



Clinical trial results:

A Placebo-Controlled, Single-Blind, Single-Center Phase 1 Study in Normal Healthy Volunteers and Open-Label Multi-Center Study in Patients with Primary Hyperoxaluria to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single Ascending Doses of DCR-PHXC Solution for Injection (subcutaneous use)

Summary

EudraCT number	2017-003534-89
Trial protocol	DE GB NL FR
Global end of trial date	19 November 2019

Results information

Result version number	v1 (current)
This version publication date	03 January 2021
First version publication date	03 January 2021

Trial information

Trial identification

Sponsor protocol code	DCR-PHXC-101
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dicerna Pharmaceuticals, Inc.
Sponsor organisation address	75 Hayden Avenue, Suite 400, Lexington, MA, United States, 02421
Public contact	Kerry S. Russell, MD, PhD, Dicerna Pharmaceuticals, Inc., +1 617-621-8097, krussell@dicerna.com
Scientific contact	Kerry S. Russell, MD, PhD, Dicerna Pharmaceuticals, Inc., +1 617-621-8097, krussell@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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 November 2019
Global end of trial reached?	Yes
Global end of trial date	19 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The overall objective of this study was to evaluate the safety and tolerability of single doses of DCR-PHXC for injection (SC use) ("DCR-PHXC") in HV (Group A) and in participants with PH (Group B).

The primary objective for part A of the study was to evaluate the safety and tolerability of single doses of DCR-PHXC in healthy volunteers.

The primary objective for part B of the study was to evaluate the safety and tolerability of single doses of DCR-PHXC in participants with PH.

Protection of trial subjects:

The study was conducted in accordance with the principles set forth in the Declaration of Helsinki as amended in 2013, the Guidelines of the International Conference on Harmonisation (ICH) on Good Clinical Practice (GCP) (CPMP/ICH/135/95), as well as the requirements of the European Union Data Protection Directive 95/46/EC, General Data Protection Regulation (GDPR) and other applicable regulatory requirements.

Background therapy:

Not applicable.

Evidence for comparator:

No comparators were used in this study - study was controlled using placebo. Use of a placebo control was only implemented in Part A, the healthy volunteer part of the study which utilised a single-blind design.

Part B of the study was an open-label part which did not utilise any placebo control or comparator product.

Actual start date of recruitment	29 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 1
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	United Kingdom: 28
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 7
Worldwide total number of subjects	43
EEA total number of subjects	42

Notes:

Subjects enrolled per age group	
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)	0
Adolescents (12-17 years)	3
Adults (18-64 years)	40
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment process for Part A was undertaken in the UK. 65 volunteers were screened in order to successfully recruit 25 eligible participants.

The recruitment process for Part B was undertaken in the UK, France, Germany, Netherlands and US. 19 patients were screened in order to successfully recruit 18 eligible patients.

Pre-assignment

Screening details:

Volunteers were screened to the inclusion/exclusion criteria of the study protocol. The following assessments were performed for both parts: Physical Exam, Demographics and Medical History, ECG, Safety Laboratory Testing/Urinalysis.

Period 1

Period 1 title	Overall Trial Period - Part A and Part B (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

Part A had a single-blind, placebo-controlled design. Participants remained blinded to treatment assignment throughout the safety assessment period. The design was labelled as single-blind, as the pharmacist was unblinded; however, the Medical Monitors at the Sponsor and CRO, study site personnel, PK analyst, and members of the SRC did not have knowledge of the treatment assignment throughout the safety assessment period.

Part B was open-label so there was no blinding procedure implemented.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A HV - 0.3 mg/kg

Arm description:

This was the first and lowest dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 0.3 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose.

Dose escalation to the next planned dose level only occurred after the SRC had reviewed available safety data (through to Day 3 for all subjects) and made a determination that it was acceptable to continue to the next planned dose level.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Arm type	Experimental
Investigational medicinal product name	DCR-PHXC Solution for Injection 170 mg/mL sodium salt - equivalent to 160 mg/mL free acid
Investigational medicinal product code	
Other name	Nedosiran
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dosing frequency was one single dose on the morning of Day 1. The dose may have been administered as 2 or more subcutaneous injections (dependent on injection volume).

Arm title	Part A HV - 1.5 mg/kg
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Arm description:

This was the second dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 1.5 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose.

Dose escalation to the next planned dose level only occurred after the SRC had reviewed available safety data (through to Day 3 for all subjects) and made a determination that it was acceptable to continue to the next planned dose level.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Arm type	Experimental
Investigational medicinal product name	DCR-PHXC Solution for Injection 170 mg/mL sodium salt - equivalent to 160 mg/mL free acid
Investigational medicinal product code	
Other name	Nedosiran
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dosing frequency was one single dose on the morning of Day 1. The dose may have been administered as 2 or more subcutaneous injections (dependent on injection volume).

Arm title	Part A HV - 3.0 mg/kg
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Arm description:

This was the third dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 3.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose.

Dose escalation to the next planned dose level only occurred after the SRC had reviewed available safety data (through to Day 3 for all subjects) and made a determination that it was acceptable to continue to the next planned dose level.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Arm type	Experimental
Investigational medicinal product name	DCR-PHXC Solution for Injection 170 mg/mL sodium salt - equivalent to 160 mg/mL free acid
Investigational medicinal product code	
Other name	Nedosiran
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dosing frequency was one single dose on the morning of Day 1. The dose may have been administered as 2 or more subcutaneous injections (dependent on injection volume).

Arm title	Part A HV - 6.0 mg/kg
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Arm description:

This was the fourth dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 6.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose.

Dose escalation to the next planned dose level only occurred after the SRC had reviewed available safety data (through to Day 3 for all subjects) and made a determination that it was acceptable to continue to the next planned dose level.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Arm type	Experimental
Investigational medicinal product name	DCR-PHXC Solution for Injection 170 mg/mL sodium salt - equivalent to 160 mg/mL free acid
Investigational medicinal product code	
Other name	Nedosiran
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Dosing frequency was one single dose on the morning of Day 1. The dose may have been administered as 2 or more subcutaneous injections (dependent on injection volume).	
Arm title	Part A HV - 12.0 mg/kg

Arm description:

This was the fifth and final dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 12.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Arm type	Experimental
Investigational medicinal product name	DCR-PHXC Solution for Injection 170 mg/mL sodium salt - equivalent to 160 mg/mL free acid
Investigational medicinal product code	
Other name	Nedosiran
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Dosing frequency was one single dose on the morning of Day 1. The dose may have been administered as 2 or more subcutaneous injections (dependent on injection volume).	
Arm title	Part B Patient - 1.5 mg/kg

Arm description:

This was the first dose level administered in Part B (PH Patient) of the study. 6 participants were administered 1.5 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. All participants received active IMP.

In Part B, subjects were only dosed once the SRC had determined acceptable safety of the same dose in Part A. Subjects were enrolled into this cohort in accordance with the inclusion & exclusion criteria of the protocol. Within each cohort, 1 subject was dosed first. After an 8-day observation period, if the dose was deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were dosed. Escalation to the next dose cohort only occurred after the SRC had reviewed available safety data (through to Day 15 for a set number of subjects) and made a determination that it was acceptable to continue.

