

**Clinical trial results:****A 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  
Summary**

EudraCT number	2018-003098-91
Trial protocol	FR GB DE NL ES PL IT RO
Global end of trial date	29 June 2021

**Results information**

Result version number	v1 (current)
This version publication date	15 July 2022
First version publication date	15 July 2022

**Trial information****Trial identification**

Sponsor protocol code	DCR-PHXC-201
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03847909
WHO universal trial number (UTN)	U1111-1224-6881

Notes:

**Sponsors**

Sponsor organisation name	Dicerna Pharmaceuticals, Inc.
Sponsor organisation address	75 Hayden Avenue, Lexington, United States, MA 02421
Public contact	Sarb Shergill, Dicerna Pharmaceuticals INC., 001 617-621-8097, sshergill@dicerna.com
Scientific contact	Sarb Shergill, Dicerna Pharmaceuticals INC., 001 617-621-8097, sshergill@dicerna.com

Notes:

**Paediatric regulatory details**

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-002493-PIP01-18
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	29 June 2021
Is this the analysis of the primary completion data?	No

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Global end of trial reached?	Yes
Global end of trial date	29 June 2021
Was the trial ended prematurely?	No

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Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the efficacy of DCR PHXC in reducing urinary oxalate burden in patients with primary hyperoxaluria (PH) (types 1 and 2)

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Protection of trial subjects:

This study was conducted in accordance with the protocol and with the following: Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines, applicable ICH Good Clinical Practice (GCP) Guidelines and applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

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Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	Lebanon: 5
Worldwide total number of subjects	35
EEA total number of subjects	12

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Notes:

<b>Subjects enrolled per age group</b>	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	5
Adolescents (12-17 years)	10
Adults (18-64 years)	20
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 19 sites in France, Spain, Italy, Netherlands, Germany, United Kingdom, Australia, United States, Canada, Lebanon, and Japan.

### Pre-assignment

Screening details:

A total of 57 subjects were screened, of which 35 subjects were randomised: 23 to DCR-PHXC and 12 to placebo. All 35 randomised subjects received at least one dose of study drug.

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

Treatment assignment was blinded for the Investigators and any personnel (other than the unblinded pharmacist or designee) involved with the study conduct or evaluation at the investigational sites, the contract research organisation (CRO), and the Sponsor.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	DCR-PHXC

Arm description:

Subjects aged greater than or equal to ( $\geq$ ) 12 years weighing  $\geq$ 50 kilograms (kg) received nedosiran 170 milligram (mg) (160 milligrams per millilitre [mg/mL] free acid equivalent [FAE]); subjects  $\geq$ 12 year weighing less than ( $<$ ) 50 kg received 136 mg (128 mg FAE); and subjects 6-11 years received 3.5 milligrams per kilogram (mg/kg) (3.3 mg/kg FAE) not exceeding 136 mg, subcutaneous (SC) injection into the abdomen or thigh on Days 1, 30, 60, 90, 120 and 150.

Arm type	Experimental
Investigational medicinal product name	DCR-PHXC
Investigational medicinal product code	
Other name	Nedosiran
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Nedosiran was administered as a SC injection into the abdomen or thigh at the following dose levels based on age and weight: 1) 170 mg (160 mg FAE) for  $\geq$  12 years and  $\geq$  50 kg; ; 2) 136 mg (128 mg FAE) for  $\geq$  12 years and weight  $<$  50 kg; 3.5 mg/kg (3.3 mg/kg FAE), not to exceed 136 mg for 6-11 years. Subjects who began the study weighing less than 50 kg had their dose increased to the 170 mg dose when they reach the 50 kg threshold. Subjects receiving the 170 mg dose had not decreased their dose to the 136 mg dose if they fell below the 50 kg threshold. The total dose for 6 to 11 year-old subjects was based upon body weight recorded on study Day 1 and was constant throughout the study, regardless of any weight gain or loss or change in age.

<b>Arm title</b>	Placebo
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Arm description:

Subjects received the equivalent volume of nedosiran matching placebo SC injection into the abdomen or thigh on Days 1, 30, 60, 90, 120 and 150.

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received nedosiran matching placebo (normal saline 0.9%) SC injection into the abdomen or thigh on Days 1, 30, 60, 90, 120 and 150.

