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An assessment of the natural progression of drug associated changes in liver fat levels following completion of chemotherapy for deposits of cancer in the liver which have spread from the large bowel

Submission date	Recruitment status	[ ] Prospectively registered
28/04/2016	No longer recruiting	[ ] Protocol
Registration date	Overall study status	[ ] Statistical analysis plan
01/07/2016	Completed	[ ] Results
Last Edited	Condition category	[ ] Individual participant data
13/03/2020	Digestive System	[ ] Record updated in last year

Plain English summary of protocol

Background & Aims

The presence of liver fat with or without inflammation is an independent risk factor for disease and death mortality and morbidity) following the removal (resection) of colorectal liver metastases (bowel cancer tumours that have spread to the liver). High levels of fat in the liver can be linked with obesity (being very overweight) and insulin resistance or it may be caused through neoadjuvant chemotherapy (chemotherapy before surgery). Dietary programmes (interventions) have been proposed for patients that are not receiving chemotherapy and have an excess of liver fat, but it is not known if similar interventions would be benefit patients with chemotherapy induced fatty changes (fatty changes caused by chemotherapy) . This is because it is not known to what extent this naturally resolves after chemotherapy has been completed in the conventional 4-6 week period between chemotherapy and surgery (washout period). This study looks to investigate changes in liver fat levels within this washout period after chemotherapy.

Who can participate?

Anybody over the age of 18 years old who has or will receive chemotherapy before surgery to remove colorectal liver metastases.

What does the study involve?

Each participant is asked to attend Royal Blackburn Hospital on 2 occasions. The first visit takes place around the time that the participant completes their course of chemotherapy. During this first visit a blood sample is taken to assess liver function, circulating blood fat levels and sugar level control. An indocyanine green clearance test is performed which is a newer more sensitive test of liver function than older blood tests. The participant also has a short chemical shift magnetic resonance scan. On the second visit, 4-5 weeks later, these investigations are performed again.

What are the possible benefits?
There are no perceived benefits to participants. Travel expenses will be reimbursed to alleviate any financial burden.

When is the study starting?
October 2015 to August 2017

Who is funding the study?
Rosemere Cancer Foundation (UK)

Where is the study running?
East Lancashire Hospitals NHS Trust, Blackburn (UK)

Who is the main contact?
1. Mr Daren Subar (scientific) daren.subar@elht.nhs.uk
2. Ms Linda Gregson (public) linda.gregson@elht.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Mr Daren Subar

Contact details
Department of Hepatpancreatbiliary Surgery
Royal Blackburn Hospital
Haslingden Road
Blackburn
United Kingdom
BB2 3HH
01254 263555
daren.subar@elht.nhs.uk

Type(s)
Public

Contact name
Ms Linda Gregson

Contact details
Research and Development Department
Royal Blackburn Hospital
Haslingden Road
Balckburn
United Kingdom
BB2 3HH
01254 263555
linda.gregson@elht.nhs.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Study Protocol v2.0

Study information

Scientific Title
An assessment of the natural progression of iatrogenic changes in intra-hepatic fat levels following cessation of neoadjuvant chemotherapy for colorectal liver metastases

Acronym
LiverPRIMEii

Study objectives
Iatrogenic increases in intra-hepatic fat levels remain static follwing cessation of neoadjuvant chemotherapy before hepatic resection of colorectal liver metastases.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West – Preston Research Ethics Committee, 11/05/2016, ref: 16/NW/0416

Study design
Observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet

Health condition(s) or problem(s) studied
Hepatic steatosis/intra-hepatic fat in patients with colorectal liver metastases who are undergoing neoadjuvant chemotherapy

Interventions
30 patients in receipt of neoadjuvant chemotherapy for metachronous colorectal liver metastases will be asked to attend Royal Blackburn Hospital on 2 occassions.

During first visit, at cessation of neoadjuvant chemotherapy, participants will undergo chemical shift magnetic resonance scan, indocyanine green clearance test, serum liver function tests, serum markers of glycaemic control and lipid profile.

These investigations will be repeated 4-5 weeks later in the immediate pre-operative period.

Statistical analysis will be carried out to test for significant differences in quantification of intra-hepatic fat.

Intervention Type
Procedure/Surgery

Primary outcome measure
Intrahepatic fat fraction as measured by 2 Chemical Shift Magnetic Resonance scans greater than 24 hours apart.

Secondary outcome measures
1. Indocyanine Green Plasma Disappearance Rate and Retention at 15 minutes, measured using a PULSiON Indocyanine Green Clearance Testing Device. This will be measured at visit 1 (Week 0 - at cessation of chemotherapy) and 4 weeks later (pre-operatively)
2. BMI, Height, Weight and Hip to Waist ratio, measured at visit 1 (Week 0 - at cessation of chemotherapy) and 4 weeks later (pre-operatively)
3. Assessment of Liver function, Glycaemic control and Lipid profile, including Bilirubin, AST, ALT, ALP GGT, HbA1c, Random Glucose, Triglycerides and Cholesterol at visit 1 and 2

Overall study start date
01/10/2015

Completion date
08/08/2017

Eligibility

Key inclusion criteria
1. Patients must be able to receive and understand verbal and written information regarding the study and give written, informed consent.
2. Patients in receipt of neoadjuvant chemotherapy for CRLM.
3. Persons over 18 years old

Participant type(s)
Patient

Age group
Adult

Lower age limit

18 Years

Sex
Both

Target number of participants
30

Key exclusion criteria
1. Persons under 18 years of age.
2. Conditions in which the supine position and breath holds required for MR scanning are not possible.
3. Persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs.
4. Persons with contraindications to MR imaging- presence of cardiac pacemaker/artificial heart valve/aneurysm clips/metallic fragments in eyes/cochlear implants
5. Pre-existing chronic liver pathology such as haemachromatosis, viral hepatitis or primary hepatic malignancy.

Date of first enrolment
01/06/2016

Date of final enrolment
01/07/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
East Lancashire Hospitals NHS Trust
Royal Blackburn Hospital
Haslingden Road
Blackburn
United Kingdom
BB2 3HH

Sponsor information

Organisation
East Lancashire Hospitals NHS Trust

Sponsor details
Royal Blackburn Hospital
Haslingden Road
Blackburn
England
United Kingdom
BB2 3HH
01254 263555
linda.gregson@elht.nhs.uk

Sponsor type
Hospital/treatment centre

Website
www.elht.nhs.uk

ROR
https://ror.org/002pa9318

Funder(s)

Funder type
Charity

Funder Name
Rosemere Cancer Foundation

Results and Publications

Publication and dissemination plan
We anticipate the results of this study to be published by peer-reviewed journals and presented at international surgical, anaesthetic and perioperative medicine conferences.

Intention to publish date
08/08/2018

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from research@elht.nhs.uk

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

HRA research summary	28/06/2023	No	No