Arm type	Experimental
Investigational medicinal product name	DCR-PHXC Solution for Injection 170 mg/mL sodium salt - equivalent to 160 mg/mL free acid
Investigational medicinal product code	
Other name	Nedosiran
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dosing frequency was one single dose on the morning of Day 1. The dose may have been administered as 2 or more subcutaneous injections (dependent on injection volume).

Arm title	Part B Patient - 3.0 mg/kg
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Arm description:

This was the second dose level administered in Part B (PH Patient) of the study. 8 participants were administered 3.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. All participants received active IMP.

In Part B, subjects were only dosed once the SRC had determined acceptable safety of the same dose in Part A. Subjects were enrolled into this cohort in accordance with the inclusion & exclusion criteria of the protocol. Within each cohort, 1 subject was dosed first. After an 8-day observation period, if the dose was deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were dosed. Escalation to the next dose cohort only occurred after the SRC had reviewed available safety data (through to Day 15 for a set number of subjects) and made a determination that it was acceptable to continue.

Arm type	Experimental
Investigational medicinal product name	DCR-PHXC Solution for Injection 170 mg/mL sodium salt - equivalent to 160 mg/mL free acid
Investigational medicinal product code	
Other name	Nedosiran
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dosing frequency was one single dose on the morning of Day 1. The dose may have been administered as 2 or more subcutaneous injections (dependent on injection volume).

Arm title	Part B Patient - 6.0 mg/kg
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Arm description:

This was the third and final dose level administered in Part B (PH Patient) of the study. 4 participants were administered 6.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. All participants received active IMP.

In Part B, subjects were only dosed once the SRC had determined acceptable safety of the same dose in Part A. Subjects were enrolled into this cohort in accordance with the inclusion & exclusion criteria of the protocol. Within each cohort, 1 subject was dosed first. After an 8-day observation period, if the dose was deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were dosed. This was the final dose level evaluated in Part B and therefore no further dose escalation was undertaken.

Arm type	Experimental
Investigational medicinal product name	DCR-PHXC Solution for Injection 170 mg/mL sodium salt - equivalent to 160 mg/mL free acid
Investigational medicinal product code	
Other name	Nedosiran
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dosing frequency was one single dose on the morning of Day 1. The dose may have been administered as 2 or more subcutaneous injections (dependent on injection volume).

Arm title	Part A Placebo Group
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Arm description:

This arm relates to the reporting group for the participants within Part A of the study who were randomised to receive placebo within all cohorts. This totals 10 participants across the 5 cohorts in Part A.

Arm type	Placebo
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Investigational medicinal product name	0.9% Saline Solution for Injection
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dosing frequency was one single placebo dose on the morning of Day 1. The dose was matched to the active IMP and therefore may have been administered as 2 or more subcutaneous injections (dependent on injection volume).

Number of subjects in period 1	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg
Started	3	3	3
Completed	3	3	3

Number of subjects in period 1	Part A HV - 6.0 mg/kg	Part A HV - 12.0 mg/kg	Part B Patient - 1.5 mg/kg
Started	3	3	6
Completed	3	3	6

Number of subjects in period 1	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg	Part A Placebo Group
Started	8	4	10
Completed	8	4	10

Baseline characteristics

Reporting groups

Reporting group title	Part A HV - 0.3 mg/kg
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Reporting group description:

This was the first and lowest dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 0.3 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose. Dose escalation to the next planned dose level only occurred after the SRC had reviewed available safety data (through to Day 3 for all subjects) and made a determination that it was acceptable to continue to the next planned dose level.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Reporting group title	Part A HV - 1.5 mg/kg
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Reporting group description:

This was the second dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 1.5 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose.

Dose escalation to the next planned dose level only occurred after the SRC had reviewed available safety data (through to Day 3 for all subjects) and made a determination that it was acceptable to continue to the next planned dose level.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Reporting group title	Part A HV - 3.0 mg/kg
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Reporting group description:

This was the third dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 3.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose.

Dose escalation to the next planned dose level only occurred after the SRC had reviewed available safety data (through to Day 3 for all subjects) and made a determination that it was acceptable to continue to the next planned dose level.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Reporting group title	Part A HV - 6.0 mg/kg
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Reporting group description:

This was the fourth dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 6.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose.

Dose escalation to the next planned dose level only occurred after the SRC had reviewed available safety data (through to Day 3 for all subjects) and made a determination that it was acceptable to continue to the next planned dose level.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Reporting group title	Part A HV - 12.0 mg/kg
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Reporting group description:

This was the fifth and final dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 12.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Reporting group title	Part B Patient - 1.5 mg/kg
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Reporting group description:

This was the first dose level administered in Part B (PH Patient) of the study. 6 participants were administered 1.5 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. All participants received active IMP.

In Part B, subjects were only dosed once the SRC had determined acceptable safety of the same dose in Part A. Subjects were enrolled into this cohort in accordance with the inclusion & exclusion criteria of the protocol. Within each cohort, 1 subject was dosed first. After an 8-day observation period, if the dose was deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were dosed. Escalation to the next dose cohort only occurred after the SRC had reviewed available safety data (through to Day 15 for a set number of subjects) and made a determination that it was acceptable to continue.

Reporting group title	Part B Patient - 3.0 mg/kg
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Reporting group description:

This was the second dose level administered in Part B (PH Patient) of the study. 8 participants were administered 3.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. All participants received active IMP.

In Part B, subjects were only dosed once the SRC had determined acceptable safety of the same dose in Part A. Subjects were enrolled into this cohort in accordance with the inclusion & exclusion criteria of the protocol. Within each cohort, 1 subject was dosed first. After an 8-day observation period, if the dose was deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were dosed. Escalation to the next dose cohort only occurred after the SRC had reviewed available safety data (through to Day 15 for a set number of subjects) and made a determination that it was acceptable to continue.

Reporting group title	Part B Patient - 6.0 mg/kg
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Reporting group description:

This was the third and final dose level administered in Part B (PH Patient) of the study. 4 participants were administered 6.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. All participants received active IMP.

In Part B, subjects were only dosed once the SRC had determined acceptable safety of the same dose in Part A. Subjects were enrolled into this cohort in accordance with the inclusion & exclusion criteria of the protocol. Within each cohort, 1 subject was dosed first. After an 8-day observation period, if the dose was deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were dosed. This was the final dose level evaluated in Part B and therefore no further dose escalation was undertaken.

Reporting group title	Part A Placebo Group
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Reporting group description:

This arm relates to the reporting group for the participants within Part A of the study who were randomised to receive placebo within all cohorts. This totals 10 participants across the 5 cohorts in Part A.

Reporting group values	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg
Number of subjects	3	3	3
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)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	3	3
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	28.7	28.0	37.3
full range (min-max)	24 to 35	22 to 36	20 to 55
Gender categorical Units: Subjects			
Female	1	2	2
Male	2	1	1
Race Units: Subjects			
White	3	3	3
Other	0	0	0
British Asian	0	0	0
Pakistani	0	0	0
Not Reported	0	0	0
Primary Hyperoxaluria Type - Patient Population Units: Subjects			
PH1	0	0	0
PH2	0	0	0
Healthy Volunteer	3	3	3
Body Mass Index Units: kg/m2			
arithmetic mean	26.37	24.36	26.93
full range (min-max)	21.44 to 28.95	20.58 to 26.75	23.49 to 29.64
Estimated Glomerular Filtration Rate (Part B PH Patients Only)			
This characteristic will report the measured estimated glomerular filtration rate for the patients who undertook Part B of the study. It is noted that this parameter was not evaluated for the healthy volunteer part of the study (Part A) and therefore values for these groups are entered as 0. This also includes the participants within the Part A Placebo Group.			
Units: mL/min/1.73m2			
arithmetic mean	0.0	0.0	0.0
full range (min-max)	0.0 to 0.0	0.0 to 0.0	0.0 to 0.0
Reporting group values	Part A HV - 6.0 mg/kg	Part A HV - 12.0 mg/kg	Part B Patient - 1.5 mg/kg
Number of subjects	3	3	6

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)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	3	6
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	35.3	29.3	26.5
full range (min-max)	25 to 46	22 to 34	19 to 45
Gender categorical Units: Subjects			
Female	1	3	3
Male	2	0	3
Race Units: Subjects			
White	3	3	4
Other	0	0	0
British Asian	0	0	1
Pakistani	0	0	0
Not Reported	0	0	1
Primary Hyperoxaluria Type - Patient Population Units: Subjects			
PH1	0	0	5
PH2	0	0	1
Healthy Volunteer	3	3	0
Body Mass Index Units: kg/m2			
arithmetic mean	21.96	23.81	28.74
full range (min-max)	20.69 to 23.48	21.00 to 25.91	23.98 to 33.64
Estimated Glomerular Filtration Rate (Part B PH Patients Only)			
This characteristic will report the measured estimated glomerular filtration rate for the patients who undertook Part B of the study. It is noted that this parameter was not evaluated for the healthy volunteer part of the study (Part A) and therefore values for these groups are entered as 0. This also includes the participants within the Part A Placebo Group.			
Units: mL/min/1.73m2			
arithmetic mean	0.0	0.0	72.31
full range (min-max)	0.0 to 0.0	0.0 to 0.0	41.20 to 94.30
Reporting group values	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg	Part A Placebo Group
Number of subjects	8	4	10
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)	0	0	0
Adolescents (12-17 years)	1	2	0
Adults (18-64 years)	7	2	10
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	25.4	16.5	35.5
full range (min-max)	16 to 38	13 to 20	19 to 49
Gender categorical Units: Subjects			
Female	4	2	2
Male	4	2	8
Race Units: Subjects			
White	4	3	10
Other	0	0	0
British Asian	0	0	0
Pakistani	1	0	0
Not Reported	3	1	0
Primary Hyperoxaluria Type - Patient Population Units: Subjects			
PH1	6	4	0
PH2	2	0	0
Healthy Volunteer	0	0	10
Body Mass Index Units: kg/m2			
arithmetic mean	21.99	22.81	26.47
full range (min-max)	15.15 to 25.83	20.80 to 27.32	22.52 to 31.74
Estimated Glomerular Filtration Rate (Part B PH Patients Only)			
This characteristic will report the measured estimated glomerular filtration rate for the patients who undertook Part B of the study. It is noted that this parameter was not evaluated for the healthy volunteer part of the study (Part A) and therefore values for these groups are entered as 0. This also includes the participants within the Part A Placebo Group.			
Units: mL/min/1.73m2			
arithmetic mean	77.45	106.34	0.0
full range (min-max)	32.87 to 113.04	83.35 to 130.30	0.0 to 0.0
Reporting group values	Total		
Number of subjects	43		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		

Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	3		
Adults (18-64 years)	40		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years arithmetic mean full range (min-max)	-		
Gender categorical Units: Subjects			
Female	20		
Male	23		
Race Units: Subjects			
White	36		
Other	0		
British Asian	1		
Pakistani	1		
Not Reported	5		
Primary Hyperoxaluria Type - Patient Population Units: Subjects			
PH1	15		
PH2	3		
Healthy Volunteer	25		
Body Mass Index Units: kg/m2 arithmetic mean full range (min-max)	-		
Estimated Glomerular Filtration Rate (Part B PH Patients Only)			
This characteristic will report the measured estimated glomerular filtration rate for the patients who undertook Part B of the study. It is noted that this parameter was not evaluated for the healthy volunteer part of the study (Part A) and therefore values for these groups are entered as 0. This also includes the participants within the Part A Placebo Group.			
Units: mL/min/1.73m2 arithmetic mean full range (min-max)	-		

End points

End points reporting groups

Reporting group title	Part A HV - 0.3 mg/kg
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Reporting group description:

This was the first and lowest dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 0.3 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose. Dose escalation to the next planned dose level only occurred after the SRC had reviewed available safety data (through to Day 3 for all subjects) and made a determination that it was acceptable to continue to the next planned dose level.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Reporting group title	Part A HV - 1.5 mg/kg
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Reporting group description:

This was the second dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 1.5 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose.

Dose escalation to the next planned dose level only occurred after the SRC had reviewed available safety data (through to Day 3 for all subjects) and made a determination that it was acceptable to continue to the next planned dose level.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Reporting group title	Part A HV - 3.0 mg/kg
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Reporting group description:

This was the third dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 3.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose.

Dose escalation to the next planned dose level only occurred after the SRC had reviewed available safety data (through to Day 3 for all subjects) and made a determination that it was acceptable to continue to the next planned dose level.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Reporting group title	Part A HV - 6.0 mg/kg
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Reporting group description:

This was the fourth dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 6.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose.

Dose escalation to the next planned dose level only occurred after the SRC had reviewed available safety data (through to Day 3 for all subjects) and made a determination that it was acceptable to continue to the next planned dose level.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Reporting group title	Part A HV - 12.0 mg/kg
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Reporting group description:

This was the fifth and final dose level administered in Part A (Healthy Volunteer) of the study. 3 participants received a single dose of 12.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on Day 1.

Subjects were enrolled in accordance with the protocol inclusion & exclusion criteria. In each cohort, 2 subjects (sentinel pair - 1 active and 1 placebo) were dosed on the same day. After a 3-day observation period, if deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were randomised (2 active: 1 placebo) and received the dose.

This arm only relates to the 3 participants who received active IMP in this cohort; 2 placebo participants are reported in a separate group.

Reporting group title	Part B Patient - 1.5 mg/kg
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Reporting group description:

This was the first dose level administered in Part B (PH Patient) of the study. 6 participants were administered 1.5 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. All participants received active IMP.

In Part B, subjects were only dosed once the SRC had determined acceptable safety of the same dose in Part A. Subjects were enrolled into this cohort in accordance with the inclusion & exclusion criteria of the protocol. Within each cohort, 1 subject was dosed first. After an 8-day observation period, if the dose was deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were dosed. Escalation to the next dose cohort only occurred after the SRC had reviewed available safety data (through to Day 15 for a set number of subjects) and made a determination that it was acceptable to continue.

Reporting group title	Part B Patient - 3.0 mg/kg
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Reporting group description:

This was the second dose level administered in Part B (PH Patient) of the study. 8 participants were administered 3.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. All participants received active IMP.

In Part B, subjects were only dosed once the SRC had determined acceptable safety of the same dose in Part A. Subjects were enrolled into this cohort in accordance with the inclusion & exclusion criteria of the protocol. Within each cohort, 1 subject was dosed first. After an 8-day observation period, if the dose was deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were dosed. Escalation to the next dose cohort only occurred after the SRC had reviewed available safety data (through to Day 15 for a set number of subjects) and made a determination that it was acceptable to continue.

Reporting group title	Part B Patient - 6.0 mg/kg
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Reporting group description:

This was the third and final dose level administered in Part B (PH Patient) of the study. 4 participants were administered 6.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. All participants received active IMP.

In Part B, subjects were only dosed once the SRC had determined acceptable safety of the same dose in Part A. Subjects were enrolled into this cohort in accordance with the inclusion & exclusion criteria of the protocol. Within each cohort, 1 subject was dosed first. After an 8-day observation period, if the dose was deemed safe and tolerated (with no medically important AEs) by the SRC, the remaining participants in the cohort were dosed. This was the final dose level evaluated in Part B and therefore no further dose escalation was undertaken.

Reporting group title	Part A Placebo Group
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Reporting group description:

This arm relates to the reporting group for the participants within Part A of the study who were randomised to receive placebo within all cohorts. This totals 10 participants across the 5 cohorts in Part A.

Primary: Treatment Emergent Adverse Events (Part A & Part B)

End point title	Treatment Emergent Adverse Events (Part A & Part B) ^[1]
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End point description:

This primary endpoint relates to the number of subjects who reported a treatment emergent adverse event (TEAE) across all study parts. In Part A, 3 participants receiving placebo and 4 participants receiving DCR-PHXC experienced at least 1 TEAE. All TEAEs with severity assessed were considered mild or moderate in severity and no TEAEs with relationship assessed were considered related to treatment.

In Part B, 17 participants experienced at least 1 TEAE. The majority of TEAEs were considered mild or moderate in severity; 3 participants had TEAEs that were considered severe. Treatment-related TEAEs were reported in 11 participants and did not appear to increase with increasing dose. Treatment-emergent SAEs were reported in 4 participants and were not considered treatment related.

There were no DLTs or TEAEs which resulted in discontinuation of study drug in either part.

End point type	Primary
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End point timeframe:

For Part A, TEAEs were collected beginning with Day 1 through Day 29/EOS. For Part B, TEAEs were collected beginning with the signing of informed consent through Day 57/EOS following the dose of IMP, or until the final follow-up visit for participants.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Treatment Emergent Adverse Events were listed as descriptive statistics with no statistical analyses conducted.

End point values	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg	Part A HV - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Number of Subjects	0	0	1	2

End point values	Part A HV - 12.0 mg/kg	Part B Patient - 1.5 mg/kg	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	8	4
Units: Number of Subjects	1	5	8	4

End point values	Part A Placebo Group			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Number of Subjects	3			

Statistical analyses

No statistical analyses for this end point

Primary: Potentially Clinically Significant Shifts in haematologic parameters including coagulation and cytokines at any study visit from baseline value

End point title	Potentially Clinically Significant Shifts in haematologic parameters including coagulation and cytokines at any study visit from baseline value ^[2]
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End point description:

This primary endpoint will report the number of subjects who had a potentially clinically significant shift in any measured haematologic or cytokine parameters from the baseline measurement at any study visit from dose administration of the IMP (excluding screening and Day -1) through to the end of study visit on Day 29 or Day 57 (Part A and B, respectively).

Shifts are defined as any value that was flagged as outside of normal within the pre-defined study ranges for each parameter. These shifts do not necessarily confer clinical significance.

There were no clinically significant changes or obvious trends observed in any haematology parameters during Part A or Part B of the study. There were no treatment or dose-related changes in any parameters during Part A or Part B.

End point type	Primary
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End point timeframe:

Haematology parameters including coagulation for all study parts were measured at set time points from Day 0 until the end of study visit (Day 29 in Part A and Day 57 in Part B).

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Shifts in hematologic and coagulation parameters, including CBC were listed as descriptive statistics with no statistical analyses conducted.

End point values	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg	Part A HV - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Number of Subjects	0	0	0	0

End point values	Part A HV - 12.0 mg/kg	Part B Patient - 1.5 mg/kg	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	8	4
Units: Number of Subjects	0	0	0	0

End point values	Part A Placebo Group			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Number of Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Potentially Clinically Significant Shifts in other clinical laboratory parameters including serum chemistry and urinalysis at any study visit from baseline value

End point title	Potentially Clinically Significant Shifts in other clinical laboratory parameters including serum chemistry and urinalysis at any study visit from baseline value ^[3]
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End point description:

This primary endpoint reports the number of subjects who had a potentially clinically significant shift in any measured serum chemistry or urinalysis parameter from the baseline measurement at any study visit from dose administration of the IMP (excluding screening and Day -1) through to the end of study visit on Day 29 or Day 57 (Part A and B, respectively).

Shifts are defined as any value that was flagged as outside of normal within the pre-defined ranges for each parameter. These shifts do not necessarily confer clinical significance.

There was one potentially clinically significant shift in one subject in Part B in the 6.0 mg/kg group (elevated liver function tests, including AST, ALT, and bilirubin, throughout the study). There were no clinically significant changes or obvious trends observed in any serum chemistry or urinalysis parameters during Part A or Part B of the study. There were no treatment or dose-related changes in any parameters during Part A or Part B.

End point type	Primary
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End point timeframe:

Clinical laboratory parameters including serum chemistry and urinalysis for all study parts were measured at set time points from Day 0 until the end of study visit (Day 29 in Part A and Day 57 in Part B).

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Shifts in other clinical laboratory test results, including serum chemistries and urinalysis were listed as descriptive statistics with no statistical analyses conducted.

End point values	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg	Part A HV - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Number of Subjects	0	0	0	0

End point values	Part A HV - 12.0 mg/kg	Part B Patient - 1.5 mg/kg	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	8	4
Units: Number of Subjects	0	0	0	1

End point values	Part A Placebo Group			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Number of Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Potentially Clinically Significant Shifts in vital sign measurements at any study visit from baseline value

End point title	Potentially Clinically Significant Shifts in vital sign measurements at any study visit from baseline value ^[4]
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End point description:

This primary endpoint will report the number of subjects who had a potentially clinically significant shift in any measured vital signs parameter from the baseline measurement at any study visit from dose administration of the IMP (excluding screening and Day -1) through to the end of study visit on Day 29 or Day 57 (Part A and B, respectively).

Shifts are defined as any value that was flagged as outside of normal within the pre-defined study ranges for each parameter. These shifts do not necessarily confer clinical significance.

There were no clinically significant changes in individual participant's vital signs during the study. There were no treatment or dose-related trends or changes in vital signs data observed between any treatment group.

End point type	Primary
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End point timeframe:

Vital Signs parameters for all study parts were measured at set time points from Day 0 until the end of study visit (Day 29 in Part A and Day 57 in Part B).