<b>Number of subjects in period 1</b>	DCR-PHXC	Placebo
Started	23	12
Safety population	23	12
Intent to treat (ITT) population	23	12
Modified ITT (MITT) population	22	12
Completed	22	11
Not completed	1	1
Consent withdrawn by subject	1	1

## Baseline characteristics

### Reporting groups

Reporting group title	DCR-PHXC
Reporting group description:	
Subjects aged greater than or equal to ( $\geq$ ) 12 years weighing $\geq$ 50 kilograms (kg) received nedosiran 170 milligram (mg) (160 milligrams per millilitre [mg/mL] free acid equivalent [FAE]); subjects $\geq$ 12 year weighing less than ( $<$ ) 50 kg received 136 mg (128 mg FAE); and subjects 6-11 years received 3.5 milligrams per kilogram (mg/kg) (3.3 mg/kg FAE) not exceeding 136 mg, subcutaneous (SC) injection into the abdomen or thigh on Days 1, 30, 60, 90, 120 and 150.	
Reporting group title	Placebo
Reporting group description:	
Subjects received the equivalent volume of nedosiran matching placebo SC injection into the abdomen or thigh on Days 1, 30, 60, 90, 120 and 150.	

Reporting group values	DCR-PHXC	Placebo	Total
Number of subjects	23	12	35
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age $<$ 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	3	2	5
Adolescents (12-17 years)	6	4	10
Adults (18-64 years)	14	6	20
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	23.7	23.6	
standard deviation	$\pm$ 11.95	$\pm$ 11.48	-
Gender categorical			
Units: Subjects			
Female	12	6	18
Male	11	6	17

## End points

### End points reporting groups

Reporting group title	DCR-PHXC
Reporting group description: Subjects aged greater than or equal to ( $\geq$ ) 12 years weighing $\geq$ 50 kilograms (kg) received nedosiran 170 milligram (mg) (160 milligrams per millilitre [mg/mL] free acid equivalent [FAE]); subjects $\geq$ 12 year weighing less than ( $<$ ) 50 kg received 136 mg (128 mg FAE); and subjects 6-11 years received 3.5 milligrams per kilogram (mg/kg) (3.3 mg/kg FAE) not exceeding 136 mg, subcutaneous (SC) injection into the abdomen or thigh on Days 1, 30, 60, 90, 120 and 150.	
Reporting group title	Placebo
Reporting group description: Subjects received the equivalent volume of nedosiran matching placebo SC injection into the abdomen or thigh on Days 1, 30, 60, 90, 120 and 150.	
Subject analysis set title	DCR-PHXC: Adults
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subject analysis set included all adult subjects (age $\geq$ 18 years) from DCR-PHXC arm who received 170 mg nedosiran.	
Subject analysis set title	DCR-PHXC: Adolescents
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subject analysis set included all adolescents (aged 12-17 years) from DCR-PHXC arm who received 170 mg nedosiran.	

### **Primary: Percentage of subjects with a reduction from baseline in 24-hour urinary oxalate excretion (Uox) of at least 70%, based on an area under the curve (AUC) and/or reaching normalization or near-normalization of 24-hour Uox on at least 2 consecutive visits**

End point title	Percentage of subjects with a reduction from baseline in 24-hour urinary oxalate excretion (Uox) of at least 70%, based on an area under the curve (AUC) and/or reaching normalization or near-normalization of 24-hour Uox on at least 2 consecutive visits
End point description: Percentage of subjects with a reduction from baseline in 24-hour Uox of at least 70%, based on an area under the curve (AUC) and/or reaching normalization or near-normalization of 24-hour Uox on at least 2 consecutive visits are presented. Normalization of Uox was defined as less than ( $<$ ) 0.46 millimole per 24 hours (mmol/24 hours) and near-normalization was defined as greater than or equal to ( $\geq$ ) 0.46 to $<$ 0.60 mmol/24 hours (values adjusted per 1.73 square metre [ $1.73 \text{ m}^2$ ] body surface area [BSA] in subjects aged $<$ 18 years). Modified Intent-to-treat population (MITT) included all subjects in the intent-to-treat (ITT) population who had at least one efficacy assessment after the Day 90 dosing visit where ITT population included all subjects who were randomised and had at least one post-baseline efficacy assessment.	
End point type	Primary
End point timeframe: From Day 90 to 180	

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	12		
Units: Percentage of subjects				
number (not applicable)	59.1	0		

## Statistical analyses

Statistical analysis title	DCR-PHXC versus Placebo
Comparison groups	DCR-PHXC v Placebo
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0005
Method	Fisher exact

## Secondary: AUC from Day 90 to Day 180, based on percent change from baseline in 24-hour Uox

End point title	AUC from Day 90 to Day 180, based on percent change from baseline in 24-hour Uox
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End point description:

AUC from Day 90 to Day 180 based on percent change from baseline in 24-hour Uox is presented. MITT population included all subjects in the ITT population who had at least one efficacy assessment after the Day 90 dosing visit, where the ITT population included all subjects who were randomized and had at least one post-baseline efficacy assessment. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 90 and 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	12		
Units: Percent change in 24-hour Uox AUC				
least squares mean (standard error)	3507.4 ( $\pm$ 788.49)	-1664.4 ( $\pm$ 1189.96)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent change from baseline to Day 180 in the summed surface area of



