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A two-part study to investigate the effects in adults of two doses of golexanolone in patients with primary biliary cholangitis with fatigue and cognitive dysfunction

Submission date
01/12/2025

Recruitment status
No longer recruiting

Registration date
09/12/2025

Overall study status
Completed

Last Edited
05/10/2026

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
Primary biliary cholangitis (PBC) is a serious chronic liver disease that harms the liver's ability to function. Patients with PBC can experience cognitive dysfunction: inability to think, learn and remember clearly. Also, they experience significant fatigue (tiredness).
The active investigational medicinal product - golexanolone – is a new drug that was developed for the treatment of the spectrum of cognitive dysfunction associated with chronic liver disease. Based on research in animals and patients with cirrhosis, it is assumed that golexanolone may offer normalization of cognitive dysfunction and fatigue in patients with PBC.
The present study has been designed to evaluate how safe and well-tolerated golexanolone is, how golexanolone is absorbed, modified, and removed from the body, and to evaluate the effects of golexanolone on PBC symptoms. The effects of golexanolone will be compared with a placebo (inactive substance).

Who can participate?
Adult patients who are diagnosed with PBC, fatigue and cognitive dysfunction and who meet all the specified criteria for the study, according to the doctor.

What does the study involve?
The study is divided into two parts, Part A and Part B.

In Part A (completed), participants who qualified were randomly assigned in a 3:1 ratio to receive either golexanolone 40 mg or a placebo orally twice daily for 5 days at the clinic.

In Part B, participants who qualify will be randomly assigned in a 1:1:1 ratio to receive either golexanolone 40 mg or golexanolone 80 mg or placebo orally twice daily for 28 days. Previously prescribed PBC therapy will be allowed as long as it is stable during the study.

The total duration of part B for a participant will be a maximum of 8 weeks (± 3 days), with 5 visits to a clinic and 2 phone calls.

The following examinations, tests and procedures are planned to be done during different periods of the study:
- Collection of basic information regarding age, gender, race, and ethnic origin, medical history and PBC treatment history, as well as medications currently being taken, including vitamins and supplements, and any recent changes to medications.
- Physical examination will be done.
- Blood and urine samples will be collected for analysis.
- Questions about their current health condition will be asked.
- Questionnaires about overall health, fatigue, anxiety, mental well-being, sleep, and sleepiness are to be completed. One of the questionnaires, called the Clinical Global Impression Scale, requires a 30-45-minute interview with an independent, qualified clinician who does not belong to the study team. The interview will be conducted at Visit 2 and Visit 6 in the local language as a video call. This interview will be organised by the company working on behalf of the Sponsor, called Signant Health. The study doctor will schedule and organise it for you at the study centre. The clinician will ask questions, make notes, and the interview will be video-recorded. Notes are needed to assess changes in the condition during the second interview and might also be used for quality control. Video recordings will be used by a second independent clinician to make sure that all assessments are made correctly. The second clinician also doesn't belong to the study team.
- Cognitive tests (such as recall words or say words) will be conducted.
- Each participant will be asked to record the date and time of study drug self-administration and recording of changes in medications and medical events occurring between visits in the Participant's Diary.

What are the possible benefits and risks of participating?
There may or may not be direct medical benefits from taking part in this study. Based on research in animals and patients with cirrhosis, it is assumed that golexanolone may offer normalisation of cognitive dysfunction and fatigue in patients with PBC. There is no guarantee, however, that the study drug will have an influence on the disease.
If the participant receives a placebo, there are no medical benefits.

The participation in this study will contribute to increasing information that may help treat patients with PBC and may contribute to improvements in medicine in general.

Where is the study run from?
This study is organised by Umecrine Cognition AB (the "Sponsor" of the study) from Sweden. Hospitals in several countries (the United Kingdom, Germany, Hungary, Italy, Spain, Serbia and Turkey) are involved in the study.

When is the study starting and how long is it expected to run for?
April 2023 to September 2026

Who is funding the study?
Umecrine Cognition AB (Sweden)

Who is the main contact?
Dr David Jones, david.jones@newcastle.ac.uk

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Scientific, Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2024-515907-20-00

Integrated Research Application System (IRAS)
1003871

Central Portfolio Management System (CPMS)
52532

Protocol serial number
UCAB-CT-05

Study information

Scientific Title

A randomised, double-blind, placebo-controlled, two-part study to evaluate the pharmacokinetics, safety and tolerability, and preliminary efficacy of two dose levels of golexanolone in subjects with primary biliary cholangitis, fatigue, and cognitive dysfunction

Study objectives

Part A: Primary objective is to assess the safety and tolerability of treatment with 40 mg golexanolone BID for 5 days in non-cirrhotic or Child-Pugh class A cirrhotic PBC subjects with clinically significant fatigue and cognitive symptoms. Secondary objectives is to assess the PK characteristics of golexanolone administered 40 mg BID for 5 days in the target population, and to investigate the metabolite profile of golexanolone in human plasma and urine.

Part B: The primary objective is to assess the safety and tolerability of 28 days BID treatment with two dose levels of golexanolone in non-cirrhotic or Child-Pugh class A PBC subjects with clinically significant fatigue and cognitive symptoms. Secondary objectives include assessment of: effects of golexanolone on health-related quality of life (HRQoL), including fatigue, effects of golexanolone on day-time sleepiness, effects of golexanolone on cognitive function, evaluation of the Investigator's overall impression of treatment effect, and the exposure of two dose levels of golexanolone in the target population treated for 28 days.

Ethics approval required

Ethics approval required

Ethics approval(s)

1. Approved 12/10/2022, East Midlands – Leicester Central Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 02071048066; leicestercentral.rec@hra.nhs.uk), ref: 22/EM/0196

2. Approved 08/11/2023, CET (Comitato Etico Territoriale [Territorial Ethics Committee]) Lombardia 5 (Via Manzoni 56, Milan, 20089, Italy; 0882247216; comitato.etico@humanitas.it), ref: 25/23

3. Approved 21/04/2023, Hellenic Republic Ministry of Health National Ethics Committee (284 Mesogeion Ave., Cholargos, 155 62, Greece; 213-2040259; eed@eof.gr), ref: 5/23

4. Approved 16/02/2023, Ethics Committee of the Hamburg Medical Association (Weidestraße 122 b, Hamburg, 22083, Germany; 040/202299-240; ethik@aekhh.de), ref: 2022-100928-AMG-ff

5. Approved 28/06/2022, Medical Research Council Ethics Committee for Clinical Pharmacology (ETT-KFEB) (Báthory str. 10, Budapest, 1054, Hungary; (+36 1) 795 1192; kfebtitkarsag@emmi.gov.hu), ref: IV/4297-0/2022-EKL

6. Approved 28/02/2023, Drug Research Ethics Committee (Comité de Ética de Investigacón de Investigación con Medicamentos) (Hospital 12 de Octubre, Avda. de Córdoba, s/n 28041, Madrid, Spain, Madrid, 28041, Spain; +34 91 779 28 39; info.imas12@h12o.es), ref: 22/603

7. Approved 28/03/2023, Ethical Board of Serbia (11221 Belgrade, 458 Vojvode Stepe Str., Belgrade, 458, Serbia; +381113951131; hygia@alims.gov.rs), ref: 515-20-27325-22-003

8. Approved 25/07/2023, Hacetiepe Oniversitesi Klinik Ara~tirmalar Etik Kurulu (06100 Altmdag, Ankara, 06100, Türkiye; 0312 305 34 98; kliniketik@hacettepe.edu.tr), ref: 2023/13-02(KA-22108)

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Treatment

Study type(s)
Efficacy, Safety, Treatment

Health condition(s) or problem(s) studied
Patients with primary biliary cholangitis with fatigue and cognitive dysfunction

