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Safety and tolerability of Yaq-001 in patients with cirrhosis

Submission date
08/03/2017

Recruitment status
No longer recruiting

Registration date
22/05/2017

Overall study status
Completed

Last Edited
18/02/2022

Condition category
Digestive System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Current plain English summary as of 14/08/2018:
Background and study aims
Cirrhosis is the result of long-term, continuous damage to the liver. There are several causes of liver damage but the increasing amount of obesity and excessive alcohol usage is causing a rapid rise in the number of cases seen across Europe. The damage leads to scarring, known as fibrosis. Irregular bumps (nodules) replace the smooth liver tissue and the liver becomes harder. Cirrhosis can take many years to develop and can do so without any noticeable symptoms until the damage to the liver is very serious. In patients with cirrhosis, bacterial fragments can leak from the gut into the blood which can cause liver failure and can damage other organs. This study looks into a new way to lower the leakage of bacterial fragments into the blood. Yaq-001, a new type of carbon medical product has shown in previous laboratory studies to have the ability to bind these bacterial fragments and so keep them together so that they stay in the gut. The purpose of this study is to test Yaq-001 for the first time in patients with cirrhosis in order to assess if the treatment with Yaq-001 is safe, is well tolerated, and if it helps improve the overall health status of the cirrhotic patients.

Who can participate?
Adults aged 18 or older with a diagnosis of cirrhosis (women must be postmenopausal or have surgical sterilization).

What does the study involve?
Participants undergo a screening test 4 weeks prior to the start of the study to test for eligibility. This includes a physical exam, heart rate test, measuring vital signs, reviewing medical history and giving blood and urine tests. Participants have to undertake additional tests to assess their bowel transit times (the time it takes for food to move through the body until it needs to be passed) by swallowing a tracer pill and then undergoing an scan to see how far it has moved. They also may have to undergo a capsule endoscopy (swallowing a pill with a tiny camera that records images inside the body and is passed naturally with bowel movements) or have an MRI (a full body scan) to confirm eligibility. Eligible participants are randomly allocated to one of two groups. Those in the first group are randomly allocated to receive either a daily dose of four grams of Yaq-001 or a dummy pill (placebo) for 12 weeks (taken by mouth). After information is collected about the participants in the first group, those in the second group are randomly

allocated either receiving an eight gram daily dose of Yaq-001 or a placebo for 12 weeks (taken by mouth). The two different doses of the treatments are done to assess the safety and tolerability of Yaq-001. Participants are assessed during the study period at the initial visit and again at week one, four, eight and 12. This includes a physical examination, testing vital signs, an electrocardiogram and reviewing medical status and medications taken between visits. It also includes an assessment of appetite and body measurements. Also, at the first visit, week four and week 12 visits, participants are asked to provide samples of their blood, morning urine and stool. Participants are followed up seven days after the study is complete to assess the safety and tolerability of the Yaq-001 treatment.

What are the possible benefits and risks of participating?
There are no direct benefits to participants however participants may benefit from a reduction in the bacteria in the blood and improvement organ function. There are small risks associated with blood tests such as pain or temporary dizziness. Assessing bowel transit times requires participants to be exposed to small amount of radiation due to the X-ray scan. If necessary, a capsule endoscopy test or MRI scan can be performed. Capsule endoscopy is associated with a small risk of capsule retention and MRI scans are associated with a risk of claustrophobia. There may be other side effects and risks that are unknown at this time.

Where is the study run from?
This study is being run by YAQRIT Ltd. (UK) and takes place in 9 public hospitals in UK, France, Italy, Portugal, Spain and Switzerland.

When is the study starting and how long is it expected to run for?
January 2017 to August 2020 (updated 18/10/2019, previously: June 2019)

Who is funding the study?
European Union's Horizon 2020 Research and Innovation Programme Grant No 634579 (EU)

Who is the main contact?
1. Dr Rajiv Jalan (Scientific)
2. Dr CR Stabile-Barnett (Public)

Previous plain English summary:
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Cirrhosis is the result of long-term, continuous damage to the liver. There are several causes of liver damage but the increasing amount of obesity and excessive alcohol usage is causing a rapid rise in the number of cases seen across Europe. The damage leads to scarring, known as fibrosis. Irregular bumps (nodules) replace the smooth liver tissue and the liver becomes harder. Cirrhosis can take many years to develop and can do so without any noticeable symptoms until the damage to the liver is very serious. In patients with cirrhosis, bacterial fragments can leak from the gut into the blood which can cause liver failure and can damage other organs. This study looks into a new way to lower the leakage of bacterial fragments into the blood. Yaq-001, a new type of carbon medical product has shown in previous laboratory studies to have the ability to bind these bacterial fragments and so keep them together so that they stay in the gut. The purpose of this study is to test Yaq-001 for the first time in patients with cirrhosis in order to assess if the treatment with Yaq-001 is safe, is well tolerated, and if it helps improve the overall health status of the cirrhotic patients.