## kidney stones

End point title	Percent change from baseline to Day 180 in the summed surface area of kidney stones
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### End point description:

Percent change from baseline to Day 180 in the summed surface area measured in millimetre square (mm<sup>2</sup>) of kidney stones is presented. The ITT population included all subjects who were randomised and had at least one post-baseline efficacy assessment. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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### End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	10		
Units: Percent change in summed surface area				
median (full range (min-max))	-2.13 (-100.0 to 228.6)	21.77 (-24.3 to 1500.0)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent change from baseline to Day 180 in the number of kidney stones

End point title	Percent change from baseline to Day 180 in the number of kidney stones
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### End point description:

Percent change from baseline to Day 180 in the number of kidney stones is presented. The ITT population included all subjects who were randomised and had at least one post-baseline efficacy assessment. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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### End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	10		
Units: Percent change in kidney stone numbers				
median (full range (min-max))	0.00 (-100.0 to 200.0)	0.00 (-94.1 to 100.0)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percent change from baseline to Day 180 in plasma oxalate (for adults only)

End point title	Percent change from baseline to Day 180 in plasma oxalate (for adults only)
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End point description:

Percent change from baseline to Day 180 in plasma oxalate (for adults only) is presented. Analysis population included all adult subjects from ITT population who were randomised and had at least one post-baseline efficacy assessment. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	5		
Units: Percent change in plasma oxalate				
median (full range (min-max))	-25.00 (-61.9 to 22.2)	-0.00 (-25.0 to 350.0)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Rate of change in estimated glomerular filtration rate (eGFR) from baseline to Day 180

End point title	Rate of change in estimated glomerular filtration rate (eGFR) from baseline to Day 180
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End point description:

Monthly rate of eGFR decline is presented. eGFR was calculated using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) and creatinine-based equation. The ITT population included all subjects who were randomised and had at least one post-baseline efficacy assessment. Number analysed (n) signifies subjects with available data for each specified category.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	12		
Units: mL/minute/1.73 <sup>2</sup>				
arithmetic mean (standard error)	0.3533 (± 0.39610)	1.1008 (± 0.54849)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of treatment emergent adverse events (TEAEs) and treatment emergent serious adverse events (TESAEs)

End point title	Number of treatment emergent adverse events (TEAEs) and treatment emergent serious adverse events (TESAEs)
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End point description:

Number of TEAEs and TESAEs are presented. An adverse event (AE) is any untoward medical occurrence in a patient or clinical study subject, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An SAE was defined as any untoward medical occurrence that, at any dose: results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalisation, results in persistent disability/incapacity or is a congenital anomaly/birth defect. TEAE was defined as any AE with an onset date/time on or after administration (including any partial administration) of the first dose of study intervention and through the study completion date from the end of study CRF. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention.

End point type	Secondary
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End point timeframe:

From Baseline up to Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	12		
Units: Events				
number (not applicable)				
TEAEs	101	54		
TESAEs	1	3		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in electrocardiogram (ECG): heart rate

End point title	Change from baseline in electrocardiogram (ECG): heart rate
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End point description:

Change from baseline in heart rate is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
End point timeframe:	
Baseline, Day 180	

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	11		
Units: beats per minute (beats/min)				
arithmetic mean (standard deviation)	0.4 (± 8.36)	-1.8 (± 9.18)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in ECG: PR interval, QRS duration, QT interval, QTcB interval, QTcF interval and RR interval

End point title	Change from baseline in ECG: PR interval, QRS duration, QT interval, QTcB interval, QTcF interval and RR interval
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End point description:

Change from baseline in PR interval, QRS duration, QT interval, QTcB interval, QTcF interval and RR interval is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
End point timeframe:	
Baseline, Day 180	

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	11		
Units: milliseconds (msec)				
arithmetic mean (standard deviation)				
PR interval	-0.5 (± 13.92)	1.3 (± 8.14)		
QRS duration	1.3 (± 6.01)	-1.5 (± 7.53)		
QT interval	-2.4 (± 23.73)	4.0 (± 22.97)		
QTcB interval	-0.8 (± 15.60)	-0.7 (± 17.31)		
QTcF interval	-1.1 (± 15.80)	1.2 (± 15.59)		
RR interval	-7.6 (± 99.35)	17.8 (± 109.73)		

### Statistical analyses

**Secondary: Number of subjects with most abnormal post-baseline shift in physical examination**

End point title	Number of subjects with most abnormal post-baseline shift in physical examination
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End point description:

Number of subjects who had most abnormal post-baseline shift in physical examination are presented. Physical examination shifts were categories into 4 categories: 1) missing; 2) normal; 3) abnormal-not clinically significant (NCS) and 4) abnormal-clinically significant (CS). Each category was presented according body systems including: 1) eyes, ears, nose and throat; 2) chest/respiratory; 3) heart/cardiovascular; 4) gastrointestinal/liver; 5) musculoskeletal/extremities; 6) dermatological/skin; 7) thyroid/neck; 8) lymph nodes; 9) neurological. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention.

End point type	Secondary
End point timeframe:	
Baseline up to Day 180	

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	12		
Units: Subjects				
Eyes, ears, nose and throat: missing	1	1		
Eyes, ears, nose and throat: normal	21	11		
Eyes, ears, nose and throat: abnormal-NCS	1	0		
Eyes, ears, nose and throat: abnormal-CS	0	0		
Chest/respiratory: missing	0	0		
Chest/respiratory: normal	23	12		
Chest/respiratory: abnormal-NCS	0	0		
Chest/respiratory: abnormal-CS	0	0		
Heart/cardiovascular: missing	0	0		
Heart/cardiovascular: normal	22	12		
Heart/cardiovascular: abnormal-NCS	1	0		
Heart/cardiovascular: abnormal-CS	0	0		
Gastrointestinal/liver: missing	0	0		
Gastrointestinal/liver: normal	22	8		
Gastrointestinal/liver: abnormal-NCS	1	4		
Gastrointestinal/liver: abnormal-CS	0	0		
Musculoskeletal/extremities: missing	1	1		
Musculoskeletal/extremities: normal	22	10		
Musculoskeletal/extremities: abnormal-NCS	0	1		
Musculoskeletal/extremities: abnormal-CS	0	0		
Dermatological/skin: missing	0	0		
Dermatological/skin: normal	18	8		
Dermatological/skin: abnormal-NCS	4	4		
Dermatological/skin: abnormal-CS	1	0		
Thyroid/neck: missing	1	1		

Thyroid/neck: normal	22	10		
Thyroid/neck: abnormal-NCS	0	1		
Thyroid/neck: abnormal-CS	0	0		
Lymph nodes: missing	0	1		
Lymph nodes: normal	23	10		
Lymph nodes: abnormal-NCS	0	1		
Lymph nodes: abnormal-CS	0	0		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in vital signs: height

End point title	Change from baseline in vital signs: height
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End point description:

Change from baseline to Day 180 in height is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	11		
Units: centimetres (cm)				
arithmetic mean (standard deviation)	0.70 (± 2.383)	1.08 (± 1.446)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in vital signs: weight

End point title	Change from baseline in vital signs: weight
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End point description:

Change from baseline to Day 180 in weight is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	11		
Units: kilograms				
arithmetic mean (standard deviation)	1.134 (± 3.4794)	1.350 (± 3.4330)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in vital signs: body mass index (BMI)

End point title	Change from baseline in vital signs: body mass index (BMI)
End point description: Change from baseline to Day 180 in BMI is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.	
End point type	Secondary
End point timeframe: Baseline, Day 180	

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	11		
Units: Kilograms per square meter (kg/m <sup>2</sup> )				
arithmetic mean (standard deviation)	0.23 (± 1.175)	0.14 (± 1.293)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in vital signs: oral body temperature

End point title	Change from baseline in vital signs: oral body temperature
End point description: Change from baseline to Day 180 in oral body temperature is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.	
End point type	Secondary
End point timeframe: Baseline, Day 180	

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	11		
Units: Degree Celsius (C)				
arithmetic mean (standard deviation)	0.01 (± 0.399)	0.05 (± 0.446)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in vital signs: heart rate

End point title	Change from baseline in vital signs: heart rate
End point description: Change from baseline to Day 180 in heart rate is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.	
End point type	Secondary
End point timeframe: Baseline, Day 180	

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	11		
Units: beats/min				
arithmetic mean (standard deviation)	0.8 (± 10.64)	-3.1 (± 6.35)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in vital signs: respiratory rate

End point title	Change from baseline in vital signs: respiratory rate
End point description: Change from baseline to Day 180 in respiratory rate is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.	
End point type	Secondary
End point timeframe: Baseline, Day 180	



End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	10		
Units: Breaths per minute (breaths/min)				
arithmetic mean (standard deviation)	-0.2 (± 3.02)	-1.1 (± 5.00)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in vital signs: systolic and diastolic blood pressure

End point title	Change from baseline in vital signs: systolic and diastolic blood pressure
End point description: Change from baseline to Day 180 in systolic and diastolic blood pressure is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.	
End point type	Secondary
End point timeframe: Baseline, Day 180	

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	11		
Units: millimetres of mercury (mmHg)				
arithmetic mean (standard deviation)				
Systolic blood pressure	-2.0 (± 13.64)	-3.0 (± 9.82)		
Diastolic blood pressure	0.8 (± 9.20)	-2.6 (± 11.84)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical chemistry laboratory tests: alanine aminotransferase, aspartate aminotransferase, glutamate dehydrogenase, gamma glutamyl transferase, alkaline phosphatase, lactate dehydrogenase and creatine kinase

End point title	Change from baseline in clinical chemistry laboratory tests: alanine aminotransferase, aspartate aminotransferase, glutamate dehydrogenase, gamma glutamyl transferase, alkaline phosphatase, lactate dehydrogenase and creatine kinase
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**End point description:**

Change from baseline to Day 180 in alanine aminotransferase, aspartate aminotransferase, glutamate dehydrogenase, gamma glutamyl transferase, alkaline phosphatase, lactate dehydrogenase and creatine kinase are presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data and number analysed (n) signifies subjects with available data for each specified category.

End point type	Secondary
End point timeframe:	
Baseline, Day 180	

<b>End point values</b>	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	11		
Units: Units per litre (U/L)				
arithmetic mean (standard deviation)				
Alanine aminotransferase (n= 22, 11)	1.0 (± 8.59)	-1.1 (± 4.59)		
Aspartate aminotransferase (n= 22, 11)	-0.2 (± 4.95)	-1.3 (± 4.73)		
Glutamate dehydrogenase (n= 22, 11)	-0.15 (± 1.913)	-0.38 (± 1.064)		
Gamma glutamyl transferase (n= 22, 11)	2.7 (± 4.12)	-0.2 (± 3.03)		
Alkaline phosphatase (n= 22, 11)	3.0 (± 29.11)	-16.8 (± 41.78)		
Lactate dehydrogenase (n= 20, 10)	4.1 (± 20.51)	1.0 (± 20.72)		
Creatine kinase (n= 22, 11)	7.5 (± 59.28)	-34.1 (± 160.46)		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change from baseline in clinical chemistry laboratory tests: bilirubin, direct bilirubin and creatinine**

End point title	Change from baseline in clinical chemistry laboratory tests: bilirubin, direct bilirubin and creatinine
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**End point description:**

Change from baseline to Day 180 in bilirubin, direct bilirubin and creatinine are presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data and number analysed (n) signifies subjects with available data for each specified category.

End point type	Secondary
End point timeframe:	
Baseline, Day 180	

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	11		
Units: micromoles per litre (umol/L)				
arithmetic mean (standard deviation)				
Bilirubin (n= 22, 11)	1.0 (± 3.18)	0.4 (± 1.80)		
Direct bilirubin (n= 22, 10)	0.1 (± 1.32)	0.1 (± 0.32)		
Creatinine (n= 22, 11)	-1.2 (± 10.81)	4.3 (± 11.02)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical chemistry laboratory tests: protein, albumin

End point title	Change from baseline in clinical chemistry laboratory tests: protein, albumin
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End point description:

Change from baseline to Day 180 in protein and albumin are presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	11		
Units: grams per litre (g/L)				
arithmetic mean (standard deviation)				
Protein	0.4 (± 4.47)	1.5 (± 6.27)		
Albumin	0.5 (± 3.22)	1.2 (± 3.63)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical chemistry laboratory tests: sodium, chloride, potassium and urea

End point title	Change from baseline in clinical chemistry laboratory tests: sodium, chloride, potassium and urea
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End point description:

Change from baseline to Day 180 in sodium, chloride, potassium and urea are presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data and number analysed (n) signifies subjects with available data for each specified category.

End point type Secondary

End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	11		
Units: mmol/L				
arithmetic mean (standard deviation)				
Sodium (n= 22, 11)	0.4 (± 2.44)	0.2 (± 3.03)		
Chloride (n= 22, 11)	0.6 (± 3.30)	-0.4 (± 4.08)		
Potassium (n= 21, 10)	-0.04 (± 0.425)	0.05 (± 0.360)		
Urea (n= 22, 11)	0.01 (± 0.895)	0.40 (± 1.197)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in clinical chemistry laboratory tests: vitamin B6

End point title Change from baseline in clinical chemistry laboratory tests: vitamin B6

End point description:

Change from baseline to Day 180 in vitamin B6 is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type Secondary

End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: nanomoles per litre (nmol/L)				
arithmetic mean (standard deviation)	34.60 (± 99.278)	-215.73 (± 337.775)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical hematology laboratory tests: erythrocytes

End point title	Change from baseline in clinical hematology laboratory tests: erythrocytes
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End point description:

Change from baseline to Day 180 in erythrocytes is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: 10 <sup>12</sup> per litre (10 <sup>12</sup> /L)				
arithmetic mean (standard deviation)	-0.04 (± 0.365)	0.02 (± 0.230)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical hematology laboratory tests: hemoglobin and erythrocytes mean corpuscular hemoglobin concentration

End point title	Change from baseline in clinical hematology laboratory tests: hemoglobin and erythrocytes mean corpuscular hemoglobin concentration
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End point description:

Change from baseline to Day 180 in hemoglobin and erythrocytes mean corpuscular hemoglobin concentration are presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: g/L				
arithmetic mean (standard deviation)				
Hemoglobin	-1.7 (± 8.90)	0.1 (± 6.62)		
Ery. mean corpuscular hemoglobin concentration	1.5 (± 15.10)	-4.8 (± 10.80)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical hematology laboratory tests: hematocrit

End point title	Change from baseline in clinical hematology laboratory tests: hematocrit
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End point description:

Change from baseline to Day 180 in hematocrit is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: Litre/litre				
arithmetic mean (standard deviation)	-0.004 (± 0.0271)	0.006 (± 0.0288)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical hematology laboratory tests: erythrocytes (ery.) mean corpuscular volume and mean platelet volume

End point title	Change from baseline in clinical hematology laboratory tests: erythrocytes (ery.) mean corpuscular volume and mean platelet volume
-----------------	--

End point description:

Change from baseline to Day 180 in ery. mean corpuscular volume and mean platelet volume are presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
End point timeframe:	
Baseline, Day 180	

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: femtoliter (fL)				
arithmetic mean (standard deviation)				
Ery. mean corpuscular volume	0.0 (± 2.31)	1.1 (± 3.57)		
Mean platelet volume	-0.03 (± 0.864)	0.61 (± 0.547)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical hematology laboratory tests: erythrocytes mean corpuscular hemoglobin

End point title	Change from baseline in clinical hematology laboratory tests: erythrocytes mean corpuscular hemoglobin
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End point description:

Change from baseline to Day 180 in erythrocytes mean corpuscular hemoglobin is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: picogram (pg)				
arithmetic mean (standard deviation)	-0.1 (± 1.37)	-0.1 (± 0.99)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical hematology laboratory tests: reticulocytes, platelets, leukocytes, lymphocytes, monocytes, eosinophils, basophils, neutrophils

End point title	Change from baseline in clinical hematology laboratory tests: reticulocytes, platelets, leukocytes, lymphocytes, monocytes, eosinophils, basophils, neutrophils
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End point description:

Change from baseline to Day 180 in reticulocytes, platelets, leukocytes, lymphocytes, monocytes, eosinophils, basophils, neutrophils are presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data and number analysed (n) signifies subjects with available data for each specified category.

End point type	Secondary
End point timeframe:	
Baseline, Day 180	

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: 10 <sup>9</sup> /L				
arithmetic mean (standard deviation)				
Reticulocytes (n= 20, 9)	0.2 (± 30.08)	-23.1 (± 32.21)		
Platelets (n= 21, 10)	-11.4 (± 54.50)	2.3 (± 53.30)		
Leukocytes (n= 21, 10)	0.18 (± 1.573)	-1.03 (± 1.931)		
Lymphocytes (n= 21, 10)	-0.03 (± 0.621)	0.06 (± 0.331)		
Monocytes (n= 21, 10)	0.07 (± 0.085)	-0.02 (± 0.103)		
Eosinophils (n= 21, 10)	0.03 (± 0.072)	0.04 (± 0.126)		
Basophils (n= 21, 10)	0.01 (± 0.062)	-0.04 (± 0.097)		
Neutrophils (n= 21, 10)	0.14 (± 1.195)	-1.07 (± 1.700)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in clinical hematology laboratory tests: lymphocytes/leukocytes

End point title	Change from baseline in clinical hematology laboratory tests: lymphocytes/leukocytes
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End point description:

Change from baseline to Day 180 in lymphocytes/leukocytes is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: Percentage of lymphocytes/leukocytes				
arithmetic mean (standard deviation)	-1.3 ( $\pm$ 10.26)	5.1 ( $\pm$ 10.21)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical hematology laboratory tests: monocytes/leukocytes

End point title	Change from baseline in clinical hematology laboratory tests: monocytes/leukocytes
-----------------	--

End point description:

Change from baseline to Day 180 in monocytes/leukocytes is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: Percentage of monocytes/leukocytes				
arithmetic mean (standard deviation)	1.0 ( $\pm$ 2.04)	0.9 ( $\pm$ 2.51)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical hematology laboratory tests:

## eosinophils/leukocytes

End point title	Change from baseline in clinical hematology laboratory tests: eosinophils/leukocytes
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End point description:

Change from baseline to Day 180 in eosinophils/leukocytes is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: Percentage of eosinophils/leukocytes				
arithmetic mean (standard deviation)	0.4 (± 1.56)	0.9 (± 1.66)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in clinical hematology laboratory tests: basophils/leukocytes

End point title	Change from baseline in clinical hematology laboratory tests: basophils/leukocytes
-----------------	--

End point description:

Change from baseline to Day 180 in basophils/leukocytes is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: Percentage of basophils/leukocytes				
arithmetic mean (standard deviation)	0.0 (± 0.77)	0.1 (± 0.74)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical hematology laboratory tests: neutrophils/leukocytes

End point title	Change from baseline in clinical hematology laboratory tests: neutrophils/leukocytes
-----------------	--

End point description:

Change from baseline to Day 180 in neutrophils/leukocytes is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: Percentage of neutrophils/leukocytes				
arithmetic mean (standard deviation)	-0.3 ( $\pm$ 11.45)	-7.1 ( $\pm$ 13.14)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical urinalysis laboratory tests: specific gravity

End point title	Change from baseline in clinical urinalysis laboratory tests: specific gravity
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End point description:

Change from baseline to Day 180 in urine specific gravity is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: Ratio				
arithmetic mean (standard deviation)	0.0000 ( $\pm$ 0.00872)	-0.0008 ( $\pm$ 0.00480)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in clinical urinalysis laboratory tests: pH

End point title	Change from baseline in clinical urinalysis laboratory tests: pH
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End point description:

Change from baseline to Day 180 in urine pH is presented. The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data.

End point type	Secondary
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End point timeframe:

Baseline, Day 180

End point values	DCR-PHXC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: Units on a scale				
arithmetic mean (standard deviation)	0.29 (± 1.067)	-0.10 (± 0.738)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum observed plasma concentration (C<sub>max</sub>) of DCR-PHXC

End point title	Maximum observed plasma concentration (C <sub>max</sub> ) of DCR-PHXC
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End point description:

The C<sub>max</sub> was defined as the maximum observed plasma concentration during a dosing interval. The Pharmacokinetic (PK) population included all subjects in the safety population without major dosing violations, where safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data and number analysed (n) signifies subjects with available data for each specified category. Data for this endpoint is reported only for adults and adolescent subjects from PK population. Here '99999' signifies data for adolescents group was not collected on Day 150.

End point type	Secondary
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End point timeframe:

For adults: Day 1 and 30: predose, 5, 15, and 30 minutes and 1, 2, 4, 6, 10, and 12 hours (hrs) postdose; Day 150: predose, 2, 6, and 12 hours postdose

For adolescents:

Days 1 and 30: predose, 30 minutes and 2 and 10 hours postdose

End point values	DCR-PHXC: Adults	DCR-PHXC: Adolescents		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	5		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1 (n= 12, 5)	778 (± 35.7)	363 (± 76.7)		
Day 30 (n= 11, 5)	774 (± 46.1)	350 (± 48.6)		
Day 150 (n= 8, 0)	648 (± 55.5)	99999 (± 99999)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Area under the curve from time of administration to the last measurable concentration (AUC0-last) of of DCR-PHXC

End point title	Area under the curve from time of administration to the last measurable concentration (AUC0-last) of of DCR-PHXC
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End point description:

AUC0-last was defined as the area under the curve from time of administration to the last measurable concentration. The PK population included all subjects in the safety population without major dosing violations, where safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. Number of subjects analysed signifies subjects with available data and number analysed (n) signifies subjects with available data for each specified category. Data for this endpoint is reported only for adults and adolescent subjects from PK population. Here '99999' signifies data for adolescents group was not collected on Day 150.

End point type	Secondary
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End point timeframe:

For adults: Day 1 and 30: predose, 5, 15, and 30 minutes and 1, 2, 4, 6, 10, and 12 hours postdose;  
Day 150: predose, 2, 6, and 12 hours postdose

For adolescents:

Days 1 and 30: predose, 30 minutes and 2 and 10 hours postdose

End point values	DCR-PHXC: Adults	DCR-PHXC: Adolescents		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	5		
Units: hours*nanograms per millilitre (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
Day 1 (n= 12, 5)	12500 (± 29.3)	6450 (± 54.5)		
Day 30 (n= 11, 5)	12800 (± 38.4)	6400 (± 45.1)		
Day 150 (n= 8, 0)	6100 (± 46.2)	99999 (± 99999)		

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From Day 1 up to end of the study (Day 180)

Adverse event reporting additional description:

The safety population included all subjects randomly assigned to study intervention and who took at least 1 partial or full dose of study intervention. All serious and non-serious adverse events presented here are treatment emergent adverse events.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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### Reporting groups

Reporting group title	DCR-PHXC
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Reporting group description:

Subjects aged  $\geq 12$  years weighing  $\geq 50$  kg received nedosiran 170 mg (160 mg/mL FAE); subjects  $\geq 12$  year weighing  $< 50$  kg received 136 mg (128 mg FAE); and subjects 6-11 years received 3.5 kg/mg (3.3 mg/kg FAE) not exceeding 136 mg, SC injection into the abdomen or thigh on Days 1, 30, 60, 90, 120 and 150.

Reporting group title	Placebo
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Reporting group description:

Subjects received the equivalent volume of nedosiran matching placebo SC injection into the abdomen or thigh on Days 1, 30, 60, 90, 120 and 150.

Serious adverse events	DCR-PHXC	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 23 (4.35%)	2 / 12 (16.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 23 (4.35%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Blood creatinine increased			
subjects affected / exposed	0 / 23 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			

subjects affected / exposed	0 / 23 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	0 / 23 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	DCR-PHXC	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 23 (69.57%)	10 / 12 (83.33%)	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	5 / 23 (21.74%)	0 / 12 (0.00%)	
occurrences (all)	11	0	
Injection site pain			
subjects affected / exposed	2 / 23 (8.70%)	0 / 12 (0.00%)	
occurrences (all)	3	0	
Fatigue			
subjects affected / exposed	1 / 23 (4.35%)	2 / 12 (16.67%)	
occurrences (all)	2	2	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	2 / 23 (8.70%)	0 / 12 (0.00%)	
occurrences (all)	6	0	
Menstrual disorder			
subjects affected / exposed	0 / 23 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 23 (8.70%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Cough			



subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Investigations Neutrophil count decreased subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2	0 / 12 (0.00%) 0	
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	1 / 12 (8.33%) 1	
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Glutamate dehydrogenase increased subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Injury, poisoning and procedural complications Adverse event following immunisation subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 2	
Meniscus injury subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	4 / 23 (17.39%) 6	3 / 12 (25.00%) 3	
Sensory disturbance			

subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 23 (17.39%)	1 / 12 (8.33%)	
occurrences (all)	4	1	
Abdominal pain			
subjects affected / exposed	2 / 23 (8.70%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Abdominal pain upper			
subjects affected / exposed	0 / 23 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Chronic gastritis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 23 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 23 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 23 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	2 / 23 (8.70%)	2 / 12 (16.67%)	
occurrences (all)	3	7	
Renal colic			
subjects affected / exposed	1 / 23 (4.35%)	1 / 12 (8.33%)	
occurrences (all)	1	2	
Hydronephrosis			

subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Musculoskeletal and connective tissue disorders			
Pain in extremity subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 4	1 / 12 (8.33%) 1	
Arthralgia subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	1 / 12 (8.33%) 1	
Neck pain subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	1 / 12 (8.33%) 3	
Arthritis subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Back pain subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	2 / 12 (16.67%) 2	
Flank pain subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Intervertebral disc protrusion subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Osteoarthritis subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Infections and infestations			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	1 / 12 (8.33%) 1	
COVID-19 subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Rhinitis			

subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Hypercholesterolaemia			
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	
Vitamin D deficiency			
subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 June 2019	Principal changes included a change in the primary endpoint to a responder analysis and addition of a "key secondary" endpoint; a change in how the completeness of 24-hour urine collections will be assessed; addition of a subgroup of participants with very high baseline Uox levels; addition of a spot urine sample collection for Uox determination; expanded details regarding modeling and simulation of PK/PD data; expanded details regarding kidney assessments; addition of information for the calculation of eGFR; and updates to the statistical analyses.
12 March 2020	Principal changes included updates in the equations used to calculate eGFR, a change in the dose of DCR-PHXC to be administered in adults weighing less than 50 kg, changed laboratory testing requirements to limit blood loss in children, added additional immunogenicity testing, updated instructions for monitoring of liver injury, clarified the performance of an interim analysis, and specified that metabolites of DCR-PHXC will be included in pharmacokinetic analyses.
13 August 2020	Principal change was to include the dose of DCR-PHXC to be administered in children aged 6-to-11 years. An appendix detailing measures to be undertaken during the COVID-19 pandemic was added.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported