



# A Phase 2 Open-Label Multicenter Study to Evaluate the Safety, Pharmacokinetics, and Efficacy of Nedosiran in Pediatric Patients from Birth to 5 Years of Age with Primary Hyperoxaluria and Relatively Intact Renal Function

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## Main Information

**Primary registry identifying number**

LBCTR2021104866

**Protocol number**

DCR-PHXC-203

**MOH registration number**

**Study registered at the country of origin**

Yes

**Study registered at the country of origin: Specify**

**Type of registration**

Prospective

**Type of registration: Justify**

N/A

**Date of registration in national regulatory agency**

04/11/2019

**Primary sponsor**

Dicerna Pharmaceuticals

**Primary sponsor: Country of origin**

United States of America

**Date of registration in primary registry**

27/01/2022

**Date of registration in national regulatory agency**

04/11/2019

**Public title**

A Phase 2 Open-Label Multicenter Study to Evaluate the Safety, Pharmacokinetics, and Efficacy of Nedosiran in Pediatric Patients from Birth to 5 Years of Age with Primary Hyperoxaluria and Relatively Intact Renal Function

**Acronym**

**Scientific title**

A Phase 2 Open-Label Multicenter Study to Evaluate the Safety, Pharmacokinetics, and Efficacy of Nedosiran in Pediatric Patients from Birth to 5 Years of Age with Primary Hyperoxaluria and Relatively Intact Renal Function

**Acronym**

**Brief summary of the study: English**

This is a Phase 2, multi-dose (3.5 mg/kg), open-label, single-arm, uncontrolled, multicenter study of nedosiran in pediatric participants (birth to 5 years of age) with genetically confirmed PH type 1 (PH1), type 2 (PH2), or type 3 (PH3) with relatively intact renal function based upon eGFR and serum creatinine.

Participants will receive monthly SC doses (3.5 mg/kg) of nedosiran over 6 months.

The primary objective of this study is to characterize the safety of nedosiran in pediatric participants (birth to 5 years of age) with PH1, PH2, and PH3. The secondary objective of this study is to characterize the efficacy of nedosiran in pediatric participants (birth to 5 years of age) with PH1, PH2, and PH3. The efficacy of nedosiran in lowering Uox will be assessed via monthly spot urine samples.

Participants completing this study may be eligible for long-term treatment with nedosiran in Study DCR-PHXC-301.





### Brief summary of the study: Arabic

مجم / كجم) ، علامة مفتوحة ، ذراع واحدة ، غير خاضعة للرقابة ، دراسة متعددة المراكز عن 3.5 ، جرعات متعددة (2 هذه مرحلة PH 2النوع ، (PH1) 1 مؤكداً وراثياً من النوع PH سنوات) مع نوع 5 في المشاركين في طب الأطفال (من الولادة حتى سن nedosiran وكرياتينين المصل (eGFR) مع وظيفة كلوية سليمة نسبياً على أساس معدل الترشيح الكبيبي (PH3) أو النوع ، (PH2) أشهر 6 على مدى nedosiran مجم / كجم) من 3.5 SC سيحصل المشاركون على جرعات شهرية من PH1 و سنوات من العمر) مع 5 عند الأطفال المشاركين (من الولادة إلى nedosiran الهدف الأساسي من هذه الدراسة هو توصيف سلامة سنوات من العمر) مع 5 في الأطفال المشاركين (من الولادة إلى nedosiran الهدف الثانوي لهذه الدراسة هو توصيف فعالية PH3 و PH2 من خلال عينات البول الموسمية الشهرية Uox في خفض nedosiran سيتم تقييم فعالية PH3 و PH2 و PH1 DCR-PHXC-301 في دراسة nedosiran قد يكون المشاركون الذين أكملوا هذه الدراسة مؤهلين للعلاج طويل الأمد باستخدام

### Health conditions/problem studied: Specify

Primary Hyperoxaluria Type 1, 2 & 3.

### Interventions: Specify

monthly SC doses (3.5 mg/kg) of nedosiran over 6 months.

### Key inclusion and exclusion criteria: Inclusion criteria

Key inclusion criteria include

- Estimated glomerular filtration rate (eGFR) at Screening  $\geq 30$  mL/min normalized to 1.73 m<sup>2</sup> body surface area (BSA).
- Average spot Uox-to-creatinine ratio at Screening above 2 times the 95th percentile for age based on Matos et al, 1999:
  - o  $> 0.44$  mol/mol in participants  $< 6$  months
  - o  $> 0.34$  mol/mol in participants from 6 months to  $< 12$  months
  - o  $> 0.26$  mol/mol in participants 12 months to  $< 2$  years
  - o  $> 0.20$  mol/mol in participants from 2 to  $< 3$  years and
  - o  $> 0.16$  mol/mol in participants from 3 to 5 years

### Key inclusion and exclusion criteria: Gender

Both

### Key inclusion and exclusion criteria: Specify gender

### Key inclusion and exclusion criteria: Age minimum

0

### Key inclusion and exclusion criteria: Age maximum

5

### Key inclusion and exclusion criteria: Exclusion criteria

Key exclusion criteria include

- Renal or hepatic transplantation (prior or planned within the study period)
- Plasma oxalate (Pox)  $> 30$   $\mu\text{mol/L}$  at Screening
- Documented evidence of clinical manifestations of severe systemic oxalosis (including preexisting retinal, heart, or skin calcifications, or history of severe bone pain, pathological fractures, or bone deformations)

### Type of study

Interventional

### Type of intervention

Pharmaceutical

### Type of intervention: Specify type

N/A

### Trial scope

Safety

### Trial scope: Specify scope

N/A

### Study design: Allocation

Single Arm Study

### Study design: Masking

Open (masking not used)

### Study design: Control

Dose comparison

### Study phase

2

### Study design: Purpose

Treatment

### Study design: Specify purpose

N/A

### Study design: Assignment

Single

### Study design: Specify assignment

N/A

### IMP has market authorization

### IMP has market authorization: Specify



No

**Name of IMP**

Nedosiran

**Year of authorization**

**Month of authorization**

**Type of IMP**

Others

**Pharmaceutical class**

DCR-PHXC consists of the drug substance (DCR-L1360) in WFI) DCR-L1360 is a synthetic double-stranded (hybridized duplex) RNA oligonucleotide conjugated to GalNAc aminosugar residues. After SC administration, the GalNAc sugars conjugated to the RNA oligonucleotide bind to asialoglycoprotein receptors (ASGR) to deliver DCR-L1360 to hepatocytes.

**Therapeutic indication**

DCR-PHXC (Nedosiran sodium) reduces the level of mRNA encoding the dominant form of the LDH enzyme, specifically, the LDHA isoenzyme. Lactate dehydrogenase catalyzes the cytosolic conversion of glyoxylate to oxalate in the liver and this biochemical reaction is believed to be critical for oxalate generation for all 3 genetic forms of PH.

**Therapeutic benefit**

DCR-PHXC (Nedosiran sodium) reduces the level of mRNA encoding the dominant form of the LDH enzyme, specifically, the LDHA isoenzyme. Lactate dehydrogenase catalyzes the cytosolic conversion of glyoxylate to oxalate in the liver and this biochemical reaction is believed to be critical for oxalate generation for all 3 genetic forms of PH.

**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**

blood samples, urine samples and buccal cells.

**Target sample size**

5

**Actual enrollment target size**

5

**Date of first enrollment: Type**

**Date of first enrollment: Date**



Anticipated	06/12/2021
<b>Date of study closure: Type</b> Anticipated	<b>Date of study closure: Date</b> 02/01/2023
<b>Recruitment status</b> Pending	<b>Recruitment status: Specify</b>
<b>Date of completion</b> 09/12/2022	
<b>IPD sharing statement plan</b> No	<b>IPD sharing statement description</b> N/A
<b>Additional data URL</b>	
<b>Admin comments</b>	
<b>Trial status</b> Approved	

## Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Dicerna Pharmaceuticals	N/A

## Sources of Monetary or Material Support

Name
Dicerna Pharmaceuticals

## Secondary Sponsors

Name
Premier Research



## Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Sarah Kharsa	Beirut	Lebanon	+96181209199	sarah.kharsa@clinart.net	Clinart MEA
Scientific	Nancy Choucair	Beirut	Lebanon	+9611421000	nancy.alam@usj.edu.lb	Hotel Dieu De France Ethics Committee

## Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hotel Dieu De France Hospital	Chebl Mourani	Pediatric Nephrology	Approved

## Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Hotel Dieu de France	07/07/2021	Nancy Choucair	nancy.alam@usj.edu.lb	01-421000

## Countries of Recruitment

Name
Lebanon
United States of America
United Kingdom
France
Poland
Turkey

## Health Conditions or Problems Studied

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



## Interventions

Intervention	Description	Keyword
Nedosiran	DCR-PHXC 170 mg/mL Solution for Injection	Nedosiran

## Primary Outcomes

Name	Time Points	Measure
To characterize the safety of nedosiran in neonates, infants, and young children with PH and relatively intact renal function based upon eGFR and serum creatinine	6 months	Change from Baseline in 12-lead ECG, physical examination findings, vital sign assessments, and clinical laboratory tests

## Key Secondary Outcomes

Name	Time Points	Measure
To assess the efficacy of nedosiran in neonates, infants, and young children with PH and relatively intact renal function based upon eGFR and serum creatinine	6 months	Percent and absolute change from Baseline to Month 6 in spot urinary oxalate-to-creatinine ratio



## 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**