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A study to evaluate the effect of Obeticholic Acid to treat patients with a recent Primary Biliary Cholangitis (PBC) diagnosis who also experience issues with cognitive function around memory and problem solving

Submission date 26/07/2021	**Recruitment status** Stopped	[X] Prospectively registered [_] Protocol
Registration date 02/08/2021	**Overall study status** Stopped	[_] Statistical analysis plan [_] Results
Last Edited 13/01/2026	**Condition category** Digestive System	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims

Bile is a substance produced in the liver to digest fats and remove waste products from the body. Primary Biliary Cholangitis (PBC) is a disease where the body's immune system mistakenly attacks the bile ducts which can become damaged, causing bile to build up, which causes more damage and scarring to the liver. PBC can get worse over time and lead to liver failure. Obeticholic acid is a drug that works by causing the liver to produce less bile and helps bile flow out of the liver.

The aim of this study is to evaluate the effect of Obeticholic Acid (OCALIVA) in patients with a recent diagnosis of Primary Biliary Cholangitis (PBC) who also experience issues with cognitive function around memory and problem solving.

Who can participate?

Adults between the ages of 18 and 65 years with an established diagnosis of recent-onset PBC.

What does the study involve?

Potential participants will be screened and if eligible, and willing to take part, they will be asked for their consent to participate in the trial. Participants will be allocated to one of two groups, with an equal chance of being in either group (like tossing a coin) to receive either Obeticholic acid or matched placebo for approximately 26 weeks. Neither the participant nor the study team will know what treatment allocation participants have received. Participant assessments will include MRI scans, blood tests, questionnaires and a series of cognitive assessments on a validated research software tool. Participants recruited and randomised out of Newcastle will be required to travel to Newcastle for their MRI scan and cognitive assessments.

What are the possible benefits and risks of participating?
If the study hypothesis is correct then study participants in the active drug arm will receive direct benefit through the actions of Obeticholic Acid on their cognitive symptoms.

The PBC Research Programme has been in place for over 3 decades in PBC with a very high proportion of the clinical patient population participating. Feedback from the patient groups, with whom we work very closely, suggests that participation in the research programme, which is highly focused on the aspects of disease which matter most to patients is associated with a high degree of satisfaction. Fatigue with cognitive symptoms, the target of the OACS-2 trial, is the number one patient priority for research because of the nature and scale of its impact. We therefore believe that there will be indirect participant benefit from participating in the programme.

Obeticholic acid is currently licensed for the treatment of PBC in the UK. The treating Clinicians in the study have clinical experience with Obeticholic acid and there is no reason to suspect a different safety profile in treating patients with PBC at an earlier stage of their disease course. However as with any medication there is potential for side effects to occur. Patients will be advised of the known side effects and will be provided with contact details of their local study team should they have any safety concerns. If side effects are reported, participant dosage may be reduced or withheld or they may treated with additional medication until side effects have resolved. Clinicians will refer to the British Society of Gastroenterology/UK-PBC Primary Biliary Cholangitis Treatment and Management Guidelines.

The safety profile of pregnant women taking Obeticholic acid is not known. All participants will be asked to use effective contraception (e.g. barrier/ hormonal/ sterilisation) or to practice sexual abstinence for the entire duration of the treatment period. If a participant were to become pregnant during the course of study, the patient will be withdrawn from study treatment but will be followed up until completion (i.e. termination, miscarriage, stillbirth or live birth). We will also follow up any pregnancies of partners of participants who become pregnant while the participant is on the trial.

Where is the study run from?
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
August 2019 to October 2026

Who is funding the study?
Intercept Pharmaceuticals (UK) and the National Institute for Health Research (UK)

Who is the main contact?
Ana Alvarez Franco, oacstrials@newcastle.ac.uk

Contact information

Type(s)
Public, Scientific

Contact name
Ms Ana Alvarez Franco

Contact details
1-4 Claremont Terrace
Newcastle-Upon-Tyne
United Kingdom
NE2 4AE
+44 (0)191 208 8753
oacstrials@newcastle.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2020-004613-12

Integrated Research Application System (IRAS)
280025

Central Portfolio Management System (CPMS)
49122

Study information

Scientific Title
Obeticholic acid for the Amelioration of Cognitive Symptoms trial- 2

Acronym
OACS-2

Study objectives
To evaluate the effect of Obeticholic Acid (OCALIVA) in patients with a recent diagnosis (<2 years) of Primary Biliary Cholangitis (PBC) who also experience issues with cognitive function around memory and problem-solving.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/04/2021, North East - Tyne & Wear South Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ; +44 (0) 2071048285; tyneandwearsouth.rec@hra.nhs.uk), ref: 21/NE/0084

Primary study design
Interventional

Study design
Multicentre double-blind randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Primary biliary cholangitis (PBC) with cognitive symptoms around memory and problem solving

Interventions

OACS-2 is a multicentre study that will take place in 4 Specialist PBC centres within an NHS setting across the UK.

OACS-2 is looking at obeticholic acid (brand name OCALIVA) in treating patients with recent-onset PBC who experience cognitive symptoms around memory and problem-solving. 25 participants will be randomised to receive either Obeticholic acid or matched placebo.

Potential participants will be screened and if eligible, and willing to take part, they will be asked for their consent to participate in the trial. Trial participants will be randomised to receive either obeticholic acid or placebo. Neither the participant nor the study team will know what treatment allocation participants have received.

As part of the trial, the participant will undertake a number of trial assessments including questionnaires and imaging assessments. The imaging assessments will all take place at Centre for Ageing and Vitality (CAV) at Newcastle upon Tyne Hospitals NHS Foundation Trust (NuTH).

Once written informed consent has been obtained from the patient, screening assessments will take place to assess the patients eligibility for the trial. The screening activities will include:
1. Recording participant demographics, medical history and vital signs
2. Clinical examination of the participant
3. Blood samples will be taken from participant
4. Female participants will undertake a pregnancy test
5. Fibroscan

As soon as the participant is confirmed as eligible, participants will be randomised using the randomisation system to receive either obeticholic acid or matched placebo.

Following randomisation, participants will attend a baseline visit where the participant will complete trial questionnaires (EQ-5D-5L, PBC 40, COGFAIL, HADS, ESS, PSQI).

As part of the baseline visit, participants will also complete CANTAB assessments on an iPad. CANTAB are a series of cognitive assessments completed using an iPad. They will also undergo an MRI scan. The CANTAB assessment and MRI scan will take place at CAV. Some of these participants will be required to travel to Newcastle for their CANTAB and MRI assessments, not all baseline assessments will be carried out on the same day. While completing the baseline activity at Newcastle, if participants have consented to give an optional additional blood sample to be analysed and stored in a biobank on top of their safety blood sample, this will be taken. Study medication will be prescribed by the Clinician at the recruiting centre.

Once a patient has been prescribed their study medication, a telephone call will take place at 2 weeks from start of trial treatment.

Visits will take place at 2 weeks (telephone call), 4 weeks, 12 weeks, 26 weeks, and 30 weeks.

At the 2-week telephone call, study treatment compliance, along with concomitant medications and adverse events will be checked.

Participants will undertake the following activities:
1. Study therapy will be prescribed at the 4 and 12-week visits and study treatment compliance

checked at 4, 12, and 26-week visits
2. Concomitant medication checked at 4, 12, and 26 weeks
3. Adverse events checked at 4, 12, 26, and 30 weeks
4. Clinical examination at 26 weeks
5. Vital signs assessed at 4, 12, 26 and 30 weeks
6. Blood samples taken at 4, 12, 26 and 30 weeks
7. Fibroscan at 26 weeks
8. Questionnaires (EQ-5D-5L, PBC 40, COGFAIL, HADS, ESS, PSQI) at 12, 26, and 30 weeks
9. CANTAB assessments at 26 weeks.
10. MRI at 26 weeks.
11. Optional blood sample for the biobank taken at 26 weeks (at Newcastle CAV)

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Obeticholic acid

Primary outcome(s)
Cognitive function measured using a composite CANTAB score derived from individual scores from four core tests (via the CANTAB cognitive testing platform https://www.cambridgecognition.com/cantab) at baseline and 26 weeks:
1. One Touch Stockings of Cambridge (OTS)
2. Paired Associates Learning (PAL)
3. Rapid Visual Information Processing (RVP)
4. Spatial Working Memory (SWM)

Key secondary outcome(s)
1. Cognitive function measured using scores from the following CANTAB domains (via the CANTAB cognitive testing platform https://www.cambridgecognition.com/cantab) at baseline and 26-weeks:
1.1. Emotion Recognition Task (ERT)
1.2. Multitasking Test (MTT)
1.3. Reaction Time (RTI)
2. Patient self-reported cognitive symptom impact measured using the following at baseline, 12, and 26 weeks:
2.1. PBC-40 Cognitive domain
2.2. COGFAIL tool
3. Patient self-reported PBC symptoms measured using the following at baseline, 12, and 26 weeks:
3.1. PBC-40 Cognitive domain
3.2. Hospital Anxiety and Depression Scale (HADS)
3.3. Epworth Sleepiness Scale (ESS)
3.4. Pittsburgh Sleep Quality Index (PSQI)
4. Patient self-reported quality of life measured using the EuroQol 5-dimension 5-level (EQ-5D-5L) questionnaire at baseline, 12, and 26 weeks
5. Mechanistic brain changes measured using MRI at baseline and 26 weeks:
5.1. Change in diffusion fractional anisotropy (FA) in the Bilateral Forceps Minor white matter

tract measured using Diffusion Tensor Imaging (DTI)
5.2. Change in frontal grey matter T1 relaxation time measured using T1 mapping

Completion date
30/10/2026

Reason abandoned (if study stopped)
Conflicting studies affecting recruitment as of 08/12/2025.

Eligibility

Key inclusion criteria
1. Established diagnosis of PBC based on the presence of 2 out of the 3 key disease characteristics:
1.1. AMA or PBC-specific ANA at a titre of 1/40 or greater
1.2. Elevated alkaline phosphatase (above the upper limit of normal for the relevant laboratory)
1.3. Compatible or diagnostic liver biopsy
2. Diagnosed disease duration of <2 years
3. PBC-40 Cognitive Domain score of ≥12 at screening
4. Stable UDCA dose for 3 months (either at 13-15 mg/kg) or not on UDCA if intolerant
5. Willing to complete the study assessment protocols
6. For participants of childbearing potential: willing to use highly effective contraception or to practice true abstinence to avoid pregnancy for the entire duration of the treatment period
7. Good command of the English language (to ensure that participants are able to comply with cognitive testing)
8. Ability to consent, to comply with the study protocol, and to attend clinic visits
9. Aged ≥18 and ≤65 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
65 Years

Sex
All

Total final enrolment
0

Key exclusion criteria

1. Clinical suspicion of advanced disease evidenced by a history of one or more of the following:
1.1. Ascites requiring diuretic therapy or percutaneous drainage
1.2. Endoscopically confirmed varices
1.3. Liver biopsy suggesting cirrhosis
1.4. Platelet count <150
1.5. Bipolar spleen length >12 cm on ultrasound
1.6. Hepatocellular carcinoma conformed by biopsy or 2 imaging modalities
2. Bilirubin >1.5 x upper limit of normal (ULN)
3. Complete biliary obstruction
4. Fibroscan >17.6 kPa within the year prior to or at screening
5. Inter-current disease characterised by cognitive dysfunction (e.g. dementia or neurodegenerative disease) or clinical suspicion of age-related cognitive decline
6. Inter-current medication characterised by cognitive dysfunction (benzodiazepines, opiates other than codeine phosphate, sleeping pills, anti-psychotic agents, regular daily anti-histamine use in the last four weeks, or recreational drug use).
7. Anticipated change in PBC medication within the duration of the study
8. Contraindications to contrast free MRI assessment (active medical implants such as Cardiac pacemaker or metal implants)
9. Previous exposure to OCA (either in clinical trials or in clinical practice) or Fibrate therapy for ≥3 months and within the last 3 months
10. Regular (more than one week per month) alcohol consumption in excess of recommended safe limits (14 units per week)
11. Active participation in another interventional trial or exposure to another experimental drug within 5 half-lives
12. Pregnancy or planning to get pregnant
13. Clinical diagnosis of AIH overlap
14. Concurrent liver disease of another aetiology
15. Severe pruritus (>11 on PBC-40 pruritus domain)
16. Hypersensitivity to the active substance or to any of the excipients
17. Treating clinician deems the patient is not suitable to participate in the trial based on other criteria apparent during screening or from medical history

Date of first enrolment
31/08/2021

Date of final enrolment
06/03/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Newcastle upon Tyne Hospitals NHS Foundation Trust
1-4 Claremont Terrace
Newcastle upon Tyne

England
NE2 4AE

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Industry

Funder Name
Intercept Pharmaceuticals Inc.

Funder Name
National Institute for Health Research (NIHR) (UK)

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

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