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Macrophage therapy for liver cirrhosis

Submission date 29/06/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 04/07/2016	**Overall study status** Completed	
Last Edited 14/01/2025	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Liver disease can overtime cause scarring and damage to the liver and eventually lead to a condition called liver cirrhosis. When this happens the liver is unable to work properly and the person can become tired and unwell. A malfunctioning liver makes people prone to infection, bruising, swelling, confusion and jaundice (yellowing of the skin). Cirrhosis is the fifth most common cause of death in UK. Currently we have no cure for liver cirrhosis but liver transplant. This is a very big operation which requires lifelong treatment with immunosuppressant drugs. Not everyone is suitable to have a liver transplant and there aren't enough transplantable livers to cure all the patients. Our group has demonstrated using animals models that selected cells (monocytes) taken from the patient's own blood can be grown in the laboratory into cells called macrophages and infused back into the patient to replace damaged liver cells. The aim of this study is to test the safety and effectiveness of autologous macrophage infusion in humans.

Who can participate?
Adults age 16-75 with liver cirrhosis

What does the study involve?
The first part of the study is to check that the macrophages are safe and find out the best number of macrophages to use. Three patients receive the same dose and if there are no side effects the dose is increased for the second group of three patients, until the maximum safe dose is reached. The second part of the study looks at whether the treatment can benefit patients with liver disease. Patients are randomly allocated to receive either the macrophage treatment or standard medical care. Liver function is then assessed after 3 months.

What are the possible benefits and risks of participating?
Patients may not gain direct benefit from the study but this could lead to the development in the future of a treatment for liver cirrhosis. This is a first in human study so the side effects are not known. We could potentially witness side effects similar to blood transfusion reactions or allergic reactions. Macrophages Activation Syndrome is a very rare condition that could potential arise from this treatment. This will be characterised by low blood pressure and difficulties in breathing. Appropriate measures are in place in the remote eventuality this may occur. Liver function could worsen. There is no information available to support the increased risk of cancer but it is difficult to predict. Patients could experience discomfort during blood sampling.

Where is the study run from?
Edinburgh Royal Infirmary (UK)

When is the study starting and how long is it expected to run for?
August 2016 to August 2021

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Prof. Stuart Forbes
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2015-000963-15

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
MR/M007588/1

Study information

Scientific Title
Macrophage therapy for liver cirrhosis

Acronym

MATCH01

Study objectives
Autologous macrophages therapy can improve liver function and reduce fibrosis in patients with established liver cirrhosis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
REC - Research Ethics Committee South East Scotland, 24/06/2016, REC ref: 15/SS/0121

Study design
Dose-escalation phase I single-centre study with 3+3 design followed by randomized controlled single-centre phase II study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Liver cirrhosis

Interventions
Dose-escalation phase I single-centre study with 3+3 design: 3 patients will receive the same dose, if no dose-limiting toxicity recorded dose will be escalated to the second group of 3 patients until maximum tolerated dose.

Followed by randomised controlled single centre phase II study of autologous activated macrophage infusion versus standard medical care. Macrophages will be infused via peripheral vein for the duration of 30 minutes. Participants will be randomised 1:1 via computer system based on a minimisation algorithm using the key variable aetiology of disease. No blinding will be possible but efficacy data will be analysed at the end of the trail to avoid bias.

Intervention Type
Biological/Vaccine

Pharmaceutical study type(s)
Not Applicable

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
Autologous activated macrophage infusion

Primary outcome measure
Phase I: The safety and feasibility of re-infusion of autologous macrophages, measured 14 days after infusion of 3rd patient in each dose escalation group (model 3+3), and the maximum safe dose of infusion
Phase II: Liver function (MELD score) at 3 months

Secondary outcome measures
1. Markers of liver fibrosis
2. Disease-related quality of life
3. Liver-related clinical events
4. Transplant-free survival
Measured at 3 months and 1 year (improvement in markers of fibrosis of the liver, improvement of quality of life, transplant free)

Overall study start date
01/08/2016

Completion date
01/08/2021

Eligibility

Key inclusion criteria
1. Age 17-65
2. Liver cirrhosis
3. Model for End-Stage Liver Disease (MELD) score 10-16
4. Aetiology liver disease: ALRD, NAFLD, PBC, hemochromatosis, alpha 1 anti trypsin deficiency, previous Hep C with SVR

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
55-74

Total final enrolment
63

Key exclusion criteria
1. Refusal or inability to give informed consent to participate in the study
2. Other cause of chronic liver disease/cirrhosis not included in listed aetiologies – this is left to the clinical judgement of the investigator based on previous investigations and trial screening
3. Portal hypertensive bleeding; active episode of bleeding requiring hospitalisation in the last 3 months where varices have not been eradicated by banding
4. Ascites unless, in the opinion of the investigator, the ascites is minimal and well controlled with no increase to diuretic therapy in last 3 months
5. Encephalopathy; current or requiring hospitalisation for treatment in last 3 months
6. Hepatocellular carcinoma – uncertain cases to be discussed at local hepatobiliary multidisciplinary meeting, dysplastic or indeterminate nodules to be excluded, regenerative or other nodules to be included at discretion of MDM
7. Previous diagnosis of hepatocellular carcinoma
8. Previous organ transplant or previous recipient of tissue
9. Listed for liver transplantation
10. Any situation that in the Investigators' opinion may interfere with optimal study participation such as alcohol or drug abuse, domicile too distant from study site, potential non-compliance or inability to co-operate
11. Presence of clinically relevant acute illness that in the opinion of the investigator might compromise the participant’s safe participation in the study
12. Presence or history of cancer within past 5 years with exception of adequately treated localised skin carcinoma, in situ cervical cancer or solid malignancy surgically excised in total without recurrence for 5 years
13. Pregnancy or breastfeeding

Date of first enrolment
01/08/2016

Date of final enrolment
26/11/2021

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Edinburgh Royal Infirmary
Little France Crescent
Edinburgh
United Kingdom
EH16 4SA

Study participating centre

Ninewells Hospital
Ninewells Avenue
Dundee
United Kingdom
DD1 9SY

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
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G4 0SF

Sponsor information

Organisation
ACCORD (UK)

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Queens Medical Research Institute
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Sponsor type
University/education

Website
http://accord.scot/

ROR
https://ror.org/01x6s1m65

Funder(s)

Funder type
Research council

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
Not provided at time of registration

Intention to publish date
01/08/2023

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

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Phase I primary safety results	01/10/2019	10/10/2019	Yes	No
Protocol article		08/11/2021	10/11/2021	Yes	No
HRA research summary			28/06/2023	No	No
Results article	Primary and secondary clinical outcomes	10/01/2025	14/01/2025	Yes	No