (IPD) sharing plan
Participants will be informed and asked for their consent for the information collected about them to be used to support other research in the future, including that outside of the EEA. In line with the principles of research transparency, data may be shared with other researchers upon reasonable request. Before sharing, data will be anonymised so that the data subject is no longer identifiable. Data will be available upon reasonable request and approval by the sponsor, please contact Dr Raha West (flicor.trial@imperial.ac.uk). Data will be anonymised and available 1 year after the end of the study.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		30/06/2023	03/07/2023	Yes	No
HRA research summary			20/09/2023	No	No