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Shifts in vital sign measurements were listed as descriptive statistics with no statistical analyses conducted.

End point values	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg	Part A HV - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Number of Subjects	0	0	0	0

End point values	Part A HV - 12.0 mg/kg	Part B Patient - 1.5 mg/kg	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	8	4
Units: Number of Subjects	0	0	0	0

End point values	Part A Placebo Group			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Number of Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Potentially Clinically Significant Shifts in 12-lead ECG parameters at any study visit from baseline value

End point title	Potentially Clinically Significant Shifts in 12-lead ECG parameters at any study visit from baseline value ^[5]
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End point description:

This primary endpoint will report the number of subjects who had a potentially clinically significant shift in any measured 12-lead ECG parameters from the baseline measurement at any study visit from dose administration of the IMP (excluding screening and Day -1) through to the end of study visit on Day 29 or Day 57 (Part A and B, respectively).

Shifts are defined as any value that was flagged as outside of normal within the pre-defined study ranges for each parameter. These shifts do not necessarily confer clinical significance.

There were no clinically significant changes or obvious trends observed in any ECG parameters during Part A or Part B of the study. There were no treatment or dose-related changes in any parameters during Part A or Part B.

End point type	Primary
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End point timeframe:

12-lead ECG parameters for all study parts were measured at set time points from Day 0 until the end of study visit (Day 29 in Part A and Day 57 in Part B).

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Shifts in 12-lead ECG findings were listed as descriptive statistics with no statistical analyses conducted.

End point values	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg	Part A HV - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Number of Subjects	0	0	0	0

End point values	Part A HV - 12.0 mg/kg	Part B Patient - 1.5 mg/kg	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	8	4
Units: Number of Subjects	0	0	0	0

End point values	Part A Placebo Group			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Number of Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Potentially Clinically Significant Shifts in physical examination parameters at any study visit from screening visit observation

End point title	Potentially Clinically Significant Shifts in physical examination parameters at any study visit from screening visit observation ^[6]
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End point description:

This primary endpoint will report the number of subjects who had a potentially clinically significant shift in any measured physical examination parameter/finding from the baseline measurement (defined as screening assessment) at any study visit from dose administration of the IMP (excluding screening and Day -1) through to the end of study visit on Day 29 or Day 57 (Part A and B, respectively).

Shifts are defined as any value that was flagged as abnormal for each body system evaluated as part of the physical examination deemed to be clinically significant.

There were no abnormal clinically significant findings in Part A. There were 4 abnormal clinically significant PE findings in Group B. Details of these are listed descriptively within the full CSR.

End point type	Primary
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End point timeframe:

Physical Examination for all study parts was conducted at set time points from Day -1 until the end of study visit.

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Shifts in physical examination findings were listed as descriptive statistics with no statistical analyses conducted.

End point values	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg	Part A HV - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Number of Subjects	0	0	0	0

End point values	Part A HV - 12.0 mg/kg	Part B Patient - 1.5 mg/kg	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	8	4
Units: Number of Subjects	0	1	0	3

End point values	Part A Placebo Group			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Number of Subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve from time 0 to 24 hr (AUC0-24) in plasma - Part A

HV

End point title	Area under the curve from time 0 to 24 hr (AUC0-24) in plasma - Part A HV ^[7]
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End point description:

This secondary endpoint will report the relevant summary values for subjects who had evaluable results for the respective pharmacokinetic parameter listed.

End point type	Secondary
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End point timeframe:

Time points for pharmacokinetic evaluation of AUC0-24 in plasma in all cohorts of Part A were as follows: pre-dose on Day 1, and at 5, 15, and 30 minutes and 1, 2, 4, 6, 8, and 12 hours, and at Days 2, 3, 8, 15, 22 and 29.

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This end point relates to Part A of the study only. Area under the curve from time 0 to 24 hr parameters were reported independently for each study part. Therefore the reported values reflect the analyses carried out for this parameter as they relate to the subjects in Part A only.

End point values	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg	Part A HV - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: ng.hr/mL				
geometric mean (geometric coefficient of variation)	1060.0 (± 23.1)	5650.0 (± 27.2)	11300.0 (± 44.9)	24400.0 (± 13.4)

End point values	Part A HV - 12.0 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ng.hr/mL				
geometric mean (geometric coefficient of variation)	65700.0 (± 5.74)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve from time 0 to time of last measurable plasma concentration (AUClast) - Part A HV

End point title	Area under the curve from time 0 to time of last measurable plasma concentration (AUClast) - Part A HV ^[8]
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End point description:

This secondary endpoint will report the relevant summary values for subjects who had evaluable results for the respective pharmacokinetic parameter listed.

End point type	Secondary
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End point timeframe:

Time points for pharmacokinetic evaluation of AUClast in plasma in all cohorts of Part A were as follows: pre-dose on Day 1, and at 5, 15, and 30 minutes and 1, 2, 4, 6, 8, and 12 hours, and at Days 2, 3, 8, 15, 22 and 29.

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This end point relates to Part A of the study only. Area under the curve from time 0 to time of last measurable plasma concentration parameters were reported independently for each study part. Therefore the reported values reflect the analyses carried out for this parameter as they relate to the subjects in Part A only.

End point values	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg	Part A HV - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: ng.hr/mL				
geometric mean (geometric coefficient of variation)	1190.0 (\pm 22.9)	6160.0 (\pm 29.9)	15500.0 (\pm 25.0)	35700.0 (\pm 24.8)

End point values	Part A HV - 12.0 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ng.hr/mL				
geometric mean (geometric coefficient of variation)	84500.0 (\pm 3.32)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve from time 0 extrapolated to infinity (AUC0-inf) in plasma - Part A HV

End point title	Area under the curve from time 0 extrapolated to infinity (AUC0-inf) in plasma - Part A HV ^[9]
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End point description:

This secondary endpoint will report the relevant summary values for subjects who had evaluable results for the respective pharmacokinetic parameter listed.

End point type	Secondary
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End point timeframe:

Time points for pharmacokinetic evaluation of AUC0-inf in plasma in all cohorts of Part A were as follows: pre-dose on Day 1, and at 5, 15, and 30 minutes and 1, 2, 4, 6, 8, and 12 hours, and at Days 2, 3, 8, 15, 22 and 29.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This end point relates to Part A of the study only. Area under the curve from time 0 extrapolated to infinity parameters were reported independently for each study part. Therefore the reported values reflect the analyses carried out for this parameter as they relate to the subjects in Part A only.

End point values	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg	Part A HV - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2 ^[10]	3	1 ^[11]	3
Units: ng.hr/mL				
geometric mean (geometric coefficient of variation)	1440.0 (± 6.41)	6380.0 (± 27.1)	13100.0 (± 0.0)	35800.0 (± 24.5)

Notes:

[10] - 3 subjects within the cohort received active DCR-PHXC. 1 subject excluded from analysis set.

[11] - 3 subjects within the cohort received active DCR-PHXC. 2 subjects excluded from analysis set.

End point values	Part A HV - 12.0 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[12]			
Units: ng.hr/mL				
geometric mean (geometric coefficient of variation)	()			

Notes:

[12] - 3 subjects in the cohort received active DCR-PHXC. No result obtained for any subject within set.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of AUC due to extrapolation from Tlast to infinity (AUCext) in plasma - Part A HV

End point title	Percentage of AUC due to extrapolation from Tlast to infinity (AUCext) in plasma - Part A HV ^[13]
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End point description:

This secondary endpoint will report the relevant summary values for subjects who had evaluable results for the respective pharmacokinetic parameter listed.

End point type	Secondary
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End point timeframe:

Time points for pharmacokinetic evaluation of AUCext in plasma in all cohorts of Part A were as follows: pre-dose on Day 1, and at 5, 15, and 30 minutes and 1, 2, 4, 6, 8, and 12 hours, and at Days 2, 3, 8, 15, 22 and 29.

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This end point relates to Part A of the study only. Percentage of AUC due to extrapolation from Tlast to infinity parameters were reported independently for each study part. Therefore the reported values reflect the analyses carried out for this parameter as they relate to the subjects in Part A only.

End point values	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg	Part A HV - 6.0 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2 ^[14]	3	1 ^[15]	3
Units: percent				
geometric mean (geometric coefficient of variation)	5.96 (± 108.0)	4.03 (± 94.2)	5.99 (± 0.0)	0.364 (± 119.0)

Notes:

[14] - 3 subjects within the cohort received active DCR-PHXC. 1 subject excluded from analysis set.

[15] - 3 subjects within the cohort received active DCR-PHXC. 2 subjects excluded from analysis set.

End point values	Part A HV - 12.0 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[16]			
Units: percent				
geometric mean (geometric coefficient of variation)	()			

Notes:

[16] - 3 subjects within the cohort received active DCR-PHXC. No result obtained for any subject within set

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve from time 0 to 24 hr (AUC0-24) in plasma - Part B PH Patient

End point title	Area under the curve from time 0 to 24 hr (AUC0-24) in plasma - Part B PH Patient ^[17]
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End point description:

This secondary endpoint will report the relevant summary values for subjects who had evaluable results for the respective pharmacokinetic parameter listed.

End point type	Secondary
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End point timeframe:

Time points for evaluation of AUC0-24 in plasma in all cohorts of Part B were as follows: pre-dose Day 1 & 5, 15, 30 mins & 1, 2, 4, 6, 8, 12 hr & Days 2, 3, 8, 15, 22/29, 43 & 57 for participants aged 12 to 17 years (inclusive) and adults.

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This end point relates to Part B of the study only. Area under the curve from time 0 to 24 hr parameters were reported independently for each study part. Therefore the reported values reflect the analyses carried out for this parameter as they relate to the subjects in Part B only.

End point values	Part B Patient - 1.5 mg/kg	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	8	4	
Units: h.ng/mL				
geometric mean (geometric coefficient of variation)	7940.0 (± 27.9)	15000.0 (± 41.1)	33400.0 (± 32.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve from time 0 to time of last measurable plasma

concentration (AUClast) - Part B PH Patient

End point title	Area under the curve from time 0 to time of last measurable plasma concentration (AUClast) - Part B PH Patient ^[18]
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End point description:

This secondary endpoint will report the relevant summary values for subjects who had evaluable results for the respective pharmacokinetic parameter listed.

End point type	Secondary
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End point timeframe:

Time points for evaluation of AUC0-last in plasma in all cohorts of Part B were as follows: pre-dose Day 1 & 5, 15, 30 mins & 1, 2, 4, 6, 8, 12 hr & Days 2, 3, 8, 15, 22/29, 43 & 57 for participants aged 12 to 17 years (inclusive) and adults.

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This end point relates to Part B of the study only. Area under the curve from time 0 to time of last measurable plasma concentration parameters were reported independently for each study part. Therefore the reported values reflect the analyses carried out for this parameter as they relate to the subjects in Part B only.

End point values	Part B Patient - 1.5 mg/kg	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	8	4	
Units: h.ng/mL				
geometric mean (geometric coefficient of variation)	9860.0 (± 18.7)	19200.0 (± 39.2)	43300.0 (± 35.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve from time 0 extrapolated to infinity (AUC0-inf) in plasma - Part B PH Patient

End point title	Area under the curve from time 0 extrapolated to infinity (AUC0-inf) in plasma - Part B PH Patient ^[19]
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End point description:

This secondary endpoint will report the relevant summary values for subjects who had evaluable results for the respective pharmacokinetic parameter listed.

End point type	Secondary
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End point timeframe:

Time points for evaluation of AUC0-inf in plasma in all cohorts of Part B were as follows: pre-dose Day 1 & 5, 15, 30 mins & 1, 2, 4, 6, 8, 12 hr & Days 2, 3, 8, 15, 22/29, 43 & 57 for participants aged 12 to 17 years (inclusive) and adults.

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This end point relates to Part B of the study only. Area under the curve from time 0 extrapolated to infinity parameters were reported independently for each study part. Therefore the reported values reflect the analyses carried out for this parameter as they relate to the subjects in Part B only.

End point values	Part B Patient - 1.5 mg/kg	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4 ^[20]	1 ^[21]	1 ^[22]	
Units: h.ng/mL				
geometric mean (geometric coefficient of variation)	10700.0 (± 5.90)	15900.0 (± 0.0)	28200.0 (± 0.0)	

Notes:

[20] - All subjects within the cohort received active DCR-PHXC. 2 subjects excluded from analysis set.

[21] - All subjects within the cohort received active DCR-PHXC. 7 subjects excluded from analysis set.

[22] - All subjects within the cohort received active DCR-PHXC. 3 subjects excluded from analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of AUC due to extrapolation from Tlast to infinity (AUCext) in plasma - Part B PH Patient

End point title	Percentage of AUC due to extrapolation from Tlast to infinity (AUCext) in plasma - Part B PH Patient ^[23]
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End point description:

This secondary endpoint will report the relevant summary values for subjects who had evaluable results for the respective pharmacokinetic parameter listed.

End point type	Secondary
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End point timeframe:

Time points for evaluation of AUCext in plasma in all cohorts of Part B were as follows: pre-dose Day 1 & 5, 15, 30 mins & 1, 2, 4, 6, 8, 12 hr & Days 2, 3, 8, 15, 22/29, 43 & 57 for participants aged 12 to 17 years (inclusive) and adults.

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This end point relates to Part B of the study only. Percentage of AUC due to extrapolation from Tlast to infinity parameters were reported independently for each study part. Therefore the reported values reflect the analyses carried out for this parameter as they relate to the subjects in Part B only.

End point values	Part B Patient - 1.5 mg/kg	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4 ^[24]	1 ^[25]	1 ^[26]	
Units: percent				
geometric mean (geometric coefficient of variation)	0.130 (± 73.9)	0.298 (± 0.0)	1.20 (± 0.0)	

Notes:

[24] - All subjects within the cohort received active DCR-PHXC. 2 subjects excluded from analysis set.

[25] - All subjects within the cohort received active DCR-PHXC. 7 subjects excluded from analysis set.

[26] - All subjects within the cohort received active DCR-PHXC. 3 subjects excluded from analysis set.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For Part A, AEs were collected beginning with Day 1 through Day 29/EOS. For Part B, AEs were collected beginning with the signing of informed consent through Day 57/EOS following the dose of IMP, or until the final follow-up visit for participants.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	Part A HV - 0.3 mg/kg
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Reporting group description:

This was the first and lowest dose level administered in Part A (Healthy Volunteer) of the study. 3 participants were administered 0.3 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. The remaining 2 participants received matching placebo.

Reporting group title	Part A HV - 1.5 mg/kg
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Reporting group description:

This was the second dose level administered in Part A (Healthy Volunteer) of the study. 3 participants were administered 1.5 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. The remaining 2 participants received matching placebo.

Reporting group title	Part A HV - 3.0 mg/kg
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Reporting group description:

This was the third dose level administered in Part A (Healthy Volunteer) of the study. 3 participants were administered 3.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. The remaining 2 participants received matching placebo.

Reporting group title	Part A HV - 6.0 mg/kg
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Reporting group description:

This was the fourth dose level administered in Part A (Healthy Volunteer) of the study. 3 participants were administered 6.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. The remaining 2 participants received matching placebo.

Reporting group title	Part A HV - 12.0 mg/kg
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Reporting group description:

This was the fifth and final dose level administered in Part A (Healthy Volunteer) of the study. 3 participants were administered 12.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. The remaining 2 participants received matching placebo.

Reporting group title	Part B Patient - 1.5 mg/kg
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Reporting group description:

This was the first dose level administered in Part B (PH Patient) of the study. 6 participants were administered 1.5 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. All participants received active IMP.

Reporting group title	Part B Patient - 3.0 mg/kg
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Reporting group description:

This was the second dose level administered in Part B (PH Patient) of the study. 8 participants were administered 3.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. All participants received active IMP.

Reporting group title	Part B Patient - 6.0 mg/kg
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Reporting group description:

This was the third and final dose level administered in Part B (PH Patient) of the study. 4 participants were administered 6.0 mg/kg of DCR-PHXC (administered as a subcutaneous injection) on one occasion on Day 1. All participants received active IMP.

Reporting group title	Part A Placebo Group
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Reporting group description:

This reporting group relates to the participants across all cohorts in Part A who received placebo rather than active DCR-PHXC. Across all 5 cohorts of Part A, this totals 10 participants.

Serious adverse events	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Appendicitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteral stone			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part A HV - 6.0 mg/kg	Part A HV - 12.0 mg/kg	Part B Patient - 1.5 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Appendicitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteral stone			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg	Part A Placebo Group
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	2 / 4 (50.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Appendicitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Pyelonephritis			
subjects affected / exposed	2 / 8 (25.00%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteral stone			

subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0.05 %

Non-serious adverse events	Part A HV - 0.3 mg/kg	Part A HV - 1.5 mg/kg	Part A HV - 3.0 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Ureteral stent removal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site haemorrhage			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cough			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Interleukin level increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mean cell volume abnormal			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Protein urine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine leukocyte esterase			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Teething			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Calculus urinary			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cystitis noninfective			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nephrolithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Polyuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal colic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part A HV - 6.0 mg/kg	Part A HV - 12.0 mg/kg	Part B Patient - 1.5 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	5 / 6 (83.33%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			

Ureteral stent removal subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
General disorders and administration site conditions			
Injection site reaction subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 3 (33.33%) 1	1 / 6 (16.67%) 1
Asthenia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Catheter site pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Fatigue subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Injection site erythema subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1
Injection site haemorrhage subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Injection site pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Injection site paraesthesia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Injection site pruritus subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Injection site urticaria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Malaise			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Pain			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Pyrexia			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Vessel puncture site pain			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 6 (16.67%) 2
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Cough			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Epistaxis			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1
Rhinorrhoea			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1
Psychiatric disorders			
Anxiety			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Insomnia			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Investigations			

Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Interleukin level increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Mean cell volume abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Protein urine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urine leukocyte esterase			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Arthropod bite subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	3 / 6 (50.00%) 8 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Teething subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	0 / 6 (0.00%) 0 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0

Vomiting subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Skin and subcutaneous tissue disorders			
Acne subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Eczema subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Urticaria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Renal and urinary disorders			
Pollakiuria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Calculus urinary subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Cystitis noninfective subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Polyuria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Renal colic subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Renal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	3
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinitis			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Metabolism and nutrition disorders Iron deficiency subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0

Non-serious adverse events	Part B Patient - 3.0 mg/kg	Part B Patient - 6.0 mg/kg	Part A Placebo Group
Total subjects affected by non-serious adverse events subjects affected / exposed	8 / 8 (100.00%)	4 / 4 (100.00%)	3 / 10 (30.00%)
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0
Surgical and medical procedures Ureteral stent removal subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 4 (25.00%) 1	0 / 10 (0.00%) 0
General disorders and administration site conditions Injection site reaction subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0
Asthenia subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0
Catheter site pain subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0
Fatigue			

subjects affected / exposed	2 / 8 (25.00%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Injection site erythema			
subjects affected / exposed	2 / 8 (25.00%)	2 / 4 (50.00%)	0 / 10 (0.00%)
occurrences (all)	2	3	0
Injection site haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injection site pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Injection site paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Injection site pruritus			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injection site urticaria			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	2 / 8 (25.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Vessel puncture site pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Dysmenorrhoea			

subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Blood creatinine increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Interleukin level increased			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Mean cell volume abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Protein urine			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Urine leukocyte esterase			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
White blood cell count increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 8 (62.50%)	1 / 4 (25.00%)	1 / 10 (10.00%)
occurrences (all)	10	9	1
Lethargy			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 4 (25.00%) 1	0 / 10 (0.00%) 0
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	1 / 10 (10.00%) 1
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2	1 / 4 (25.00%) 1	0 / 10 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 3	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 4	1 / 4 (25.00%) 6	0 / 10 (0.00%) 0
Teething subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	5 / 8 (62.50%) 5	1 / 4 (25.00%) 3	0 / 10 (0.00%) 0
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0
Eczema subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 4 (25.00%) 1	0 / 10 (0.00%) 0
Urticaria subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	2 / 4 (50.00%) 2	0 / 10 (0.00%) 0
Renal and urinary disorders			

Pollakiuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Calculus urinary			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Cystitis noninfective			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nephrolithiasis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Polyuria			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Renal colic			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Renal pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 8 (37.50%)	2 / 4 (50.00%)	0 / 10 (0.00%)
occurrences (all)	3	4	0
Myalgia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Arthralgia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal pain			

subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	2 / 8 (25.00%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Pharyngitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	2 / 8 (25.00%)	1 / 4 (25.00%)	0 / 10 (0.00%)
occurrences (all)	4	1	0
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vitamin D deficiency			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 November 2017	This amendment concerned an update to the study protocol from v1.0 to v2.0. The summary of changes are as follows: <ul style="list-style-type: none">- Clarified that placebo will be supplied by the pharmacy at the clinical site.- Added emergency unblinding instructions.
28 November 2017	This amendment concerned an update to the study protocol from v2.0 to v3.0. The summary of changes are as follows: <ul style="list-style-type: none">- Added United States to list of sites.- Clarified that participants will be admitted to clinic on Day 0 through Day 3 and allowed participants to opt to be discharged and readmitted each day during this period.- Updated total blood volume collected for HV.- Updated schedule of events to remove urine aliquot at 6-hrs post gelatin-loading dose for oxalate and metabolite panel, to clarify ECGs were to be performed 30 mins post dose, to clarify that participants were to be re-weighed on Day 0, and to update AE collection to begin at Day 1.- Removed requirement for participants to drink 250 mL of bottled water after gelatin load and removed aliquot of urine taken 6-hours post ingestion of gelatin-loaded breakfast.- Removed requirement for participants to be admitted to clinic Day 22 and Day 43.- Corrected typographical errors and made minor administrative changes.
14 February 2018	This amendment concerned an update to the study protocol from v3.0 to v4.0. The summary of changes are as follows: <ul style="list-style-type: none">- Clarified that dosing was based on a 75 mg, adult participant.- Removed option for participants in low dose cohort to receive a second single dose at a higher dose level.- Clarified that IMP should be removed from refrigeration approximately 1 hour prior to administration and allow solution to reach room temperature.- Clarified stopping rules to reflect that any single adverse event experienced by a single patient that is "Grade 3 Severe, Serious" or higher will result in dose level suspension.- Clarified that AEs and SAEs are collected from the time of informed consent.- The window for the Day 8 visit was changed from ± 1 day to ± 2 days.- The window for the Day 15, Day 22, and Day 43 visits was changed from ± 1 day to ± 3 days.- Clarified that 24-hour urine screening sample to be collected at home.- Clarified that vital signs and ECGs were measured at 30 minutes post-dosing.- Clarified timing of urinalysis sample and urine sample for biomarkers of renal tubular injury.- Updated duration of Screening window.- Clarified which urine samples were to be collected in clinic.- Updated schedule for admission and discharge from clinic.- Minor administrative changes.
22 February 2018	This amendment concerned an update to the study protocol from v4.0 to v5.0. The summary of changes are as follows: <ul style="list-style-type: none">- Minor administrative changes.

20 March 2018	<p>This amendment concerned an update to the study protocol from v5.0 to v6.0. The summary of changes are as follows:</p> <ul style="list-style-type: none"> - Added burden assessment for pediatric participants. - Updated total blood volume collected, blood collection requirements and text relating to failed venipuncture attempts in children to align the protocol more closely with the European Commission's "Ethical considerations for clinical trials on medicinal products conducted with minors" (18 September 2017). - Clarified dosing levels. - Updated plasma requirements to not require glycolate for participants aged 6-11 years old and to not require plasma glyoxylate samples for participants aged 12-17. - Explicit endpoints added to the primary objective and endpoints section. - Added drug and alcohol screening. - Removed double barrier method of contraception as a stand-alone method of acceptable contraception in inclusion criterion for Groups A and B. - Update the minimum weight for minors in conjunction with changes to the blood sampling schedule for minors in order to align the protocol more closely with the European Commission's "Ethical considerations for clinical trials on medicinal products conducted with minors" (18 September 2017) for Groups A and B. - Updated definition of post-menopausal female. - Added a sub-bullet of 'any clinically significant (in the opinion of the Investigator), age-appropriate abnormality in screening data (including serum chemistry, hematology, coagulation parameters, blood pressure, pulse rate, and ECG findings)' to Exclusion Criterion related to medical condition or co-morbidities for Groups A and B. - Added exclusion criterion of 'Known hypersensitivity to DCR-PHXC or any of its ingredients' for Groups A and B. - Updated text relating to screen failure and completion rate estimates. - Added text to state that cytokines testing was not to be done at the central laboratory. Deleted lactate and pyruvate from clinical laboratory testing.
25 April 2018	<p>This amendment concerned an update to the study protocol from v6.0 to v7.0. The summary of changes are as follows:</p> <ul style="list-style-type: none"> - Establishment of a minimum effective dose was added as an exploratory objective for Group B and the definition of minimum effective dose was added. - Updated locations of clinical sites. - Updated the NOAEL. - Added drug anti-body testing and updated blood volumes to reflect addition of anti-drug antibody testing. - Added text stating that glyoxylate samples in adults were optional. - Updated text to reflect that the first participant must have completed Day 8 assessments for review of data by the SRC prior to continued dosing within a cohort. - Added text that no participant under the age of 18 may have enrolled until a minimum effective dose was established in adults. - Text was added to indicate that AEs were to be graded with the terms mild, moderate or severe. - Updated text to reflect changes to SRC decision making with regard to changes in enrollment, dose escalation and dose progression, in accordance with feedback from Regulatory Agencies. - Text added to list of assessments to include questioning of participants with regard to signs or symptoms of muscle pain. - Text added to indicate that collection plasma oxalate and glycolate will only occur in patients aged 12-17 inclusive. - Updated text relating to criteria for study termination to be more specific. - New section added to detail how retained samples will be processed, stored and used. - Text added to define non-serious and serious DLTs. - Added text relating to implementation of the General Data Protection Regulation. - Added text to clarify that the study is not statistically powered. - Text changed to clarify that the consent form must be signed in the presence of the PI. - Minor administrative changes and clarifications.

10 July 2018	<p>This amendment concerned an update to the study protocol from v7.0 to v8.0. The summary of changes are as follows:</p> <ul style="list-style-type: none"> - Removed CTCAE scale for grading of AEs and clarified that all AEs will be graded as mild, moderate, or severe. - Stopping rules were updated to reflect removal of CTCAE grading of AEs. - Text referring to CTCAE grading of injection site reactions was deleted. - The Day 22 visit in Group B was changed to Day 29 in order to more evenly monitor participants' safety over the course of the study. - Expanded the window surrounding the performance of multiple assessments for Group B participants from ± 10 minutes to ± 30 minutes in order to facilitate timely completion of the safety and PK assessments. - Updated the composition of the SRC to reflect the inclusion of an ethicist to further protect the rights of pediatric participants. - Text was added to allow the injection of IMP into either the abdomen or the thigh. - The requirement for the second 24-hour urine sample collection to be completed at least 14 days prior to Day 0 was deleted. - Minor administrative changes and clarifications. <p>In addition, there was a country specific amendment for the Netherlands - Protocol v8.0, date 21-Aug-2018.</p>
06 March 2019	<p>This amendment concerned an update to the study protocol from v8.0 to v9.0. The summary of changes are as follows:</p> <ul style="list-style-type: none"> - Updated protocol to allow patients whose 24-hour urinary oxalate concentration had not returned to within 80% of baseline to roll over into study DCR PXHC-301 prior to meeting the $\geq 80\%$ threshold. <p>Note that in addition to this global amendment, there were also 2 country specific protocol amendments for the Netherlands (v8.1 - 07 September 2018 and v9.1 - 06 March 2019) respectively.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

It is noted that for the Estimated Glomerular Filtration Rate parameter in baseline characteristics, where 0 values are recorded for reporting groups, this is due to the fact that this parameter was not measured within these groups.

Notes: