ISRCTN99030459 https://doi.org/10.1186/ISRCTN99030459

HMB to improve functional status in people with liver cirrhosis

Submission date
25/01/2025

Recruitment status
Not yet recruiting

Registration date
08/05/2025

Overall study status
Ongoing

Last Edited
08/07/2025

Condition category
Digestive System

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

Plain English summary of protocol
Background and study aims
Cirrhosis is liver scarring, caused mainly by alcohol or fatty liver in the UK. People with cirrhosis have poorer quality of life than healthy people. As cirrhosis worsens, they develop more symptoms and require hospital admissions. Cirrhosis causes over 75,000 admissions and costs the NHS £17 billion annually. A leaky gut, due to the breakdown of the gut lining, drives liver damage in cirrhosis. Changes in gut bacteria mean there are fewer bacteria that can break down fibre into short-chain fatty acids (SCFAs). SCFAs are important for the proper function of cells lining the gut. Without them the gut becomes leaky, letting parts of bacteria into the bloodstream leading directly to the liver. This triggers liver inflammation and scar formation. There are no treatments for liver scarring or leaky gut. Increasing gut SCFAs may be effective in treating cirrhosis by restoring the gut lining. HMB, a naturally occurring substance that is already available as a dietary supplement to increase muscle strength, also increases SCFA levels in the gut. In small test trials, HMB was safe and had only minor side effects in people with cirrhosis. We will conduct a trial of HMB compared to a dummy treatment (placebo) in 124 patients with cirrhosis from four hospital outpatient clinics in England.

Who can participate?
Patients aged 18 to 85 years with cirrhosis

What does the study involve?
Patients will be randomly allocated to HMB or placebo twice daily for 12 weeks and followed up for another 12 weeks. At the start and during the trial we will measure the Liver Frailty Index, a combination of strength and function tests, and measures of liver disease, quality of life and mental wellbeing. The researchers will consider the treatment effective if there is meaningful improvement in the Liver Frailty Index after 12 weeks of HMB compared to placebo.

What are the possible benefits and risks of participating?
If the study shows HMB is effective, the researchers will work with national societies and healthcare professionals to encourage the regular use of HMB in routine patient care without delay as it is cheap and widely available. If participants are allocated to the HMB group they might experience an improvement in their physical wellbeing, but they might not. If they are in the placebo group or do not benefit directly, their participation will help us learn more about

HMB as a treatment for liver cirrhosis. In this way, participation may benefit people with advanced cirrhosis, in the future.
This trial is categorised as: Type A: No higher than the risk of standard medical care. HMB is a nutritional supplement that is available to the public for purchase without prescription or restriction at health food shops or online vendors. Participants will be monitored for adverse events during trial participation.
There is a risk of bleeding, infection and discomfort from additional blood samples being taken that are not standard of care. Venepuncture is a common procedure that will be carried out by appropriately trained staff at site only. Where routine bloods have been carried out in the 4 weeks before a visit to calculate Child-Pugh and MELD scores, these results may be used for trial data to minimise the amount of blood taken at each visit, where possible. Participants will be informed of risks associated with venepuncture in the PIS (e.g., discomfort, bruising, redness, fainting, vein puncture and swelling at the site where the needle goes in).

Where is the study run from?
Peninsula Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?
January 2025 to January 2027

Who is funding the study?
Research for Patient Benefit Programme (UK)

Who is the main contact?
Kayle Sands, boost.penctu@plymouth.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Muchineripi Kanengoni

Contact details
1 Roscoff Rise
Derriford
United Kingdom
PL6 5FP
+44 (0)1752 01752 432842
m.kanengoni1@nhs.net

Type(s)
Principal Investigator

Contact name
Dr Ashwin Dhanda

Contact details
South West Liver Unit
Level 7

Derriford Hospital
Plymouth
United Kingdom
PL6 8DH
+44 (0)1752 432 723
ashwin.dhanda@plymouth.ac.uk

Type(s)
Public

Contact name
Ms Kayle-Anne Sands

Contact details
Peninsula Clinical Trials Unit
Faculty of Health
University of Plymouth
N16, ITTC Building 1
Plymouth Science Park
Plymouth
United Kingdom
PL6 8BX
+44 (0)1752 437513
boost.penctu@plymouth.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1010060

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
23HEP856, CPMS 64115

Study information

Scientific Title
β -hydroxy β-methylbutyrate (HMB) supplementation to improve functional status in people with advanced liver cirrhosis: a multicentre double blind placebo-controlled randomised trial: BOOST

Acronym
BOOST

Study objectives

Primary objective:
Determine the clinical effectiveness of HMB supplementation to improve physical function as measured by the Liver Frailty Index.

Secondary objectives:
1. To determine the effect of HMB supplementation on:
1.1. Liver disease severity measured by model for end-stage liver disease (MELD) score and Child-Pugh score
1.2. Quality of life and mental wellbeing measured by Short Form-36 (SF-36) and Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS)
1.3. Rate of hospitalisation
1.4. Rate of infections
1.5. Cognitive function, measured by the Animal Naming Test
1.6. Serum short-chain fatty acid concentrations
1.7. Markers of gut permeability (LPS, LBP and D-lactate)
1.8. Muscle mass measured by calf muscle circumference
2. To evaluate participant engagement with trial procedures and adherence to the intervention
3. To assess for contamination, measured by dietary intake (macronutrient intake over the preceding 24 hours at baseline, week 12 and week 24) via Intake24 tool and HMB supplement use.
4. To assess the safety of intervention.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 06/05/2025, North East - Newcastle & North Tyneside 1 Research Ethics Committee (2nd Floor, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8384; newcastlenorthtyneside1.rec@hra.nhs.uk), ref: 25/NE/0028

Study design
Double-blind randomized placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

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
Advanced liver cirrhosis

Interventions
Current interventions as of 09/05/2025:
Intervention: 3 g of HMB (nutritional supplement) daily for 12 weeks, oral administration of to 2 x 750 mg capsules twice daily
Matched placebo (maltodextrin)

Randomisation is via an online tool

Follow-up is 24 weeks post-baseline (12 weeks post-treatment).

Previous interventions:
Intervention: 3 g of HMB (nutritional supplement) daily for 12 weeks, oral administration of 3 x 500 mg capsules twice daily
Matched placebo (maltodextrin)

Randomisation is via an online tool

Follow-up is 24 weeks post-baseline (12 weeks post-treatment).

Intervention Type
Drug

Pharmaceutical study type(s)
Not Applicable

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Calcium beta-hydroxy-beta-methylbutyrate (CaHMB)

Primary outcome measure
Clinical effectiveness of HMB to improve physical function measured by change in Liver Frailty Index at 12 weeks post-baseline*
*Note, LFI is measured at baseline, week 12 and week 24 but the primary outcome is baseline vs week 12

Secondary outcome measures
1. Quality of life measured using the SF-36 questionnaire at Baseline, Weeks 12 and 24
2. Mental wellbeing measured using the WEMWBS at Baseline, Weeks 12 and 24
3. Liver disease severity measured using the Child-Pugh score at Baseline, Weeks 12 and 24
4. Liver disease severity measured using the MELD score at Baseline, Weeks 12 and 24
5. Cognitive function measured using the animal naming test at Baseline, Weeks 12 and 24
6. Serum SCFA concentrations at Baseline, Weeks 12 and 24
7. LPS, LBP and D-lactate concentrations measured using blood test at Baseline, Weeks 12 and 24
8. Muscle mass measured by calf circumference, corrected for BMI and oedema, at Baseline, Weeks 12 and 24
9. Number, duration and diagnosis of any hospital admissions (self-reported) at Weeks 4, 12 and 24
10. Infections (self-reported and by primary/secondary care records) at Weeks 4, 12 and 24

11. Attendance to and completion of the final study visit (Week 24)
12. Self-report of medication adherence at Weeks 4 and 12
13. Medication adherence measured by pill count measured at Week 12
14. Dietary intake measured using a 24-hour food recall (total macronutrient intake/24 hours - protein, carbohydrate, fat, and fibre) at Baseline, Weeks 12 and 24
15. Contamination assessed by checking HMB supplement use at Baseline, Weeks 4, 12 and 24
16. Safety of intervention measured by adverse reactions and serious adverse events measured at Weeks 4, 12 and 24

Overall study start date
23/01/2025

Completion date
31/01/2027

Eligibility

Key inclusion criteria
Current inclusion criteria as of 09/05/2025:
1. Cirrhosis diagnosed by any of the following:
1.1. Clinical features of cirrhosis as determined by an experienced clinician
1.2. Radiological features on ultrasound or cross-sectional imaging
1.3. Histological evidence of cirrhosis
1.4. Fibrosis assessment by transient elastography with stiffness >15 kPa
2. Advanced cirrhosis defined as Child Pugh score of 7 or more (based on laboratory values and clinical assessment within the previous 6 months)
3. Evidence of portal hypertension within the previous 6 months defined by:
3.1. Presence of ascites
3.2. Presence of oesophageal or gastric varices
3.3. Splenomegaly >13 cm in maximum diameter
3.4. Episode of hepatic encephalopathy
4. Ability to provide informed consent to participate
5. Participant is ≥18 years and ≤85 years of age

Previous inclusion criteria:
1. Cirrhosis diagnosed by any of the following:
1.1. Clinical features of cirrhosis as determined by an experienced clinician
1.2. Radiological features on ultrasound or cross-sectional imaging
1.3. Histological evidence of cirrhosis
1.4. Fibrosis assessment by transient elastography with stiffness >15 kPa
2. Advanced cirrhosis defined as Child Pugh score of 7 or more (based on laboratory values and clinical assessment within the previous 6 months)
3. Evidence of portal hypertension within the previous 6 months defined by:
3.1. Presence of ascites
3.2. Presence of oesophageal or gastric varices
3.3. Splenomegaly >13 cm in maximum diameter
3.4. Episode of hepatic encephalopathy
4. Ability to provide informed consent to participate or, where the participant has hepatic encephalopathy, agreement is provided by a personal or professional representative
5. Participant is ≥18 years and ≤85 years of age

Participant type(s)
Patient

Age group
Mixed

Lower age limit
18 Years

Upper age limit
85 Years

Sex
Both

Target number of participants
124

Key exclusion criteria
Current exclusion criteria as of 09/05/2025:
1. Estimated prognosis limited to less than 6 months
2. Advanced hepatocellular carcinoma
3. The consumption of HMB, or products containing HMB, within the previous 4 weeks
4. Inability to complete the Liver Frailty Index
5. Liver transplant recipient
6. On the liver transplant waiting list or being considered or under assessment for liver transplant
7. Participant in any other interventional trial within previous 4 weeks
8. Previous history of poor engagement with clinical services, at the discretion of local PI
9. Previous history of hypersensitivity reactions or allergy to exogenous HMB supplements or any of its excipients

Previous exclusion criteria:
1. Estimated prognosis limited to less than 6 months
2. Advanced hepatocellular carcinoma
3. The consumption of HMB, or products containing HMB, within the previous 4 weeks
4. Inability to complete the Liver Frailty Index
5. Liver transplant recipient
6. On the liver transplant waiting list or being considered or under assessment for liver transplant
7. Participant in any other interventional trial within previous 4 weeks
8. Previous history of poor engagement with clinical services, at the discretion of local PI

Date of first enrolment
21/07/2025

Date of final enrolment
31/05/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospitals Plymouth NHS Trust
Derriford Hospital
Derriford Road
Derriford
Plymouth
United Kingdom
PL6 8DH

Study participating centre
Hull University Teaching Hospitals NHS Trust
Hull Royal Infirmary
Anlaby Road
Hull
United Kingdom
HU3 2JZ

Study participating centre
Liverpool University Hospitals NHS Foundation Trust
Aintree University Hospital
Lower Ln
Fazakerley
Liverpool
United Kingdom
L9 7AL

Study participating centre
Nottingham University Hospitals NHS Trust
Trust Headquarters
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre

Royal Devon University Healthcare NHS Foundation Trust
Royal Devon University NHS Ft
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
St George's University Hospitals NHS Foundation Trust
St George's Hospital
Blackshaw Road
Tooting
London
United Kingdom
SW17 0QT

Study participating centre
NHS Greater Glasgow and Clyde
J B Russell House
Gartnavel Royal Hospital
1055 Great Western Road Glasgow
Glasgow
United Kingdom
G12 0XH

Study participating centre
The Royal Wolverhampton NHS Trust
New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
United Kingdom
WV10 0QP

Sponsor information

Organisation
University Hospitals Plymouth NHS Trust

Sponsor details

Plymouth Science Park
Plymouth
England
United Kingdom
PL6 8BX
-
plh-tr.rdgovernance@nhs.net

Sponsor type
Hospital/treatment centre

Website
http://www.plymouthhospitals.nhs.uk/home

ROR
https://ror.org/05x3jck08

Funder(s)

Funder type
Government

Funder Name
Research for Patient Benefit Programme

Alternative Name(s)
NIHR Research for Patient Benefit Programme, RfPB

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Peer-reviewed scientific journals
Conference presentation
Publication on website
Submission to regulatory authorities
Access to raw data and right to publish freely by all investigators in the study or by the

Independent Steering Committee on behalf of all investigators
Other

After the trial has been reported, the anonymised individual participant data that underlie the results will be available on request from the CI and Sponsor, along with supplementary files as required (e.g. data dictionaries, blank data collection forms, analysis code, etc). Data will be shared with (or access to the data will be provided to) requestors whose proposed use of the data has been approved by the CI and Sponsor, under an appropriate data-sharing agreement. It will not be possible to identify participants personally from any information shared.

Intention to publish date
16/03/2027

Individual participant data (IPD) sharing plan
The 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