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Multicentre Cohort Study in Alcoholic Hepatitis

Submission date
10/04/2019

Recruitment status
No longer recruiting

Registration date
11/07/2019

Overall study status
Completed

Last Edited
16/02/2023

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
Alcoholic hepatitis is a form of alcohol-related liver disease characterised by liver failure in the context of recent and heavy alcohol consumption. Currently, liver biopsy is used to diagnose alcoholic hepatitis and remains difficult to predict the course of the disease and how to select the best treatment.
The purpose of this study is to investigate how we can reduce mortality in patients with alcoholic hepatitis. Samples and data collected from patients will be used to investigate whether a blood test can diagnose alcoholic hepatitis and so avoid the need for liver biopsy. It will also study tests to predict disease outcome, infection and kidney damage.

Who can participate?
Adults aged 18 years and over with clinical diagnosis of either Alcoholic Hepatitis (AH) or Acute Decompensation of Cirrhosis (AD).

What does the study involve?
After consent to take part the study involves a brief interview and medical examination to ensure eligibility. Blood (about 60ml - just over four tablespoons worth) and urine samples will be collected for infection screening, standard laboratory testing and study testing. In case of ascites (fluid that has accumulated in the abdomen) the study doctor will perform an ascitic tap (collection of this fluid). Tests will also be done for viral hepatitis infections and for HIV (AIDS) (unless already available). Pre-menopausal female will be tested for pregnancy. All of these tests are standard clinical care. If agreed, we will be using samples if liver biopsy is performed as standard clinical care. Each visit should take about one hour.
- AD patients will only be required to attend the initial screening – day 0 and baseline – day 1 assessments as these samples are comparison for a diagnostic test for AH.
- For patients with AH, the study will last for 90 days (3 months). AH patients will be seen for a study/research visit at 7, 14, 21, 28, and 90 days after standard of care treatment. The condition will be monitored and we will collect the data/samples at these time points while the patient is in the hospital. After discharge from hospital, the routine weekly assessments will cease and there will only be day 28 and day 90 assessments.
- The last visit at 90 days, AH patients will have further blood, urine, and stool samples taken.

What are the possible benefits and risks of participating?
The knowledge we gain from the study and looking at samples in the laboratory should help us

improve the treatment offered to patients with alcohol-related liver disease in the future. There may be discomfort associated with the taking of blood samples via a needle. There may be the inconvenience of donating urine and stool samples.

Where is the study run from?
Imperial College London, UK

When is the study starting and how long is it expected to run for?
June 2019 to December 2023

Who is funding the study?
Medical Research Council

Who is the main contact?
Dr. Karolina Bogdanowicz, micah@imperial.ac.uk

Contact information

Type(s)
Public

Contact name
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Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
19SM5048

Study information

Scientific Title
Multicentre Cohort Study in Alcoholic Hepatitis

Acronym
MICAH

Study objectives
The aim of the study is to recruit patients with Alcoholic Hepatitis (AH), irrespective of severity, to evaluate performance of the prognostic scoring systems and diagnostic and prognostic biomarkers. In order to evaluate diagnostic biomarkers, we will also recruit control patients with acute decompensation of cirrhosis (AD).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Prospective multi-centre cohort study

Primary study design
Observational

Secondary study design
Nested case-control study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Alcoholic hepatitis or acute decompensation of cirrhosis (control group)

Interventions
Patients will continue to receive standard of care treatment throughout. Study participants will attend several test sessions where routine samples and other data will be collected.

After consent to take part the study involves a brief interview and medical examination to ensure eligibility. Blood and urine samples will be collected for infection screening, standard laboratory testing and study testing. In case of ascites, the study doctor will perform an ascitic tap. Tests will also be done for viral hepatitis infections and for HIV (AIDS) (unless already available). Pre-menopausal female will be tested for pregnancy. All of these tests are standard clinical care. If agreed, we will be using samples if liver biopsy is performed as standard clinical care. Each visit should take about 1 hour.
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- The last visit at 90 days, AH patients will have further blood, urine, and stool samples taken.

Intervention Type
Other

Primary outcome measure
Validation of diagnostic and prognostic performance parameters for (Baseline, D28, D90):
1. Taurocholic acid diagnostic test to distinguish AH from AD
2. Transferrin, ELF and PNPLA3 genotype adjusted prognostic scores
3. Bacterial DNA, monocyte HLADR expression and oxidative burst for prediction of infection
4. Bacterial DNA for risk stratification before immunosuppressive therapy
5. Micro RNAs for prediction of AKI
6. BLISS assay for prediction of response to prednisolone

Secondary outcome measures
1. Outcome at 28 and 90 days:
1.1 Mortality (rate)
1.2 Incidence of infection (rate)
1.3 Incidence of AKI (rate)
1.4 Incidence of recidivism (rate)
2. Outcome at 1, 5 and 10 years:
2.1 All-cause mortality (rate)
2.2 Liver-related mortality (rate)
2.3 Use of healthcare services (HES data)

Overall study start date
01/03/2019

Completion date
31/12/2023

Eligibility

Key inclusion criteria
1. Alcoholic Hepatitis group:
1.1 Aged 18 years or older
1.2 Clinical diagnosis of alcoholic hepatitis:
1.2.1 Serum bilirubin ≥ 50µmol/L
1.2.2 History of excess alcohol (> 80g/day male, > 60g/day female) to within 2 months of recruitment
1.3 Less than 4 weeks since admission to hospital
1.4 Informed consent
The alcoholic hepatitis cohort will be subdivided into patients with Maddrey's discriminant function ≥32, referred to as severe alcoholic hepatitis (SAH) and those with Maddrey's discriminant function <32, referred to as non-severe alcoholic hepatitis (NSAH).

2. Acute Decompensation of Cirrhosis group:
2.1 Aged 18 years or older
2.2 Clinical or radiological diagnosis of liver cirrhosis
2.3 Acute development of one or more of the following complications:
2.3.1 Ascites
2.3.2 Encephalopathy
2.3.3 Gastrointestinal haemorrhage
2.3.4 Infection
2.4 Less than 4 weeks since admission to hospital
2.5 Informed consent
2.6 History of excess alcohol (> 80g/day male, > 60g/day female) for more than 5 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
1,000

Key exclusion criteria
1. Acute Decompensation of Cirrhosis group:
1.1 Abstinence of >2 months prior to randomisation
1.2 Duration of clinically apparent jaundice > 3 months
1.3 Other causes of liver disease including:
1.3.1 Evidence of active chronic viral hepatitis (Hepatitis B or C)
1.3.2 Biliary obstruction
1.3.3 Hepatocellular carcinoma
1.4 Evidence of current malignancy (except non-melanotic skin cancer)
1.5 HIV infection
1.6 Aspartate Aminotransferase (AST) >500 U/L or Alanine Aminotransferase (ALT) >300 U/L (not

compatible with alcoholic hepatitis)
1.7 Patients with a serum creatinine >500 µmol/L or requiring renal support (see below)
1.8 Patients dependent upon inotropic support (adrenaline or noradrenaline). Terlipressin is allowed
1.9 Active gastrointestinal bleeding
1.10 Untreated infection
1.11 Pregnant or lactating women
1.12 Patients who cannot understand English

2. Acute Decompensation of Cirrhosis group:
2.1 Alcoholic Hepatitis (clinically or on histology)
2.2 Other causes of liver disease including:
2.2.1 Evidence of active chronic viral hepatitis (Hepatitis B or C)
2.2.2 Biliary obstruction
2.2.3 Hepatocellular carcinoma
2.3 Pregnant or lactating women
2.4 HIV infection
2.5 Patients who cannot understand English

Date of first enrolment
01/06/2019

Date of final enrolment
31/05/2023

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
Imperial College Healthcare NHS Foundation Trust
St Marys Hospital
Praed Street
London
United Kingdom
W2 1NY

Study participating centre
Plymouth Hospitals NHS Trust
Derriford Hospital

Plymouth
United Kingdom
PL6 8DH

Study participating centre
University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
Southampton
United Kingdom
SO16 6YD