Interventions
This is a multicenter interventional randomised, double-blind, placebo-controlled, two-part Phase Ib/2a study

Part A: Subjects are randomised using an online tool to either active treatment for 5 days (40 mg golexanolone bid) or placebo bid for 5 days (randomised 6:2)

Part B: Subjects are randomised using an online tool to either active treatment (40 mg golexanolone bid) or active treatment (80 mg golexanolone bid) or placebo bid for 28 days (randomised 1:1:1)

Intervention Type
Drug

Phase
Phase I/II

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

Primary outcome(s)
Part A:
1. Frequency, intensity, and seriousness of adverse events (AEs) recorded from baseline to Day 5
2. Changes from baseline to Day 5 in safety laboratory parameters (blood samples for analysis of clinical chemistry, haematology, and coagulation parameters, urine dipstick)
3. Changes from baseline to Day 5 in clinical safety parameters:
3.1. Physical examination, including assessments of the lungs, cardiovascular, and abdomen

3.2. Vital signs: systolic and diastolic blood pressure, pulse and body temperature
3.3. Electrocardiogram (12-lead ECG)
3.4. Hospital Anxiety and Depression Scale (HADS), to screen anxious and depressive states

Part B:
1. Frequency, intensity, and seriousness of adverse events (AEs) recorded from baseline to Day 28
2. Changes from baseline to Day 28 in safety laboratory parameters (blood samples for analysis of clinical chemistry, haematology, and coagulation parameters, urine dipstick)
3. Changes from baseline to Day 28 in clinical safety parameters:
3.1. Physical examination, including assessments of the lungs, cardiovascular, and abdomen
3.2. Vital signs: systolic and diastolic blood pressure, pulse and body temperature
3.3. Electrocardiogram (12-lead ECG)
3.4. Hospital Anxiety and Depression Scale (HADS), to screen anxious and depressive states

Key secondary outcome(s)
Part A:
1. The pharmacokinetic (PK) characteristics of golexanolone administered 40 mg BID for 5 days in the target population (baseline to Day 5):
1.1. After the first dose: area under the plasma concentration time curve (AUC) 0-24 h, maximum plasma concentration (Cmax), time to Cmax (Tmax), terminal elimination rate constant (lambdaz), terminal half-life (T1/2), apparent volume of distribution associated with the terminal elimination phase of the plasma curve (Vz/F), total apparent clearance of drug from plasma (Cl/F)
1.2. After the last dose: AUC at steady state (AUCss), Cmax and Cmin at steady state (Cmax, ss and Cmin, ss), Tmax, % fluctuation, lambdaz, T1/2, CL/F, Vz/ F
1.3. Accumulation ratio between first and last dose
2. Metabolite profile in human plasma and urine

Part B:
1. Change from baseline to Day 28 in PBC-40 scores for each of the domains (cognition, itch, fatigue, social, emotional, and general symptoms)
2. Change from baseline to Day 28 in health status measured using EQ-5D-3L
3. Change from baseline to Day 28 in daytime sleepiness related symptoms assessed using the Epworth Sleepiness Scale (ESS)
4. Change from baseline to Day 28 in Portosystemic Hepatic Encephalopathy Score (PHES) total score
5. Change from baseline to Day 28 in Rey Auditory Verbal Learning Test (RAVLT)
6. Change from baseline to Day 28 in Delis and Kaplan Executive Function System (D-KEFS) Letter and Category fluency subtests
7. The Investigator’s overall impression of treatment effect evaluated by Clinical Global Impression of Change, PBC version (CGI-C-PBC) from baseline to Day 28
8. The exposure of two dose levels of golexanolone in the target population treated for 28 days. The lowest plasma concentration before the next dose (Ctrough) assessed pre-dose on Days 1, 14, and 28.

Completion date
30/09/2026

Eligibility

Key inclusion criteria

1. Male and female subjects age ≥18 years
2. Diagnosis of PBC based on the presence of ≥2 of 3 key disease characteristics
3. Clinically significant fatigue defined for the purposes of this study as a PBC-40 fatigue domain score of ≥29 at screening
4. Clinically significant cognitive symptoms, defined for the purposes of this study as a PBC-40 cognitive domain ≥16 at screening
5. Stable PBC SoC therapy (if any),for at least 3 months prior to randomisation
6. For all women of childbearing potential (WOCBP) a negative pregnancy test at screening and a negative urine dip-stick pregnancy test at baseline, prior to first dose of IMP
7. WOCBP must be willing to use a contraceptive method with a failure rate of <1% and agree to continue use of this method for the duration of the study and thereafter for 1 month after the last dosing of the IMP
8. Females of non-childbearing potential must have documented tubal ligation or hysterectomy; or be post-menopausal
9. Fertile male subjects must be willing to use condom and assure that their female partner will use contraceptive methods with a failure rate of <1%
10. Willing and able to give informed consent
11. The subject should be judged by the Investigator to be lucid and oriented to person, place, time, and situation when giving the informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
120 Years

Sex
All

Total final enrolment
207

Key exclusion criteria
1. Child-Pugh class B or C cirrhosis
2. Clinical evidence of hepatic decompensation (e.g. current or prior HE, ascites, or variceal bleeding)
3. History of hepatocellular carcinoma
4. Bilirubin >1.5 x ULN
5. Glomerular filtration rate (GFR) <35 mL/min/1.73m2
6. Low Haemoglobin (HB), i.e. subjects with moderate/severe anaemia
7. Low S-B12 or low P-folate
8. Evidence of biliary obstruction

9. Any positive result on screening for human immunodeficiency virus (HIV), or hepatitis B (serum hepatitis B surface antigen positive)
10. Prolonged QTcF (>500 ms), or any clinically significant abnormality in the resting ECG, as judged by the Investigator (at screening)
11. Concomitant disease characterised by chronic fatigue and/or cognitive impairment
12. Clinically significant bowel disease, including obstruction, active inflammatory bowel disease, or malabsorption
13. Clinically significant sleep apnoea
14. An uncontrolled thyroid disorder
15. Subjects with a history of or currently active immune disorders (i.e. uncontrolled) other that PBC (including autoimmune disease) and/or diseases requiring immunosuppressive drugs
16. Clinical diagnosis of autoimmune hepatitis overlap
17. The presence, as judged by the Investigator, of clinically significant concomitant illness which would jeopardise safe participation in the study and /or the interpretation of study findings
18. Regular use of prescribed or over the counter (OTC) medications known to cause fatigue or cognitive dysfunction
19. Use of prohibited medications within 14 days prior to randomisation
20. Anticipated change in PBC medication and/or significant medical or surgical intervention within the duration of the study
21. Regular (more than 1 week per month) alcohol consumption in excess of 14 units per week
22. Administration of another new chemical entity or has participated in any other clinical study that included drug treatment with the last administration within 3 months prior to administration of IMP in this study
23. Females who are pregnant, nursing or actively trying to conceive a child
24. Expected inability to swallow the required number of IMP capsules at the applicable dose level
25. History of severe allergy/hypersensitivity or on-going allergy/hypersensitivity, as judged by the Investigator

Date of first enrolment
14/04/2023

Date of final enrolment
31/07/2026

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Germany

Greece

Hungary

Italy

Serbia

Spain

Türkiye

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Study participating centre
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Sponsor information

Organisation
Umecrine Cognition AB

Funder(s)

Funder type
Not defined

Funder Name
Umecrine Cognition AB

Results and Publications

Individual participant data (IPD) sharing plan
Study data will be available publicly, through publication in peer reviewed scientific journals, conference presentation and publication on website.

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file			23/09/2026	No	No