Phase 2 Placebo-Controlled, Double-Blind, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of DCR-PHXC Solution for Injection (subcutaneous use) in Patients with Primary Hyperoxaluria

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Main Information

Primary registry identifying number
LBCTR2020043435

Protocol number
DCR-PHXC-201

MOH registration number

Study registered at the country of origin
No

Study registered at the country of origin: Specify
Study registered in clinicaltrials.gov

Type of registration
Prospective

Type of registration: Justify
N/A

Date of registration in national regulatory agency
15/02/2019

Primary sponsor
Dicerna Pharmaceuticals, Inc

Primary sponsor: Country of origin
US

Date of registration in primary registry
27/04/2020

Date of registration in national regulatory agency
15/02/2019

Public title
Phase 2 Placebo-Controlled, Double-Blind, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of DCR-PHXC Solution for Injection (subcutaneous use) in Patients with Primary Hyperoxaluria

Acronym

Scientific title
Phase 2 Placebo-Controlled, Double-Blind, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of DCR-PHXC Solution for Injection (subcutaneous use) in Patients with Primary Hyperoxaluria

Acronym
PHYOX2

Brief summary of the study: English
This is a 6-month randomized, placebo-controlled, double-blind study of DCR-PHXC in patients with primary hyperoxaluria (PH1 and PH2). Potential participants are screened over an up-to- 6-week period prior to randomization to DCR-PHXC or placebo. The proposed study is designed to evaluate the efficacy, safety, tolerability, and PK of DCR-PHXC versus placebo in patients with PH1 and PH2.

Brief summary of the study: Arabic
دراسة مدتها 6 أشهر ، في المرحلة الثانية، متعددة المراكز ومزدوجة التعمية، محكومة بدواء وهمي لتقييم فعالية و سلامة محلول الحقن DCR-PHXC (تحت الجلد) ودرجة تحمله لدى المرضى الذين يعانون من فرط أوكسالات البول الأولي

Health conditions/problem studied: Specify
DCR-PHXC is designed to selectively reduce LDHA messenger ribonucleic acid (mRNA) and lactate dehydrogenase (LDH) activity in the liver, and subsequently decrease liver oxalate production. DCR-PHXC is being developed as a treatment for PH, an ultra-rare autosomal recessive

disease characterized by excessive production of oxalate in the liver.

Interventions: Specify

DCR-PHXC is a synthetic RNAi drug that consists of a double-stranded oligonucleotide conjugated to GalNAc ligands. DCR-PHXC is a sterile formulation of drug substance (DCR-L1360) in WFI, intended for SC administration.
DCR-PHXC is not commercially available in any country. The placebo comparator is 0.9% normal saline for injection.

Key inclusion and exclusion criteria: Inclusion criteria

• 24-hour Uox excretion ≥ 0.7 mmol (adjusted per 1.73 m2 body surface area [BSA] in participants < 18 years of age) in both collections performed in the screening period. Of the first 24 participants enrolled, at least 12 (50%) must have at least one 24-hour Uox excretion ≥ 1.6 mmol (adjusted per 1.73 m2 BSA in participants aged < 18 years).
• Less than 20% variation between the two 24-hour urinary creatinine excretion values [mmol/24 hr/kg] derived from the two 24-hour urine collections in the screening period.
• Estimated glomerular filtration rate (eGFR) at screening ≥ 30 mL/min normalized to 1.73 m2 BSA calculated using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula in participants aged ≥ 18 years (Levey & Stevens, 2010), or the formula by Schwartz in participants aged 6 to 17 years, (Schwartz et al., 2009; National Kidney Foundation, 2002). In Japan, the formula by Uemura et al. will be used for
participants aged 6 to 17 years.

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

6

Key inclusion and exclusion criteria: Age maximum

99

Key inclusion and exclusion criteria: Exclusion criteria

• Renal or hepatic transplantation (prior or planned within the study period)
• Current dialysis or anticipated requirement for dialysis during the study period
• Plasma oxalate > 30 µmol/L
• Documented evidence of clinical manifestations of systemic oxalosis (including preexisting retinal, heart, or skin calcifications, or history of severe bone pain, pathological fractures, or bone deformations)
• Liver function test (LFT) abnormalities: Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) >1.5 times upper limit of normal (ULN) for age and gender.

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Other

Trial scope: Specify scope

Study design: Allocation

Randomized controlled trial

Study design: Masking

Blinded (masking used)

Study design: Control

Placebo

Study phase

2

Study design: Purpose

Treatment

Study design: Specify purpose

N/A

Study design: Assignment

Parallel

Study design: Specify assignment

N/A

IMP has market authorization

No

IMP has market authorization: Specify

Name of IMP

DCR-PHXC

Year of authorization

2020

Month of authorization

1

Type of IMP

Others

Pharmaceutical class

Synthetic double-stranded (hybridized duplex) RNA oligonucleotide conjugated to GalNAc .

Therapeutic indication

DCR-PHXC is designed to selectively reduce LDHA messenger ribonucleic acid (mRNA) and lactate dehydrogenase (LDH) activity in the liver, and subsequently decrease liver oxalate production. DCR-PHXC is being developed as a treatment for PH, an ultra-rare autosomal recessive disease characterized by excessive production of oxalate in the liver.