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When is the study starting and how long is it expected to run for?
January 2017 to March 2019.

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European Union's Horizon 2020 Research and Innovation Programme Grant No 634579 (EU)

Who is the main contact?
1. Dr Rajiv Jalan (Scientific)
2. Dr CR Stabile-Barnett (Public)

Contact information

Type(s)
Public

Contact name
Dr CR Stabile-Barnett

Contact details
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Type(s)
Scientific

Contact name
Prof Rajiv Jalan

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Royal Free Campus
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United Kingdom
NW3 2PF

Additional identifiers

ClinicalTrials.gov (NCT)
NCT03202498

Protocol serial number
Yaq001-S-001

Study information

Scientific Title
Safety and tolerability of Yaq-001 in patients with cirrhosis

Acronym
CARBALIVE-SAFETY

Study objectives
The aim of this study is to ascertain the safety and tolerability of oral administration of Yaq-001 in patients with cirrhosis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. South west – Exeter Research Ethics Committee, 27/09/2017, 17/SW/0144
2. Comité de Protection des Personnes Sud-Méditerranée 2, 03/10/2017, 217 R51

Added 08/06/2018
3. CE A.O.U. di Bologna, 07/11/2017, 122/2017/U
4. Kantonale Ethikkommission Bern, 08/11/2017, 2017-01188
5. CESC della Provincia di Padova, 11/01/2018, 4384/AO/17
6. CEIm Hospital Clínic Barcelona, 22/02/2017, HCB/ 2017/1066
7. CEIC Portugal, 12/03/2018, 1712GK983

Study design
Multi-centre double blinded randomised placebo controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cirrhosis with diuretic-responsive ascites

Interventions
Current interventions as of 14/08/2018:
After providing informed consent, participants undergo a screening visit 4 weeks prior to the start of the study treatment. The screening consists of a general evaluation of medical history and medication history, physical examination, vital signs (blood pressure, pulse rate, respiratory rate and body temperature), electrocardiogram (to measure the electrical activity of your heart), blood and urine tests. These tests consist of the normal management of patients with the condition.
To confirm eligibility for the study, participants have to undertake an additional test to assess their bowel transit time. Participants are asked to swallow a small tracer pill at night and then again ten hours later the following day an X-ray is performed to see how far it has moved. It the clinician feels the participants needs another test they may be asked to swallow a small pill which takes pictures of the intestine or to have an MRI scan after swallowing a contrast pill.
Once eligibility is confirmed, participants are randomly allocated to one of two groups through computer generated randomisation using a 1:1 ratio. The treatment remains unknown throughout the study and no one involved knows what each patient is receiving. The study treatment is supplied as sachets for oral administration. At baseline, week one, four and eight visits participants receive a kit containing enough treatment to take between visits. The study doctor instructs participants on how to take the study treatment once at night after dinner. The participants are asked to carefully keep all the used and unused sachets and to return them in the same box they came in at each visit.
Group 1: Participants are randomly allocated to either receiving a daily dose of four grams Yaq-001 or of a placebo as well as continue with their standard medical treatment for 12 weeks. The Yaq-001 device or placebo is administered orally.
Group 2: Participants are randomly allocated to either receiving a daily dose of eight grams Yaq-001 or of a placebo as well as continue with their standard medical treatment for 12 weeks. The Yaq-001 device or placebo is administered orally.

Two different dosage levels are tested of Yaq-001 in order to assess the safety and tolerability. Participants in group two are not started on the higher dose until after the information of the first group (who take the lower dose) has been collected.
During the 12 week treatment period, participants are assessed by a study doctor on baseline, week one, four, eight and 12. This includes a physical examination, testing vital signs (blood pressure, pulse rate, respiratory rate and body temperature), electrocadiogram (measures the heart activity), blood and unrine samples collection for analysis at the hospital laboratory, review changes of medical status between visits, review changes of medications taken between visits.
At day one, week four and week 12 visits, participants are asked to provide 20 milliliters of blood, 9 milliliters of morning urine, a five hour urine collection and a sample of stool. The samples are collected at the visits and proceeds at the local laboratory hospital, and are then forzen and shipped to specialised laboratories in London, Barcelona, Bern and Bologna, where the analysis for all the patients' samples are done.
At each visit during the treatment period, the appetite of participants is assessed by the study doctor. Furthermore, the weight, mid-arm circumference and triceps skinfold thickness is measured in the non-dominant side of the patient's body to assess the nutritional status.
Follow-up is done seven days after the end of the study treatment and includes a physical examination, testing for vital signs (blood pressure, pulse rate, respiratory rate, and body temperature) and reviewing changes in medical status or medications taken since the previous visit.