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Northern General Hospital
Southampton
United Kingdom
S5 7AU

Study participating centre
Royal Devon and Exeter NHS Foundation Trust
Royal Devon and Exeter Hospital
Exeter
United Kingdom
Ex2 5DW

Study participating centre
Royal Liverpool and Broadgreen University Hospitals NHS Trust
Royal Liverpool University Hospital
Liverpool
United Kingdom
L7 8XP

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Addenbrookes Hospital
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Nottinghamshire Healthcare NHS Foundation Trust
The Resource, Trust HQ
Nottingham
United Kingdom
NG3 6AA

Study participating centre
Royal Free London NHS Foundation trust
Royal Free Hospital
London
United Kingdom
NW3 2QG

Study participating centre
The Newcastle Upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Newcastle
United Kingdom
NE7 7DN

Study participating centre
University Hospitals Bristol NHS Foundation Trust
Marlborough Street; Bristol Avon
Bristol
United Kingdom
BS1 3NU

Study participating centre
Derby Teaching Hospitals NHS Foundation Trust
Royal Derby Hospital
Derby
United Kingdom
DE22 3NE

Study participating centre
NHS Greater Glasgow and Clyde
Glasgow Royal Infirmary; Queen Elizabeth University Hospital
Glasgow
United Kingdom
G12 0XH

Study participating centre
Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital
Oxford
United Kingdom
OX3 9DU

Study participating centre
Aintree University Hospital NHS Foundation Trust
University Hospital AIntree
Liverpool
United Kingdom
L9 7AL

Study participating centre
Blackpool Teaching Hospitals NHS Foundation trust
Victoria Hospital
Blackpool
United Kingdom
FY3 8NR

Study participating centre
Chelsea and Westminster Hospital NHS Foundation trust
Chelsea and Westminster Hospital
London
United Kingdom
SW10 9NH

Study participating centre
Torbay and South Devon NHS Foundation Trust
Hengrave House, Torbay Hospital
Devon
United Kingdom
TQ2 7AA

Study participating centre
Nottingham University Hospitals NHS Trust
Queens Medical Centre

Nottingham
United Kingdom
NG7 2UH

Study participating centre
Kings College Hospital NHS Foundation Trust
Kings College Hospital
London
United Kingdom
SE5 9RS

Study participating centre
Gloucestershire Hospitals NHS Foundation Trust
Alexandra House
Cheltenham
United Kingdom
GL53 7AN

Study participating centre
Royal Cornwall Hospitals NHS Trust
Royal Cornwall Hospital
Cornwall
United Kingdom
TR1 3LJ

Study participating centre
The Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust
Royal Bournemouth General Hospital
Bournemouth
United Kingdom
BH7 7DW

Study participating centre
Hull and East Yorkshire Hospitals NHS Trust
Hull Royal Infirmary
Hull
United Kingdom
Hu3 2JZ

Study participating centre
Bradford Teaching Hospitals NHS Foundation Trust
Bradford Royal Infirmary
Bradford
United Kingdom
BD9 6RJ

Study participating centre
Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust
Doncaster Royal Infirmary
Doncaster
United Kingdom
DN2 5LT

Study participating centre
ST Georges University Hospitals NHS Foundation Trust
St Georges Hospital
London
United Kingdom
SW17 0QT

Study participating centre
Portsmouth Hospitals NHS Trust
Queen Alexandra Hospital
Portsmouth
United Kingdom
PO6 3LY

Study participating centre
Poole Hospital NHS Foundation Trust
Poole Hospital
Poole
United Kingdom
BH15 2JB

Study participating centre
Luton and Dunstable University Hospital NHS Foundation Trust
Luton and Dunstable University Hospital
Luton
United Kingdom
LU4 0DZ

Study participating centre
Chesterfield Royal Hospital NHS Foundation Trust
Chesterfield Royal Hospital
Chesterfield
United Kingdom
S44 5BL

Study participating centre
County Durham and Barlington NHS Foundation Trust
Darlington Hospital
Durham
United Kingdom
DL3 6HX

Study participating centre
NHS Tayside
Kings Croos
Dundee
United Kingdom
DD3 8EA

Study participating centre
Abertawe Bro Morgannwg University LHB
One Talbot Gateway
West Glamoran
United Kingdom
SA12 7BR

Study participating centre
South Tyneside NHS Foundation Trust
South Tyneside District Hospital
Southshields Tyne and Wear
United Kingdom
Ne34 0PL

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Medical Centre

West Midlands
United Kingdom
B15 2TH

Study participating centre
City Hospitals Sunderland NHS Foundation Trust
Sunderland Royal Hospital
Sunderland Tyne and Wear
United Kingdom
SR4 7TP

Study participating centre
Countess of Chester Hospital NHS Foundation Trust
Countess of Chester Hospita
Chester
United Kingdom
CH2 1UL

Study participating centre
University Hospitals of Leicester NHS Trust
Leicester Royal Infirmary
Leicester
United Kingdom
LE1 5WW

Study participating centre
Northumbria Healthcare NHS Foundation Trust
Rake Lane
North Shields Tyne and wear
United Kingdom
NW29 8NH

Study participating centre
NHS Lothian
Waverley Gate
Edingburgh
United Kingdom
EH1 3EG

Study participating centre
South Tees Hospitals NHS Foundation Trust
James Cook University Hospital
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
Taunton and Somerset NHS Foundation Trust
Musgrove Park Hospital
Taunton Somerset
United Kingdom
TA1 5DA

Study participating centre
Firmley Health NHS Foundation Trust
Portsmouth Road
Surrey
United Kingdom
GU16 7UJ

Study participating centre
Sandwell and West Birmingham Hospitals NHS Trust
City Hospital
Birmingham
United Kingdom
B18 7QH

Study participating centre
Sherwood Forest Hospitals NHS Foundation Trust
Mansfield Road
Sutton In Ashfield
United Kingdom
NG17 4JL

Study participating centre
North Staffordshire Combined Healthcare NHS Trust
Bellringer Road
Stoke on Trent
United Kingdom
St4 8HH

Study participating centre
Warrington and Halton Hospitals NHS Foundation Trust
Warrington Hospital
Cheshire
United Kingdom
Wa5 1qg

Study participating centre
Leeds Teaching Hospitals NHS Trust
St James's University Hospital
Leeds
United Kingdom
LS9 7TF

Study participating centre
NHS Forth Valley
33 Spittal Street
Stirling
United Kingdom
FK8 1DX

Study participating centre
Western Sussex Hospitals NHS Foundation Trust
Worthing Hospital
Worthing
United Kingdom
BN11 2DH

Study participating centre
NHS Grampian
Summerfield House
Aberdeen
United Kingdom
AB15 6RE

Sponsor information

Organisation
Imperial College London

Sponsor details
Medical School Building
St Marys Campus
Norfolk Place
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United Kingdom
W2 1PG
020 7589 5111
jrco@ic.ac.uk

Sponsor type
University/education

Website
http://www.imperial.ac.uk/

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The results of the MICAH study may take approximately 1 year to be reported. The results will be published in a medical journal and presented at appropriate clinical conferences.

Intention to publish date
31/12/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository.

No identifiable personal data will be included in any publications resulting from research. Data generated by the study will be held on the InForm eCRF online database. The database will not be used to store any raw data. NHS identifiable patient data will only be stored on secure computers which may only be accessed by the clinicians involved in the patients' clinical care. Paper records (consent forms etc) will be stored securely on NHS premises. Information gleaned from access will remain entirely confidential, and will only be recorded anonymously in study. Under the General Data Protection Regulation (GDPR) the study database will assign a unique identifying numerical code which is distinct from the NHS number of the hospital record number. The unique identifier will be used for all NHS or Imperial College research data stored on investigators computers accessible only to members of the research/healthcare team. This pseudoanonymised data will be kept on NHS and University computers. Such data will be encrypted to the local ICT requirements. Only fully anonymised data will be kept on University computers and laptops.

IPD sharing plan summary
Stored in non-publicly available repository