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Testing a potential new treatment for patients with severe alcohol-associated hepatitis called SZN-043

Submission date 08/03/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 07/05/2024	**Overall study status** Ongoing	
Last Edited 09/01/2025	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Hepatitis is inflammation of the liver that leads to liver cell damage and cell death. Alcoholic hepatitis is caused by drinking too much alcohol. SZN-043 is being developed to learn how safe and effective this medication is in treating severe alcohol-associated hepatitis (sAH). SZN-043 is being tested in another research study in healthy volunteers and people with liver cirrhosis (scarring of the liver). This is the first time that SZN-043 is being tested in people with sAH.

Who can participate?
Patients aged 18 years and over with severe alcohol-associated hepatitis (sAH)

What does the study involve?
Blood, urine, and tissue samples will be collected, for routine safety and study-related tests. Participants will be assigned to one of three treatment groups. The treatment groups will differ by the number of doses participants will receive and the strength of those doses. Participants may receive either 1 (Day 0), 2 (Days 0 and 4), or 3 (Days 0, 4, and 7) doses of the study medication depending on their treatment group and how the study progresses. The study medication will be administered in the hospital by intravenous infusion (IV) which will take about 30 minutes. Participants will be observed for at least 4 hours after receiving study medication. This research study could be done while participants are in either inpatient or outpatient care. Once participants have completed inpatient treatment, outpatient treatment can occur in a clinic within the hospital or at a similar location. Participants will be required to attend the study visits, including a screening period and dosing days. Some procedures would typically be conducted as a part of normal care, the main difference between regular care and this study is that participants will receive the study medication, additional blood work will be completed, and participants will have study-specific tests to assess liver function, and they will be asked to complete a questionnaire.

What are the possible benefits and risks of participating?
There may be no direct benefit to participants from taking part in this study. Participants may or may not experience improvement in their condition. The information from this research study

may help to develop better treatments for and understanding of severe alcohol-associated hepatitis.
SZN-043 has been generally well tolerated across all the populations and dosing regimens. Out of the 35 people who have received the study medication so far:
Four participants experienced mild to moderate rises in their liver enzymes. These increased levels later returned to normal. Currently, it is not known what the increase in the transaminases means or what is the risk to the liver. Ten participants have developed antibodies to SZN-043 without reporting any symptoms that might be considered related. Six participants experienced mild side effects that occurred when IV SZN-043 was administered, but no one has experienced an infusion reaction. SZN-043 is a protein that is foreign to the body and therefore, participants may experience side effects or unwanted reactions. These reactions could include rashes, shortness of breath, swelling, or changes in blood pressure, however to date, they have not been observed in any participants exposed to SZN 043. The study doctor will monitor participants' liver health very closely in the study. SZN-043 may act as a growth factor for any existing tumours, including liver. The possibility of this happening is very low since participants are checked to make sure they do not have a liver tumour to qualify for this study. SZN-043 is also expected to increase the activity of some liver enzymes that normally process certain medications. To be safe, any usage of medications that may be affected by SZN-043, including paracetamol (or acetaminophen) and chlorzoxazone, will be restricted. There is a chance that participants may experience an allergic reaction to SZN-043. Symptoms of a severe allergic reaction can include itchy rash, tongue or throat swelling, difficulty breathing, and dizziness or collapse. A severe allergic reaction requires immediate medical treatment and could result in permanent disability or death. The Study Doctor will monitor participants for symptoms closely throughout the study. It is not known whether treatment with the study drug poses a risk to an unborn child. Participants who are pregnant or nursing cannot participate in this study. Participants of childbearing potential will be given a pregnancy test before taking part in, and throughout, the study.
There is the risk of slight pain, bruising or infection when blood is drawn. Drawing blood may cause some people to feel light-headed or faint. In rare cases, bloodtaking can lead to swelling or infection of the vein. Participants must fast for at least 8 hours before any scheduled blood sample collection.
Participants will be asked about their symptoms related to their liver disease; some questions might be asked about uncomfortable topics. Participants do not have to answer any questions they do not feel comfortable answering.
The HepQuant SHUNT test is a noninvasive procedure to see how the liver works. Participants must fast 5 hours before this test (no food or liquids); they may drink water. Participants will have a cannula inserted into a vein in their arm to allow for blood sample collection. Participants will then drink an oral cholate solution. Blood samples will be collected from the cannula at 20 minutes and 60 minutes after they have finished the oral solution. This test has not yet been approved for use by regulatory authorities, like the US FDA, and is experimental. There may be unknown risks.
The methacetin breath test is a noninvasive procedure to monitor liver function. Participants will drink a solution containing 13C-methacetin, which can be tracked in the body. 13C-methacetin has no radioactive potential and does not expose participants to any radiation. Participants must fast 8 hours before this test; they may drink water. Participants will first have to breathe into two tubes, one at 10 minutes and one at 5 minutes before they drink the oral solution. Participants will then have to breathe into 1 tube every 10 minutes for up to 60 minutes after they complete the oral solution. This test has not yet been approved for use by regulatory authorities, like the US FDA, and is experimental. There may be unknown risks.
To date, the cholate solution used in this study has not been associated with any allergic reactions or side effects.
Ultrasound uses sound waves to produce an image of tissues within the body; it will be used to

view the liver. Ultrasound is not invasive and does not use radiation. The ultrasound will be completed the same as for standard of care.

Where is the study run from?
Surrozen Netherlands, B.V. (Netherlands)

When is the study starting and how long is it expected to run for?
March 2024 to December 2025

Who is funding the study?
Surrozen Operating, Inc. (Netherlands)

Who is the main contact?
Joshua Koons, CL-0043-1002@surrozen.com

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Additional identifiers

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2022-001608-16

IRAS number
1009585

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CL-0043-1002, IRAS 1009585, CPMS 61157

Study information

Scientific Title
A Phase Ib study evaluating the safety and pharmacokinetics of SZN 043 in participants with severe alcohol-associated hepatitis

Study objectives
The primary objective is to evaluate the safety and tolerability of multiple ascending doses of SZN-043 in participants with severe alcohol-associated hepatitis.

The secondary objects are to:
1. To assess the change from baseline (measuring the difference between a patient's pre-treatment score and their follow-up score) in alcohol-associated hepatitis disease progression within and across cohorts (groups) as measured by Model for End-Stage Liver Disease (MELD), Lille Model for alcohol-associated hepatitis (Lille) score, and mortality
2. To assess the change from baseline in functional measures of liver function within and across cohorts
3. To characterize the pharmacokinetics (the study of how the body interacts with administered substances for the entire duration of exposure) of SZN-043
4. To evaluate immunogenicity (the ability of cells/tissues to provoke an immune response) (measured as anti-drug antibodies [ADAs]) to SZN-043

Ethics approval required

Ethics approval required

Ethics approval(s)
Approved 01/05/2024, London - Brent Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford , London, E20 1JQ, United Kingdom; +44 (0)207 107 8117; brent.rec@hra.nhs.uk), ref: 24/LO/0239

Study design
Open-label non-randomized study

Primary study design
Interventional

Secondary study design
Non randomised study

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
Severe alcohol-associated hepatitis

Interventions
SZN-043 is an RSPO mimetic specifically targeted to hepatocytes through ASGR1 binding. SZN-043 will be administered via intravenous injection. Doses of 0.5 mg/kg, 1.0 mg/kg, and 1.5 mg/kg are planned to be tested in three separate cohorts, in which SZN-043 will be administered twice within 1 week (Day 0, Day 4). Optional cohorts may be included to test other dose levels and frequencies based on a review of the emerging and available data. The maximum exposure will not exceed a dose equivalent of 3.0 mg/kg.

This is an open-label trial. There is no active control group planned to be recruited. Results may be presented in the context of historical data from other studies that are not part of this protocol.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic, Dose response

Phase
Phase I

Drug/device/biological/vaccine name(s)

SZN-043

Primary outcome measure
The safety and tolerability of SZN-043 in participants with severe alcohol-associated hepatitis at the proposed doses, based on the frequency and severity of treatment-emergent adverse events, treatment-emergent serious adverse events, treatment-emergent laboratory, electrocardiogram (ECGs), and physical examination findings from baseline through to 90 days after receipt of treatment (safety is measured continuously)

Secondary outcome measures
1. Change from baseline in alcohol-associated hepatitis disease progression within and across cohorts as measured by Model for End-Stage Liver Disease (MELD), Lille Model for alcohol-associated hepatitis (Lille) score, and mortality. Percent of participants alive measured on Days 28, 60, and 90. Percent and absolute change in MELD score measured from baseline to Days 4, 7, 28, 60, and 90. Lille Score: Percent and absolute change from baseline measured at Days 4 and 7 and percent of participants with Lille score <0.45 measured at Days 4 and 7.
2. The change from baseline in functional measures of liver function within and across cohorts measured as percent and absolute change from baseline in ALT, AST, bilirubin, international normalised ratio, and albumin. Change in measurements from baseline through last observation carried forward on Day 90.
3. The PK of SZN-043 by measurement of PK parameters after multiple doses of SZN-043, as data allow, measured from Day 0 (prior to dose) through Day 35 at various timepoints depending on how many doses were received. This includes one sample prior to dosing, seven timepoints after dosing on the day of dosing, and one sample on up to nine different days after the first dose.
4. The immunogenicity to SZN-043 by measuring the prevalence of antidrug antibodies (ADAs) for SZN-043 at baseline and the incidence of ADA during the study, measured once Pre-Dose and again on Day 14, 28, 60 and 90. If participants are positive for ADA at Day 90, measurements will continue with participant consent every 3 months until they return to baseline or 1 year has passed, whichever comes first.

Overall study start date
05/03/2024

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Be a male or female (sex assigned at birth), 18 years of age or older AND considered to be an adult in accordance with local law
2. Have a BMI between ≥18.0 and ≤36.0 kg/m2 at Screening
3. Be willing and able to provide written informed consent
4. Have a clinical diagnosis of Alcohol-associated hepatitis (AH) that is anticipated to require inpatient care for a period to encompass at a minimum the first dose of study medication based on typical serum chemistry (as determined by local laboratory) meeting all of the following parameters:
4.1. Onset of jaundice within the prior 8 weeks
4.2. History of heavy alcohol abuse: >40 (female) or 60 (male) g alcohol/day for ≥6 months
4.3. Consumed alcohol within 8 weeks before study entry

4.4. AST >50, AST/ALT >1.5, and both values are: <400 IU/L, and
4.5. Serum total bilirubin >3.0 mg/dL
At the Investigator's discretion, a liver biopsy may be performed to confirm diagnosis in participants who meet criteria a-c above but where other causes of liver disease are not otherwise possible to rule out (viral, drug, autoimmune, etc)
5. MELD score of 21 to 30, inclusive
6. Acceptable methods of contraception defined in protocol Section 4.2.3 must be used from Screening until study completion. Surgically sterile males or females (Section 4.2.3) or women who are postmenopausal for ≥12 months do not need additional contraception methods. Postmenopausal status will be confirmed by testing follicle-stimulating hormone (FSH) levels ≥40 IU/L at Screening for amenorrhoeic female participants.
7. Must have the ability and willingness to attend the necessary visits to the study centre.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
18

Key exclusion criteria
1. Previous receipt of antibody or biologic therapy whether licensed or investigational within the past 6 months.
2. Treatment with any experimental drug within 30 days, or within 5 half-lives (whichever is longer), before Day 0 visit (Baseline).
3. Other causes of liver disease including:
3.1. Evidence of chronic viral hepatitis (hepatitis B or C)
3.2. Biliary obstruction or cholestatic liver disease (e.g., primary biliary sclerosis, sclerosing cholangitis)
3.3. Drug-induced hepatotoxicity (e.g., acetaminophen)
3.4. Hepatocellular carcinoma
3.5. Wilson’s disease
3.6. Budd Chiari Syndrome
3.7. Metabolic dysfunction-associated steatotic liver disease
3.8. Metabolic dysfunction-associated steatohepatitis
3.9. Auto-immune hepatitis
3.10. Acute hepatitis A.
4. Introduction of a new medication with potential hepatotoxicity within 60 days of screening or any anticipated increase in dose or dose regimen of any potential hepatotoxic medication.
5. Have a portosystemic shunt or scheduled for transjugular intrahepatic portosystemic shunt placement or highly likely to receive a liver transplant during the study period.
6. Dependent upon inotropic support or ventilatory or vasopressor support.
7. Organ failure: renal replacement therapy or creatinine >2.5 mg/dL (or 221 mmol/L

Uncontrolled hyperthyroidism, history of Paget's disease, osteomalacia, or fracture within 4 weeks of Screening.
9. Uncontrolled bacterial infections, after a minimum of 2 days of antibiotic therapy.
10. History of a previous severe allergic reaction with generalised urticaria, angioedema, or anaphylaxis.
11. A QT duration corrected for heart rate by Fridericia's formula (QTcF) >450 msec for males and >470 msec for females based on either single or averaged QTcF values of triplicate ECGs before study drug administration.
12. A history of malignant neoplasm, except for adequately treated non-metastatic basal or squamous cell cancers of the skin (>1 year ago) or carcinoma in situ of the uterine cervix (>3 years ago) that has been fully treated and shows no evidence of recurrence. Participants under evaluation for possible malignancy are also not eligible.
13. Gastrointestinal (GI) bleeding within 2 days of Screening requiring transfusion of more than 3 units of blood (participants with a recent upper gastrointestinal bleeding that is controlled for >48 h is allowed).
14. Grade 3 or higher encephalopathy by West Haven Criteria.
15. Acute kidney injury defined as an increase in serum creatinine (sCr) ≥0.3 mg/dL within 48 h or an increase in sCr ≥50% from baseline known or presumed (Baseline sCr: a value of sCr obtained in the previous 3 months, closest to admission; if no previous sCr value, the sCr on admission is baseline), within the prior 7 days or the requirement for renal replacement therapy.
16. Presence of portal vein thrombosis.
17. Presence of acute pancreatitis.
18. Cerebral hemorrhage, extensive retinal hemorrhage, acute myocardial infarction (within the last 6 weeks) or severe cardiac arrhythmias (not including atrial fibrillation).
19. Evidence of GI bleeding or renal failure after 7 days of treatment within 8 weeks of screening.
20. Liver imaging at screening showing any lesions (except benign lesions, i.e., hemangiomas).
21. Known infection with HIV or HIV Ab positive at screening.
22. Organ transplantation (such as liver, kidney, lung, heart, bone marrow, or stem cell etc.), other than cornea transplant.
23. Positive urine screen for amphetamines, cocaine, or opiates (i.e., heroin, morphine) at Screening. Participants receiving stable methadone or buprenorphine maintenance treatment for at least 6 months before Screening may be included in the study. Participants with positive cannabis drug screen may be included in the study. Participants with a positive urine drug screen due to prescription opioid-based medication are eligible if the prescription and diagnosis are reviewed and approved by the Investigator.
24. Pregnant or lactating at Screening or planning to become pregnant (self or partner) at any time during the study.
25. Planning to donate sperm (male) or ovum (female) within 90 days after the last dose of the study drug.
26. Prior or ongoing medical conditions, medical history, concomitant medication, physical findings, or laboratory abnormality that could adversely affect the safety of the participant.
27. Current use of anticoagulants that affect prothrombin time or international normalised ratio (INR).
28. Eligibility: All participants where HepQuant SHUNT test kit use is specified:
28.1. Extensive resection of large segments of small intestine or severe gastroparesis; On either a non-selective beta blocker or an angiotensin-converting enzyme inhibitor or angiotensin II receptor blockers who are unwilling or unable to delay taking their normal dose the morning of the HepQuant SHUNT test.
28.2. Allergy to any ingredient in the formulations or components in the HepQuant

Date of first enrolment

23/05/2024

Date of final enrolment
30/09/2025

Locations

Countries of recruitment
Australia

Canada

England

Korea, South

New Zealand

United Kingdom

Study participating centre
Kings College Hospital
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Study participating centre
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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Surrozen Operating, Inc.

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Publication on website
3. Other publication
4. Submission to regulatory authorities

Participants' records from the study are confidential unless law requires certain people to see them, such as the sponsor or representatives, monitors, auditors and regulatory agencies. Participants will be informed about this in the Patient Information Sheet and consent will be obtained. Participants will be allocated a participant number once they have signed the informed consent form. Anonymised data may be sent to the regulatory bodies, and collaborators within the pharmaceutical industry.

Intention to publish date
31/12/2026

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be published as a supplement to the results publication

IPD sharing plan summary

Published as a supplement to the results publication