Previous interventions:
After providing informed consent, participants undergo a screening visit two weeks prior to the start of the study treatment. The screening consists of a general evaluation of medical history and medication history, physical examination, vital signs (blood pressure, pulse rate, respiratory rate and body temperature), electrocardiogram (to measure the electrical activity of your heart), blood and urine tests. These tests consist of the normal management of patients with the condition.
To confirm eligibility for the study, participants have to undertake an additional test to assess their bowel transit time. Participants are asked to swallow a small tracer pill at night and then again ten hours later the following day an X-ray is performed to see how far it has moved. It the clinician feels the participants needs another test they may be asked to swallow a small pill which takes pictures of the intestine or to have an MRI scan after swallowing a contrast pill.
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Intervention Type
Device

Primary outcome(s)
Safety is assessed using a physical examination, vital signs (blood pressure, pulse rate, respiratory rate and body temperature), clinical laboratory tests (haematology, coagulation, clinical chemistry and urinalysis), 12-lead ECG and reported./observed adverse events at baseline and weeks 1, 4, 8 and 12.

Key secondary outcome(s))
1. Changes in blood endotoxin activity is measured using the Endotoxin Activity Assay (EAA) at baseline and weeks 1, 4, 8 and 12.
2. Changes in organ function (kidney, liver, brain, intestinal and immune functions) are assessed using:
2.1. CHILD-PUGH score at baseline and weeks 1, 4, 8 and 12
2.2. MELD score at baseline and weeks 1, 4, 8 and 12
2.3. Clinical laboratory tests at baseline and weeks 4 and 12
3. Nutritional status is measured using:
3.1. Global assessment (RFH-GA) at baseline and weeks 1, 4, 8 and 12
3.2. Clinical laboratory tests at baseline and weeks 4 and 12

Completion date
30/08/2020

Eligibility

Key inclusion criteria
1. Male and female patients
2. Aged 18 years old or older at screening
3. Clinical diagnosis of cirrhosis for any cause. Liver biopsy is not required
4. Cirrhotic patients with diuretic-responsive ascites and Child-Pugh score = 7-11 inclusive
5. Abstinence from alcohol for at least 4 weeks prior to screening

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Refusal or inability (lack of capacity) to give informed consent
2. Prohibited medication within 4 weeks before the start of the study treatment: all oral antibiotics, immunosuppressants, long acting benzodiazepines or barbiturates and antiviral medication
3. Change in dose of proton pump inhibitor therapy within 4 weeks before the start of the study treatment
4. Patients with once daily medications in which orocaecal transit time is greater than 10 hours
5. Patients requiring medication in which the dosing schedule is three times per day or greater
6. Antiviral therapy for hepatitis C within 3 months prior to screening
7. Hospital admission for liver-related indication for at least 4 weeks (except paracentesis)
8. BMI > 35 or BMI < 18
9. Clostridium Difficile diarrhoea within 4 weeks before the start of the study treatment
10. Uncontrolled infection (chronic viral hepatitis is not an exclusion criterion)
11. Human immunodeficiency virus
12. Presence of a transjugular intrahepatic portosystemic shunt (TIPSS)
13. Participation in any clinical study of an investigational medicinal product within 30 days of five half-lives of the investigational product, whichever is longer
14. Presence of clinically relevant cardiovascular, pulmonary, gastro-intestinal, renal, hepatic, metabolic, haematological, neurological, psychiatric, systemic, ocular, gynaecologic or any acute infection disease or signs of acute illness that, in the opinion of the investigator, might compromise the patient’s safe participation in the trial and/or result in a WHO performance status of 2 or more
15. Presence of the history of cancer within the past 5 years with exception of hepatocellular carcinoma within Milan criteria, adequately treated localised basal cell carcinoma of the skin, in situ cervical carcinoma or solid malignancy surgical excised in total without recurrence for five years
16. Women of child bearing potential (only postmenopausal women or with surgical sterilization will be included)

Date of first enrolment
01/10/2018

Date of final enrolment
30/05/2020

Locations

Countries of recruitment
United Kingdom

England

France

Italy

Portugal

Spain

Switzerland

Study participating centre
Royal Free Hospital
Rowland Street
London
United Kingdom
NW3 2PF

Study participating centre
Hospital Clínic de Barcelona
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Barcelona
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08036

Study participating centre
Hospital Ramón y Cajal
Carretera de Colmenar Viejo Km 9,100
Madrid
Spain
28034

Study participating centre
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Passeig Vall d’Hebron 119
Barcelona
Spain
08035

Study participating centre
Azienda Ospedaliera di Padova
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Padova
Italy
35128

Study participating centre
Policlinico S.Orsola - Malpighi
Via Albertoni 15
Bologna
Italy
40138

Study participating centre
Inselspital Universitaet Bern
Freiburgstrasse 4
Bern
Switzerland
3010

Study participating centre
Hospital Beaujon
100 Boulevard du General Leclerc
Clichy
France
82110

Study participating centre
Hospital of Santa Maria
Av. Prof. Egas Moniz
Lisbon
Portugal
1649-035

Sponsor information

Organisation

Yaqrit Ltd

Funder(s)

Funder type
Research council

Funder Name
European Union's Horizon 2020 Research and Innovation Programme Grant No. 634579

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results		17/09/2021	18/02/2022	No	No
HRA research summary			26/07/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes