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ECUR-506 in Neonatal OTC Deficiency Phase I/II

Submission date 16/09/2023	**Recruitment status** Recruiting	[_] 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 11/09/2025	**Condition category** Genetic Diseases	

Plain English summary of protocol

Background and study aims
The purpose of this study is to look at how safe and how well one of two dose levels of a new investigational gene editing drug, ECUR-506, works for the treatment of neonatal onset (within the first four weeks of an infant's life) Ornithine Transcarbamylase Deficiency (OTC Deficiency). Gene editing means that a corrective gene which can produce a working OTC enzyme is introduced into DNA.
Neonatal Onset OTC Deficiency is a rare genetic condition that causes a damaging substance, called ammonia, to build up in the blood because the enzyme, OTC, is missing from a child's body. It is more common in boys.
Currently there is no approved medication that cures OTC Deficiency and a liver transplant is considered the only treatment that can cure the disease. Therefore, there is an urgent need for research into new treatment options for OTC Deficiency.

Who can participate?
Approximately 9 boys, up to 9 months old, who have been diagnosed with OTC Deficiency will be dosed with one of two dose levels in this study. The study is being conducted at several hospitals globally.

What does the study involve?
There are 28 study visits over a period up to 42 weeks. Study drug will be given as an intravenous infusion (via a tube linked to a small needle in the child’s vein) over a period of approximately 1 to 2 hours. Study procedures include measurements such as blood pressure and weight, electrocardiogram, liver biopsy, ultrasound, blood test, tests on urine, faeces and questionnaires for parents/carers.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
Other AAVs (adeno-associated virus - not this study drug) used to deliver gene therapies have been evaluated in many prior clinical studies. The safety risks related to AAV gene therapy that have been reported include elevation in liver enzymes (inflammation or damage to the cells in the liver), thrombocytopenia (low platelet count), and cardiomyopathy (damage to the heart muscle). AAV treatment may also be associated with an immune response which may lead to the

need for a liver biopsy to be completed.
Other potential risks related to AAV used for gene therapy are noted below, and may include:
• Cancer: The tests performed in mice and non-human primates suggest AAV vectors carry little to no risk of causing cancer.
• Genetic Changes: The risk of "off-target" genetic changes (changes to DNA that are not the target of the study drug) and unintended consequences of on- and off-target editing of the child's DNA is unknown at this time.
• Future Reproduction: AAV gene therapy is also associated with the risk of transfer of introduced genetic material in semen to the offspring of the treated participant. Prior clinical studies have demonstrated that genetic material carried by AAV can be detected in seminal fluid, but not in the sperm portion capable of passing to offspring.
• Viral Shedding (Study Drug): Viral shedding in bodily waste (urine and stool) has been extensively assessed in previous clinical studies with other similar gene edited products and has consistently shown that other viral products were not detectable in patients after 40 days after dosing. Viral shedding will be extensively measured in this study.
• Nerve Damage: The risk for nerve damage, which is a neurologic side effect, following study drug administration is unknown at this time but considered to be low.
There are also possible risks and discomforts that the child may experience from the procedures during the study. These include:
• Infusion Reaction: If observed, the study team will treat the symptoms as needed.
• Infection, Inflammation, and Bruising at injection site: If observed, the study team will treat the symptoms as needed. If an infection at the injection site occurs, the study team will speak with the parent/carer about the best treatment option for the child.
• Blood draw volumes and frequency: The risk of blood drawing includes discomfort at the site of the blood draw with bruising, bleeding, infection, and rarely, fainting or nerve damage.
• Electrocardiogram (ECG): ECG patches placed on the child’s skin may cause itching, redness, or mild rash. It may be necessary to shave the area on the child’s chest for placement of the ECG patches directly on the child’s skin.
• Liver Biopsy: Bleeding and/or discharge at the site of the biopsy (that in rare cases may be extensive), pain, infection, damage to the organ from which biopsy was taken and/or nearby organs. The child’s study doctor will discuss specific risks of a biopsy related to the child’s procedure.
• Sedation: The risks of sedation include an allergic reaction, aspiration (fluid going into the lungs), and over-sedation. In addition, the IV used may cause a bruise. Occasionally, an infection develops at the IV site.
• Quality of Life and Bayley assessments: The parent/carer will be asked to a complete questionnaire(s) about the child's development, and quality of life. For the Bayley scale the child will actively participate in assessments that involve movement but should not cause any stress for the child. If there are any signs of stress or fatigue, the study team will provide a plan to complete the assessment at a better suited time during the visit.
There may be other side effects of the study drug that are not yet known. Side effects may go away after the treatment. It is also possible that the side effects may last a long time or may never go away. They may range from mild to life threatening and/or fatal.
The child will be closely monitored for early signs of any possible side effect(s).Parents/carers will be instructed to tell the study doctor right away about any changes in their child’s health during their participation in this study. The study doctor may give the child treatments to help control side effects.

Where is the study run from?
Fortrea Development Ltd (UK)

When is the study starting and how long is it expected to run for?
September 2023 to December 2025

Who is funding the study?
iECURE, Inc. (USA)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1008261

ClinicalTrials.gov number
NCT06255782

Secondary identifying numbers
ECUR-506-OTC-101, IRAS 1008261, CPMS 57410

Study information

Scientific Title
A Phase I/II/III first-in-human, open-label, dose-escalation study to evaluate the safety and efficacy of a single intravenous (IV) administration of ECUR-506 in males less than 9 months of age with genetically confirmed neonatal onset ornithine transcarbamylase (OTC) deficiency

Study objectives
Primary objective:
To assess the safety and tolerability of up to two dose levels of ECUR-506 following IV administration of a single dose.

Secondary objective:
To assess the pharmacokinetics and efficacy of up to two dose levels of ECUR-506 following IV administration of a single dose.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 07/12/2023, London - West London & GTAC Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8098; westlondon.rec@hra.nhs.uk), ref: 23/LO/0846

Study design
Interventional non randomized

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

Participant information sheet

Health condition(s) or problem(s) studied
Ornithine Transcarbamylase (OTC) Deficiency

Interventions
Cohort 1 - Participants will receive the Low Dose of ECUR-506 delivered one time via IV Infusion.
Cohort 2 - Participants will receive the High Dose of ECUR-506 delivered one time via IV infusion
Expansion Cohort - Participants will receive ECUR-506 at one of the doses evaluated in Cohort 1 or Cohort 2 one time via IV infusion.

Intervention Type
Drug

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

Phase
Phase II

Drug/device/biological/vaccine name(s)
ECUR-506

Primary outcome measure
1. Treatment-emergent adverse events (incidence, severity, seriousness, and relatedness)

The following will be assessed as change from last value available pre-dose at pre-specified timepoints as described in the Schedule of Events throughout the duration of the study:
2. Physical exam parameters
3. Vital signs
4. Neurologic exam parameters
5. Blood safety tests including hematology, serum chemistry, liver function tests, coagulation tests
6. Urinalysis evaluations
7. ECG parameters

Secondary outcome measures
1. Percent liver transduction at Week 24
2. Number of HAC (defined as ammonia levels > 100 µmol/L and neurological status
3. changes) from Day 1 post dose through Week 24, overall and by severity
4. Vector PK in blood and shedding in urine and feces at all scheduled time points from Day1 post dose through Week 24
5. Scavenger drug dose per BSA from Day 1 post dose through Week 24
6. Protein allowance (gm/kg) from Day 1 post dose through Week 24
7. Blood urea nitrogen at all scheduled time points from Day 1 post dose through Week 24

Overall study start date
13/09/2023

Completion date
31/12/2025

Eligibility

Key inclusion criteria

1. Male sex
2. Gestational age ≥ 37 weeks
3. Age at screening is 24 hours to 7 months
4. Genetically confirmed OTC deficiency (OTCD). Documented analysis either through prenatal testing or post-birth genetic testing. Note: a prenatal testing diagnosis will be confirmed post-birth and prior to dosing.
5. Severe neonatal OTCD defined by the following:
5.1. Current or past hyperammonemic crisis (which includes but is not limited to: severely elevated [>8 x ULN] ammonia levels, lethargy, poor feeding, coma, seizure) within first week of life
OR
5.2. Family history and genetic confirmation of pathogenic or likely pathogenic variant consistent with severe OTCD, or has same genetic mutation as previous family member who had severe disease with neonatal onset within first week of life
AND
5.3. Currently receiving treatment (e.g., dietary and scavenger therapy)
6. In participants not prenatally diagnosed, current or historical (within 2 weeks prior to Screening) biochemical profile consistent with OTCD: below LLN of plasma citrulline/arginine and urine orotic aciduria at time of diagnosis
7. Participant's parents/legally authorized representative must be able to comprehend and be willing to provide a signed IRB/IEC-approved ICF which will include consent for participation in this 24 week protocol with immediate roll-over into the 14.5 year long term follow-up (ECUR-LTFU) study.

Participant type(s)
Patient

Age group
Neonate

Lower age limit
1 Days

Upper age limit
7 Months

Sex
Male

Target number of participants
13

Key exclusion criteria
1. Neonatal diagnosis of severe to profound Hypoxic Ischemic Encephalopathy (based on standard HIE metrics) due to birth injury
2. Requiring urgent liver transplant due to liver failure as assessed by the PI.
3. Contiguous gene deletion involving the OTC gene
4. Known or suspected major organ injury/dysfunction/anomalies (brain, heart, liver, kidneys) other than what is consistent with OTCD, based on routine medical assessments performed as part of standard of care
5. Treatment with any other gene therapy or gene editing therapy

6. Co-enrollment in any other clinical study with an investigational product prior to or during the duration of this protocol would require the participant to be withdrawn from this study
7. Any condition, that in the opinion of the Investigator, would compromise the safety of the participant or study data
8. Documented vertical transmission of HSV, HIV, or HepA/HepB/HepC
9. Documented in-utero teratogen, substance, and/or alcohol exposure, which in the opinion of the Investigator may increase the participant's risk of developmental delays, congenital anomalies, and/or significant medical complications

Date of first enrolment
15/04/2024

Date of final enrolment
23/03/2027

Locations

Countries of recruitment
Australia

England

Spain

Türkiye

United Kingdom

Study participating centre
Great Ormond Street Hospital for Children
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Sponsor information

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
iECURE, Inc.

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Conference presentation
Publication on website
Other publication
Submission to regulatory authorities
Summary of study results will be posted on Clintrials.gov

Intention to publish date
31/12/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available.

IPD sharing plan summary
Not expected to be made available