Therapeutic benefit

Patients with PH are predisposed to the development of multiple and recurrent urinary tract (urolithiasis) and kidney (nephrolithiasis) stones. This deposition of calcium oxalate in the renal parenchyma produces tubular toxicity and renal damage. At present, no therapies are approved by regulatory authorities for the treatment of patients with PH. A number of supportive therapies are used in an attempt to mitigate some of the effects of the disease.
DCR-PHXC treatment has the potential benefit to reduce or eliminate the excess oxalate production in the liver and thus avoid the need for a combined liver and kidney transplantation in patients not already on renal replacement therapy.

Study model

N/A

Study model: Explain model

N/A

Study model: Specify model

N/A

Time perspective

N/A

Time perspective: Explain time perspective

N/A

Time perspective: Specify perspective

N/A

Target follow-up duration

Target follow-up duration: Unit

Number of groups/cohorts

Biospecimen retention

Samples with DNA**

Biospecimen description

Samples may be stored for a maximum of 5years (or according to local regulations) following the last participant's last visit for the study at a facility selected by the sponsor to enable further analysis of immune responses to DCR-PHXC.

Target sample size

36

Actual enrollment target size

Date of first enrollment: Type

Actual

Date of first enrollment: Date

28/10/2019

Date of study closure: Type

Actual

Date of study closure: Date

30/01/2021

Recruitment status

Recruiting

Recruitment status: Specify

Date of completion

IPD sharing statement plan

No

IPD sharing statement description

Participants will be assigned a unique identifier by the Sponsor. Any participant records or data sets that are transferred to the Sponsor will contain the identifier only; participant names or any information which would make the participant identifiable will not be transferred

Additional data URL

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
1.US NCT	NCT03847909
2.WHO Universal	U1111-1224-6881

Sources of Monetary or Material Support

Name
Dicerna pharmaceuticals inc. 87 Cambridgepark Drive Cambridge, MA 02140 US

Secondary Sponsors

Name
N/A

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Chadi Safa	Beirut	Lebanon	009617125 1819	chadi.safa@clinart.net	Clinart Mena
Scientific	Chebl Mourani	Beirut	Lebanon	009611290 090	cheblmourani@gmail.com	Hotel Dieu de France

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hotel Dieu De France	Chebl Mourani	Pediatric Nephrology	Approved
Saint George University Hospital	Pauline Abou Jaoude	Pediatric Nephrology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Hotel Dieu de France	01/10/2019	Nancy Alam	nancy.alam@usj.edu.lb	01421000
Saint George Hospital University Medical Center	29/11/2019	Sandra Berberi	smberbari@stgeorgehospital.org	01 1 44 16 30

Countries of Recruitment

Name
Australia
Canada
France
Germany
Italy
Japan
Netherlands
New Zealand
Poland
Romania
Spain
United Kingdom
United States of America
Lebanon

Health Conditions or Problems Studied

Condition	Code	Keyword
Primary Hyperoxaluria	Nephrotic syndrome, other (N04.8)	PHYOX

Interventions

Intervention	Description	Keyword
DCR-PHXC	DCR-PHXC is a synthetic RNAi drug that consists of a double-stranded oligonucleotide conjugated to GalNAc ligands. DCR-PHXC is a sterile formulation of drug substance (DCR-L1360) in WFI, intended for SC administration. DCR-PHXC is not commercially available in any country.	DCR-PHXC
Placebo	The placebo comparator is 0.9% normal saline for injection.	Placebo

Primary Outcomes

Name	Time Points	Measure
To assess the efficacy of DCR-PHXC in reducing urinary oxalate burden in patients with PH (types 1 and 2)	The proportion of participants with a reduction from baseline in 24-hour Uox of at least 70%, based on a TWS AUC and/or reaching normalization or near-normalization of 24-hour Uox on at least 2 consecutive visits, starting from Day 90. Normalization of Uox is defined as < 0.46 mmol/24 hours; near-normalization is defined as ≥ 0.46 to < 0.60 mmol/24 hours (values adjusted per 1.73 m2 BSA in participants aged < 18 years).	24-hour Uox

Key Secondary Outcomes

Name	Time Points	Measure
To evaluate the effect of DCR-PHXC on stone burden in patients with PH	Percent change in the summed surface area and number of kidney stones identified via kidney ultrasound from Baseline to Day 180	Number of Kidney stone
To evaluate the effect of DCR-PHXC on plasma oxalate in patients with PH	Percent change in plasma oxalate from Baseline to Day 180 (for adults only)	Plasma Oxalate
To evaluate the effect of DCR-PHXC on eGFR	Rate of change in eGFR from Baseline to Day 180	eGFR
To assess the safety of DCR-PHXC in patients with PH	AE and SAE; change from Baseline in 12-lead ECG, physical examination findings, vital signs, and clinical laboratory tests	12 Lead ECG, Physical Examination test, Vital signs, Clinical Laboratory test.
To characterize the PK of DCR-PHXC in patients with PH	Population and individual PK parameters for DCR-PHXC	PK

Trial Results

Summary results

Study results globally

Date of posting of results summaries

Date of first journal publication of results

Results URL link

Baseline characteristics

Participant flow

Adverse events

Outcome measures

URL to protocol files