ISRCTN10994757 https://doi.org/10.1186/ISRCTN10994757

Rifaximin to reduce infection in decompensated cirrhosis

Submission date	Recruitment status	[_] Prospectively registered
20/02/2017	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
08/03/2017	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
30/08/2023	Digestive System	

Plain English summary of protocol

Background and study aims
Cirrhosis is the result of long-term, continuous damage to the liver and may be due to many different causes. The damage leads to scarring, known as fibrosis. Irregular bumps (nodules) replace the smooth liver tissue and the liver becomes harder. Together, the scarring and the nodules are called cirrhosis. Cirrhosis can take many years to develop and can do so without any noticeable symptoms until the damage to the liver is very serious. The build-up of scar tissue can interfere with the flow of blood to the liver and stop it from functioning properly, eventually leading to liver failure. Patients with decompensated cirrhosis (when the liver is not working properly) are at risk of dying from life-threatening complications of liver disease, such as bleeding varices (internal bleeding); ascites (fluid in the belly); encephalopathy (confusion); and jaundice (yellowing of eyes and skin). Rifaximin is an antibiotic most often used to treat diarrhea caused by the common bacteria known as E. coli. The aim of this study is to find out whether use of rifaximin can reduce the risk of infection in patients admitted to hospital with cirrhosis.

Who can participate?
Patients aged between 18 and 80 who have been admitted to hospital with cirrhosis.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group take rifaximin 550 mg twice a day for 6 months. Those in the second group take a placebo (dummy drug) twice a day for 6 months. At the start of the study, during treatment, after treatement and after 9 and 12 months, participants have information collected about their use of antibiotics and whether they have had infections at routine clinic appointments.

What are the possible benefits and risks of participating?
There may not be any direct benefits for patients taking part in this study personally, but the care that participants receive as part of this study may reduce their risk of infection whilst they are being treated for their cirrhosis. The knowledge gained from the trial and looking at study samples in the laboratory during and after treatment may improve the treatment offered to patients with cirrhosis in the future. There aren’t any significant risks in participating in this trial. The medicine being used in this study is already licenced and is used in clinical care and is very well tolerated with minimal side effects.

Where is the study run from?
St Mary’s Hospital (lead centre) and four other NHS hospitals in England (UK)

When is the study starting and how long is it expected to run for?
April 2016 to January 2020

Who is funding the study?
1. Norgine Ltd (UK)
2. Alfa Wassermann S.P.A (Italy)

Who is the main contact?
Dr Rooshi Nathwani
rooshi.nathwani08@imperial.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Rooshi Nathwani

Contact details
Liver & Anti Viral Unit10th Floor
QEQM
St Mary's Hospital
South Wharf Road
London
United Kingdom
W2 1NY
+44 7415 871928
rooshi.nathwani08@imperial.ac.uk

Additional identifiers

EudraCT/CTIS number
2016-002628-96

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
33490

Study information

Scientific Title
A multi-centre, double-blind, randomised, controlled clinical trial of rifaximin to reduce infection in patients admitted to hospital with decompensated cirrhosis

Acronym
R-RID

Study objectives
The aim of the study is to investigate whether the use of Rifaximin reduces the risk of infection in patients admitted to hospital with cirrhosis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South West – Central Bristol Research Ethics Committee, 20/09/2016, ref: 16/SW/0232

Study design
Randomised; Interventional; Design type: Treatment, Prevention, Drug

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

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

Interventions
Patients will be randomised to one of two groups in a ratio of 1:1 using a blinded randomisation list drawn up by an Imperial statistician and InForm software.

Intervention group: Participants receive rifaximin 550 mg twice a day for 6 months
Control group: Participants receive placebo 550 mg twice a day for 6 months

Participants in both groups are followed up for 6 months by their consultant during their routine clinic appointments.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Rifaximin

Primary outcome measure
Incidence of secondary or recurrent infections in patients with cirrhosis during hospitalisation or after hospital discharge is assessed using clinical evaluations at baseline, 3, 7, 14, 28 and 90 days, at 6 months (EoT) and at 9 and 12 months.

Secondary outcome measures
1. Extrahepatic organ failure (e.g. renal, neurological) rate is measured by reviewing patient notes at baseline, 3, 7, 14, 28 and 90 days, at 6 months (EoT) and at 9 and 12 months
2. Mortality rate is measured by reviewing patient notes at baseline, 3, 7, 14, 28 and 90 days, at 6 months (EoT) and at 9 and 12 months
3. Readmission with sepsis rates is measured by reviewing patient notes at baseline, 3, 7, 14, 28 and 90 days, at 6 months (EoT) and at 9 and 12 months
4. Length of hospital stay is measured by reviewing patient notes at baseline, 3, 7, 14, 28 and 90 days, at 6 months (EoT) and at 9 and 12 months

Overall study start date
15/04/2016

Completion date
30/01/2020

Eligibility

Key inclusion criteria
1. Clinical/biochemical/radiological +/- histological diagnosis of cirrhosis
2. Hospital admission with complication of cirrhosis (e.g. alcoholic hepatitis, sepsis, variceal bleeding)
3. Commencement on antimicrobial therapy
4. Aged 18 - 80 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
80 Years

Sex
Both

Target number of participants
Planned Sample Size: 268; UK Sample Size: 268

Total final enrolment
78

Key exclusion criteria
1. C.difficile infection
2. HIV antibody positive
3. Immunosuppression (excluding low dose steroids/steroid sparing agents for AIH <20 mg or equivalent of prednisolone)
4. Advanced disseminated Hepatocellular Carcinoma or invasive carcinoma
5. eGFR < 30 on screening/randomisation
6. End-stage/severe cardiac, pulmonary or kidney disease
7. IDDM
8. Colitis or coeliac disease
9. Pregnancy
10. Already receiving rifamixin

Date of first enrolment
12/01/2017

Date of final enrolment
31/03/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St Mary's Hospital
Imperial College London & Imperial College Healthcare NHS Trust
South Wharf Road
London
United Kingdom
W2 1NY

Study participating centre
The Royal Liverpool University Hospital
Gastrointestinal and Liver Services
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
Frimley Park Hospital
Portsmouth Road
Frimley
United Kingdom
GU16 7UJ

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

Sponsor information

Organisation
Imperial College London

Sponsor details
Joint Research Compliance Office
2nd Floor, Medical School Building
St Mary's Hospital
Norfolk Place
London
England
United Kingdom
W2 1NY
+44 20 3311 0204
jrco.ctimp.team@imperial.ac.uk

Sponsor type
University/education

ROR

https://ror.org/041kmwe10

Funder(s)

Funder type
Industry

Funder Name
Norgine Ltd

Funder Name
Alfa Wassermann S.P.A

Results and Publications

Publication and dissemination plan
1. Interim analysis shared with study funders, interim results to be published in peer reviewed journals, and interim results to be presented at international conferences and meetings: April – June 2018
2. Final analysis shared with study funders, final results to be published in peer reviewed journals, and final results to be presented at international conferences and meetings: January 2020

Intention to publish date
31/01/2020

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Thesis results		01/06/2021	30/08/2023	No	No