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Trial exploring the benefits of different doses of baclofen for patients with alcohol addiction

Submission date
06/12/2022

Recruitment status
Recruiting

Registration date
13/10/2023

Overall study status
Ongoing

Last Edited
16/06/2025

Condition category
Mental and Behavioural Disorders

[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
Continued alcohol consumption in people diagnosed with cirrhosis quickens the time to death. It follows, that helping people stop drinking (abstinence) can lead to improvements in how the liver works, resulting in longer life expectancy. Baclofen has been identified as a promising alcohol anti-craving medicine with potential to help people to stop drinking which is clearly the most important aim of treatment.

What does the study involve?
Our proposed trial will evaluate whether baclofen is an effective treatment option in patients with alcohol-related liver cirrhosis, and which dose(s) is/are safe and effective. This trial will test 3 different doses of baclofen and a placebo (dummy treatment) in patients with alcohol-related cirrhosis over 24 weeks. Participants will be recruited from secondary care settings within NHS trusts with the trial population reflecting the range of disease severity, co-morbidities (co-existing disease), and social and ethnic groups encountered in everyday clinical practice. The patients will be aged 18-75 years. All participants will undergo screening to detect suicidal ideation using the C-SSRS Screen between day 7 and day 10 post registration. This will ensure time for patients to receive appropriate medical treatment and reduce test anxiety. An answer of 'yes' to questions 3, 4, 5, or 6 will result in referral for mental health assessment following local standard of care procedures. At the randomisation visit, results of mental health assessment will determine eligibility (i.e. patient determined to be at risk of suicide will not be eligible for the trial). After two weeks, all participants will be assessed for entry to randomisation Participants who do not meet the entry criteria will not be randomised. Participants will be randomised after the run-in period to one of the four treatment arms using double-blind methods, meaning neither the participants or the research doctors and nurses will know which treatment has been allocated. We will also undertake blood sampling to determine the relationship between the amount of baclofen in the bloodstream to and how participants respond. This will help us to identify the best dose for each individual.

What are the possible benefits and risks of participating?
Benefits: Alcohol consumption in the presence of liver cirrhosis leads to poorer patient outcomes in comparison to patients who remain abstinent. Currently there are limited options to promote abstinence in this patient group. Continued alcohol intake increases the risk of

advanced liver failure and reduces both short and longterm survival. The predicted rates of death for patients with alcohol-related cirrhosis is very poor, with mortality rates of 71% at 5 years and 91% at 15 years for patients who continue to drink. Importantly, abstinence is associated with a ~40% reduced risk of mortality from 18 months onwards. Death from alcohol-related cirrhosis usually occurs in people of working age. Also, despite shorter life expectancy, patients admitted with alcohol-related cirrhosis incur substantial costs for healthcare systems. Risks: Baclofen has a well-established safety profile, with known adverse effects documented. Furthermore, the doses to be used have been taken from evidence from trials, and the upper limit of baclofen dosing in the UK (100 mg/day). Specific exclusion criteria have been adopted to minimise the risk of serious adverse events . In addition, suicide and suicide-related events have been reported in patients treated with baclofen. In most cases, the patients had additional risk factors associated with an increased risk of suicide including alcohol use disorder. The requirement for abstinence prior to recruitment will help reduce this risk. Patients with a recent suicide attempt or a history of previous multiple suicide or self-harm episodes will be excluded as will patients exhibiting suicidal ideation at the time of planned recruitment. During the run in period participants will undergo screening to detect suicidal ideation to determine if they need to be referred for mental health assessment. Following the mental health assessment, if the participant is assessed as being at risk of suicide they will not be eligible for the trial. The common side effects of baclofen include dizziness, weakness, confusion, headache, nausea, constipation, difficulty falling asleep or staying asleep, tiredness, frequent urination.

Where is the study run from?
Liverpool University Hospitals NHS Foundation Trust is the Sponsor of this study and is responsible for managing it. They are based in United Kingdom. They have asked that the day-to-day running of the study is carried out by a team based at the Liverpool Clinical Trials Centre, UK (LCTC, part of the University of Liverpool). A separate team from the University of Liverpool is responsible for managing the sub-study blood samples.

When is the study starting and how long is it expected to run for?
November 2022 to March 2027

Who is funding the study?
National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA) programme (UK).

Who is the main contact?
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Principal investigator

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Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-000154-28

Integrated Research Application System (IRAS)
1006141

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
R&I 6040, IRAS 1006141, CPMS 54363

Study information

Scientific Title
An adaptive-design randomised placebo-controlled trial of baclofen in the treatment of alcohol use disorder in patients with liver cirrhosis

Acronym
BASIS trial

Study objectives
The primary objective is to investigate the effect of baclofen compared with placebo in the treatment of Alcohol Use Disorder (AUD) in patients with alcohol-related cirrhosis.

Secondary objectives:
1. To determine if the treatment of AUD with baclofen in patients with alcohol-related cirrhosis is superior to placebo

2. To determine which dose(s) of baclofen is/are most effective in improving AUD treatment outcomes in patients with alcohol-related cirrhosis in comparison to placebo
3. To assess the relationship between variability in baclofen exposure and efficacy and safety parameters.
4. To monitor and compare the safety profile of the baclofen arms, including dose dependency, in comparison to the placebo arm

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 05/09/2023, South Central – Berkshire B Research Ethics Committee (Whitefriars, Level 3, Block B, Lewins Mead, Bristol, BS1 2NT, United Kingdom; +44 207 104 8253 ; berkshireb.rec@hra.nhs.uk), ref: 23/SC/0006

Study design
Interventional double-blind randomized parallel-group placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Alcohol use disorder in patients with liver cirrhosis

Interventions
Current interventions as of 16/06/2025:
All participants will undergo screening to detect suicidal ideation using the C-SSRS Screen between day 7 and day 10 post registration. This will ensure time for patients to receive appropriate medical treatment and reduce test anxiety.
An answer of 'yes' to questions 3, 4, 5, or 6 will result in referral for mental health assessment following local standard of care procedures.
At the randomisation visit, results of mental health assessment will determine eligibility (i.e. patient determined to be at risk of suicide will not be eligible for the trial).
After two weeks, all participants will be assessed for entry to randomisation. Participants who do not meet the entry criteria will not be randomised

Registered participants will be required to abstain from alcohol for 2 weeks prior to randomisation.

Following the two weeks run-in period, eligible participants will be randomised via a secure (24 hour) web-based randomisation system.

Participants will be randomised to either one of three doses of baclofen or a matching placebo (in a ratio of 1:1:1:1). Participants will be instructed to take one tablet orally three times per day (TDS).

The study arms are:
• baclofen 10 mg TDS (max daily dose 30 mg)

• baclofen 20 mg TDS (max daily dose 60 mg)
• baclofen 30 mg TDS (max daily dose 90 mg)
• placebo TDS

Participants will be prescribed tablets at baseline and weeks 1, 2, 4, 8, 16 and 24.

Blinded treatment packs will be administered at baseline and weeks 1, 2, 4, 8, 16 and 24, with all participants attending titration visits at week 1 and week 2.

Participants will be titrated up to the next dose level if this is in accordance with their randomised dose allocation. Participants randomised to 20 mg TDS will be initially be given 10 mg TDS for the first week, then increasing to 20 mg TDS for the remainder of the treatment period. Participants randomised to 30 mg TDS will initially be given 10 mg TDS for the first week, then 20 mg TDS for the second week increasing to 30 mg TDS for the rest of the treatment period.

When end of treatment is reached participants will be unblinded and a phased reduction in baclofen dose applied for those in the active arms.
The protocol provides a down-titration regime; however, this can be adjusted for the individual needs of each participant. Down titration medication will be sourced via usual NHS supply arrangements.

Previous interventions:
All participants will undergo screening to detect suicidal ideation using the C-SSRS Screen between day 7 and day 10 post registration. This will ensure time for patients to receive appropriate medical treatment and reduce test anxiety.
A score of 3 or more will result in referral for mental health assessment following local standard of care procedures.
At the randomisation visit, results of mental health assessment will determine eligibility (i.e. patient determined to be at risk of suicide will not be eligible for the trial).
After two weeks, all participants will be assessed for entry to randomisation. Participants who do not meet the entry criteria will not be randomised

Registered participants will be required to abstain from alcohol for 2 weeks prior to randomisation.

Following the two weeks run-in period, eligible participants will be randomised via a secure (24 hour) web-based randomisation system.

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When end of treatment is reached participants will be unblinded and a phased reduction in baclofen dose applied for those in the active arms.
The table provided in the email illustrates a down-titration regime; however, this can be adjusted for the individual needs of each participant. Down titration medication will be sourced via usual NHS supply arrangements.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Continued abstinence post randomisation for 24 weeks measured using Timeline Followback

Key secondary outcome(s))
Current secondary outcome measures as of 16/06/2025:
At baseline and weeks 4, 8, 16 and 24 of follow-up unless noted otherwise:
1. Self-reported alcohol consumption since previous visit via Timeline Followback to measure:
1.1. Average units per drinking day
1.2. Percent days abstinent.
1.3. Number of heavy drinking days.
2. Changes in alcohol usage and dependency questionnaires (AUDIT, SADQ, APQ). SADQ to be completed at baseline and if required at follow up, when triggered by Timeline Followback and participant is drinking again.
3. Time to lapse (time to first alcoholic drink) measured using Timeline Followback.
4. Time to relapse (defined as time to consumption of ≥5 units for women, ≥6 units for men in a single day) measured using Timeline Followback.
5. Biological markers of alcohol consumption and liver function measured by:
5.1. Ethyl glucuronide test in urine using dipstick at baseline, weeks 1, 2, 4, 8, 16 and 24 of follow-up
5.2. Breath alcohol at baseline, weeks 1, 2, 4, 8, 16 and 24 of follow-up
5.3. LFTs at baseline, weeks 4, 8, 16 and 24 of follow-up
6. Delta changes in liver function as per Child-Pugh and Model of End Stage Liver Disease (MELD-Na)
7. Alcohol craving by Penn Alcohol Craving Scale (PACS)
8. Subsequent hospital attendances and admissions (including unplanned use) at weeks 4, 8, 16 and 24 of follow-up

9. Rate of survival at time of data analysis using median duration of follow-up, ONS data clarification that death data may be requested at the final analysis if required
10. Medication adherence (pill count) at weeks 1, 2, 4, 8, 16 and 24 of follow-up
11. Blood sampling to determine a population pharmacokinetic model for baclofen in patients with alcohol-related liver cirrhosis
12. Recording and assessment of related adverse events at baseline and weeks 1, 2, 4, 8, 16 and 24 of follow-up

Previous secondary outcome measures:
At baseline and weeks 4, 8, 16 and 24 of follow-up unless noted otherwise:
1. Self-reported alcohol consumption since previous visit via Timeline Followback to measure:
1.1. Average units per drinking day
1.2. Percent days abstinent.
1.3. Number of heavy drinking days.
2. Changes in alcohol usage and dependency questionnaires (AUDIT, SADQ, APQ). SADQ to be completed at baseline and if required at follow up, when triggered by Timeline Followback and participant is drinking again.
3. Quantity and Frequency of alcohol consumption measured using Timeline Followback.
4. Time to relapse (time to first alcoholic drink) measured using Timeline Followback.
5. Time to relapse (defined as time to consumption of ≥5 units for women, ≥6 units for men in a single day) measured using Timeline Followback.
6. Biological markers of alcohol consumption and liver function measured by:
6.1. Urine Ethyl glucuronide (optional; measured in around 25% of participants) at weeks 4, 8, 16 and 24 of follow-up, where optional consent has been provided
6.2. Breath alcohol at baseline, weeks 1, 2, 4, 8, 16 and 24 of follow-up
6.3. LFTs at baseline, weeks 1, 2, 4, 8, 16 and 24 of follow-up
7. Delta changes in liver function as per Child-Pugh and Model of End Stage Liver Disease (MELD-Na)
8. Alcohol craving by Penn Alcohol Craving Scale (PACS)
9. Subsequent hospital attendances and admissions (including unplanned use) at weeks 4, 8, 16 and 24 of follow-up
10. Rate of survival at time of data analysis using median duration of follow-up, ONS data clarification that death data may be requested at
the final analysis if required
11. Medication adherence (pill count) at weeks 1, 2, 4, 8, 16 and 24 of follow-up
12. Blood sampling to determine a population pharmacokinetic model for baclofen in patients with alcohol-related liver cirrhosis
13. Recording and assessment of related adverse events at baseline and weeks 1, 2, 4, 8, 16 and 24 of follow-up

Completion date
31/03/2027

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 16/06/2025:
At Registration:
1. Age 18 to 75 years
2. Confirmed diagnosis of alcohol-related cirrhosis classified according to the Child-Pugh classification

3. Abstinent from alcohol at the time of registration for between ≥1 day and <42 days
4. Capacity to provide informed consent

At Randomisation:
1. Age 18 to 75 years
2. Confirmed diagnosis of alcohol-related cirrhosis classified according to the Child-Pugh classification
3. Abstinent from alcohol at the time of the baseline/randomisation visit for between ≥14 days and <56 days
4. Capacity to provide informed consent
5. Women of reproductive potential must have a negative pregnancy test at randomisation and use highly effective contraception for the duration of the treatment period

Previous participant inclusion criteria:
At Registration:
1. Age 18 to 65 years
2. Confirmed diagnosis of alcohol-related cirrhosis classified according to the Child-Pugh classification
3. Abstinent from alcohol at the time of registration for between ≥1 day and <42 days
4. Capacity to provide informed consent

At Randomisation:
1. Age 18 to 65 years
2. Confirmed diagnosis of alcohol-related cirrhosis classified according to the Child-Pugh classification
3. Abstinent from alcohol at the time of the baseline/randomisation visit for between ≥14 days and <56 days
4. Capacity to provide informed consent
5. Women of reproductive potential must have a negative pregnancy test at randomisation and use highly effective contraception for the duration of the treatment period

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
75 years

Sex
All

Key exclusion criteria

At registration:
1. Planning to become pregnant, is pregnant or breastfeeding
2. Overt hepatic encephalopathy or trans-jugular intrahepatic porto-systemic shunt in situ
3. Severe renal impairment (stage 5 chronic kidney disease and/or current haemodialysis)
4. History of illicit drug use excluding marijuana in the previous 4 weeks
5. Concurrent use of opioid substitution therapy
6. Use of licenced alcohol anti-craving pharmacotherapy (such as acamprosate, disulfiram naltrexone, nalmefene) in previous 12 weeks
7. Use of baclofen for any purpose in previous 12 weeks
8. Peptic ulceration detected by endoscopy within 14 days of registration.
9. Known hypersensitivity to baclofen or structurally related drugs or any other component of the formulation.
10. Poorly controlled major psychiatric disorder such as schizophrenia or bipolar disorder
11. Individuals who have participated in a trial of a medicinal product within 12 weeks preceding registration
12. Poorly controlled epilepsy
13. Rare hereditary problems of galactose intolerance, total lactose deficiency or glucose-galactose malabsorption
14. Suffering from porphyria

At randomisation:
1. Planning to become pregnant, is pregnant or breastfeeding
2. Overt hepatic encephalopathy or trans-jugular intrahepatic porto-systemic shunt in situ
3. Severe renal impairment (stage 5 chronic kidney disease and/or current haemodialysis)
4. History of illicit drug use excluding marijuana in the previous 6 weeks
5. Concurrent use of opioid substitution therapy, or use in the previous 14 days
6. Use of licenced alcohol anti-craving pharmacotherapy (such as acamprosate, disulfiram naltrexone, nalmefene) in previous 14 weeks
7. Use of baclofen for any purpose in previous 14 weeks
8. Peptic ulceration detected by endoscopy within 28 days of the baseline/randomisation visit.
9. Known hypersensitivity to baclofen or structurally related drugs or any other component of the formulation
10. Scored 3 or more on the C-SSRS Screen and has been assessed by an appropriately qualified mental health practitioner as having suicidal ideation or behaviour prior to the baseline /randomisation visit
11. Poorly controlled major psychiatric disorder such as schizophrenia or bipolar disorder
12. Individuals who have participated in a trial of a medicinal product within 14 weeks preceding the baseline/ randomisation visit
13. Poorly controlled epilepsy
14. Rare hereditary problems of galactose intolerance, total lactose deficiency or glucosegalactose malabsorption
15. Suffering from porphyria

Date of first enrolment
18/03/2024

Date of final enrolment
31/03/2026

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

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

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
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Study participating centre
Royal Free Hospital
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Study participating centre
Addenbrookes
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Mapother House
De Crespigny Park
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London
United Kingdom
SE5 8AB

Study participating centre
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Newcastle upon Tyne
United Kingdom
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Study participating centre
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Fazakerley Hospital
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L9 7AL

Sponsor information

Organisation
University of Liverpool

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type

Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Anonymous data from the trial will be made available to share with external researchers. All requests for access to these data will be reviewed by the sponsor and data controllers

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes