



Clinical trial results:

A Phase 1 Placebo-Controlled, Double-Blind, Multicenter Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of a Single Dose of DCR-PHXC in Patients with Primary Hyperoxaluria Type 3

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2020-000344-67 |
| Trial protocol | GB DE FR NL |
| Global end of trial date | 07 September 2021 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 24 August 2022 |
| First version publication date | 24 August 2022 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | DCR-PHXC-104 |
|-----------------------|--------------|

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, Lexington, MA, United States, 02421 |
| Public contact | Andrew Henderson, Dicerna Pharmaceuticals, Inc., 001 617 612 6275, ahenderson@dicerna.com |
| Scientific contact | Andrew Henderson, Dicerna Pharmaceuticals, Inc., 001 617 612 6275, ahenderson@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 | 01 October 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 07 September 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 September 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of a single dose of nedosiran (DCR-PHXC) in patients with PH3

Protection of trial subjects:

The Investigator or their representative explained the nature of the study to the participant or their legally authorized representative and answered all questions regarding the study.

Participants were informed that their participation was voluntary. Participants or their legally authorized representative were required to sign a statement of informed consent that met the requirements of 21 CFR 50, local regulations, ICH guidelines, HIPAA requirements, where applicable, and the institutional review board/independent ethics committee or study center.

The medical record included a statement that written informed consent was obtained before the participant was enrolled in the study and the date the written consent was obtained. The authorized person obtaining the informed consent also signed the informed consent form (ICF).

Participants were re-consented to the most current version of the ICF(s) during their participation in the study.

A copy of the ICF(s) was provided to the participant or the participant's legally authorized representative.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 01 July 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Netherlands: 1 |
| Country: Number of subjects enrolled | Germany: 1 |
| Country: Number of subjects enrolled | United States: 4 |
| Worldwide total number of subjects | 6 |
| EEA total number of subjects | 2 |

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) | 1 |
| Adults (18-64 years) | 5 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The screening period lasted up to 35 days (with an extra 7-day period for participants who were required to repeat screening 24-hour urine collections or initially unanalyzable screening laboratory assessment samples)

Period 1

| | |
|------------------------------|------------------|
| Period 1 title | Screening Period |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | Yes |
| Arm title | Nedosiran |

Arm description: -

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nedosiran |
| Investigational medicinal product code | |
| Other name | DCR-PHXC, nedosiran sodium, DCR-L1360 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of nedosiran was given on Day 1 to those randomized to the nedosiran arm through subcutaneous injection (thigh or abdomen).

No nedosiran was administered during the Screening Period or the Follow-up Period.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description: -

| | |
|--|---------------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | 0.9% saline |
| Investigational medicinal product code | |
| Other name | sterile saline, normal saline, saline |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of 0.9% saline for injection was given on Day 1 to those randomized to the placebo arm through subcutaneous injection (thigh or abdomen).

No placebo was administered during the Screening Period or the Follow-up Period.

| Number of subjects in period 1 | Nedosiran | Placebo |
|--------------------------------|-----------|---------|
| Started | 4 | 2 |
| Completed | 4 | 2 |

Period 2

| | |
|------------------------------|---|
| Period 2 title | Dosing Period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer |

Blinding implementation details:

All participants were centrally assigned to randomized study intervention using an interactive web response system.

Arms

| | |
|--|---------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Nedosiran |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Nedosiran |
| Investigational medicinal product code | |
| Other name | DCR-PHXC, nedosiran sodium, DCR-L1360 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Sterile formulation of drug substance (DCR-L1360) was provided in water for injection at 170 mg/mL sodium salt (free acid equivalent [FAE] 160 mg/mL). A single dose of nedosiran was given on Day 1 to those randomized to the nedosiran arm through subcutaneous injection (thigh or abdomen) at the following dose levels:

Age \geq 12 years: 3 mg/kg (FAE 2.8 mg/kg)

Age 6-11 years: 3.5 mg/kg (FAE 3.3 mg/kg), not to exceed 136 mg

The maximum volume of a single SC injection was 1.0 mL in participants \geq 12 years; if the participant's weight required an injection volume $>$ 1.0 mL, the total dose was administered as 2 or more SC injections of equal volume. The maximum injection volume in participants aged less than 12 years was 0.5 mL; if the participant's weight required an injection volume $>$ 0.5 mL, the total dose was administered as 2 or more SC injections of equal volume.

| | |
|--|---------------------------------------|
| Arm title | Placebo |
| Arm description: - | |
| Arm type | Placebo |
| Investigational medicinal product name | 0.9% saline |
| Investigational medicinal product code | |
| Other name | sterile saline, normal saline, saline |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of 0.9% saline for injection was given on Day 1 through subcutaneous injection (thigh or abdomen), at a volume to match the active drug.

| Number of subjects in period 2 | Nedosiran | Placebo |
|--------------------------------|-----------|---------|
| Started | 4 | 2 |
| Completed | 4 | 2 |

Period 3

| | |
|------------------------------|---|
| Period 3 title | Follow-up Period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer |

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | Yes |
| Arm title | Nedosiran |

Arm description: -

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nedosiran |
| Investigational medicinal product code | |
| Other name | DCR-PHXC, nedosiran sodium, DCR-L1360 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of nedosiran was given on Day 1 to those randomized to the nedosiran arm through subcutaneous injection (thigh or abdomen).

No nedosiran was administered during the Screening Period or the Follow-up Period.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description: -

| | |
|--|---------------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | 0.9% saline |
| Investigational medicinal product code | |
| Other name | sterile saline, normal saline, saline |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of 0.9% saline for injection was given on Day 1 to those randomized to the placebo arm through subcutaneous injection (thigh or abdomen).

No placebo was administered during the Screening Period or the Follow-up Period.

| Number of subjects in period 3 | Nedosiran | Placebo |
|---------------------------------------|-----------|---------|
| Started | 4 | 2 |
| Completed | 4 | 2 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|-----------|
| Reporting group title | Nedosiran |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

| Reporting group values | Nedosiran | Placebo | Total |
|---|-----------|----------|-------|
| Number of subjects | 4 | 2 | 6 |
| Age categorical Units: Subjects | | | |
| Adolescents (12-17 years) | 0 | 1 | 1 |
| Adults (18-64 years) | 4 | 1 | 5 |
| Age continuous Units: years | | | |
| arithmetic mean | 44.8 | 38.0 | |
| standard deviation | ± 13.60 | ± 36.77 | - |
| Gender categorical Units: Subjects | | | |
| Female | 2 | 0 | 2 |
| Male | 2 | 2 | 4 |
| Baseline 24-hour urinary oxalate Units: mmol/day | | | |
| arithmetic mean | 1.302 | 1.018 | |
| standard deviation | ± 0.6026 | ± 0.0753 | - |

End points

End points reporting groups

| | |
|---|-------------------------------|
| Reporting group title | Nedosiran |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | Nedosiran |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | Nedosiran |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |
| Subject analysis set title | Safety Population - Nedosiran |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All participants who received a partial or full dose of nedosiran on Day 1 | |
| Subject analysis set title | Safety Population - Placebo |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All participants who received a partial or full dose of placebo on Day 1 | |
| Subject analysis set title | PK Population - Nedosiran |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All participants who received a full dose of nedosiran and had at least one evaluable postdose PK assessment | |
| Subject analysis set title | mITT Population - Nedosiran |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: All participants who were randomly assigned to nedosiran, received a partial or full dose of nedosiran, and had postdose 24-hour urinary oxalate (Uox) values on at least 2 consecutive visits | |
| Subject analysis set title | mITT Population - Placebo |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: All participants who were randomly assigned to placebo, received a partial or full dose of placebo, and had postdose 24-hour urinary oxalate (Uox) values on at least 2 consecutive visits | |

Primary: Incidence and severity of treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), and adverse events of special interest (AESIs)

| | |
|---|---|
| End point title | Incidence and severity of treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), and adverse events of special interest (AESIs) ^[1] |
| End point description: Injection site reactions were considered AESIs. Signs or symptoms at the injection site with a time to onset of 4 hours (or more) postdose were evaluated according to the CTCAE v. 5.0 criteria. All TEAEs were mild in severity. | |
| End point type | Primary |
| End point timeframe: Day 1 to End of Study | |

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: Primary endpoint refers to a count of participants and/or events, for which no statistical analyses are required.

| End point values | Safety Population - Nedosiran | Safety Population - Placebo | | |
|-----------------------------|-------------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 2 | | |
| Units: events | | | | |
| TEAEs | 6 | 5 | | |
| SAEs | 0 | 0 | | |
| AESIs | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with clinically relevant clinical laboratory test results, including hematology, serum chemistry, and urinalysis

| | |
|-----------------|--|
| End point title | Number of participants with clinically relevant clinical laboratory test results, including hematology, serum chemistry, and urinalysis ^[2] |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Screening to End of Study

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: Primary endpoint refers to a count of participants and/or events, for which no statistical analyses are required.

| End point values | Safety Population - Nedosiran | Safety Population - Placebo | | |
|-----------------------------|-------------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 2 | | |
| Units: participants | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with clinically significant vital signs measurements

| | |
|-----------------|--|
| End point title | Number of participants with clinically significant vital signs measurements ^[3] |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Screening to End of Study

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: Primary endpoint refers to a count of participants and/or events, for which no statistical analyses are required.

| End point values | Safety Population - Nedosiran | Safety Population - Placebo | | |
|-----------------------------|-------------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 2 | | |
| Units: participants | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with clinically significant 12-lead electrocardiogram findings

| | |
|-----------------|--|
| End point title | Number of participants with clinically significant 12-lead electrocardiogram findings ^[4] |
|-----------------|--|

End point description:

One participant in the nedosiran group had a potentially clinically significant ECG finding of a high QTcF interval of 452.0 msec at Day 85. Although the Baseline ECG was normal with a QTcF of 426 msec, the Screening ECG had a high QTcF of 455 msec, suggesting no significant change after nedosiran treatment.

No other potentially clinically significant ECG findings were reported.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Screening to End of Study

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: Primary endpoint refers to a count of participants and/or events, for which no statistical analyses are required.

| End point values | Safety Population - Nedosiran | Safety Population - Placebo | | |
|-----------------------------|-------------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 2 | | |
| Units: participants | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Incidence and nature of treatment-emergent clinically significant physical examination findings

| | |
|-----------------|--|
| End point title | Incidence and nature of treatment-emergent clinically significant physical examination findings ^[5] |
|-----------------|--|

End point description:

One participant in the nedosiran group had a clinically significant abnormal physical examination finding of tenderness in back in right kidney region, which was reported as a TEAE.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 1 to End of Study

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: Primary endpoint refers to a count of participants and/or events, for which no statistical analyses are required.

| End point values | Safety Population - Nedosiran | Safety Population - Placebo | | |
|-----------------------------|-------------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 2 | | |
| Units: participants | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma PK parameters of nedosiran: C(max)

| | |
|-----------------|---|
| End point title | Plasma PK parameters of nedosiran: C(max) |
|-----------------|---|

End point description:

PK samples taken predose on Day 1, then postdose (h): 0.5, 2, 10, 24, 360 (Day 15), 696 (Day 29)

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 (predose) to Day 29 postdose

| End point values | PK Population - Nedosiran | | | |
|--------------------------------------|---------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 615 (± 295) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma PK parameters of nedosiran: AUC(0-24) and AUC(0-last)

| | |
|-----------------|--|
| End point title | Plasma PK parameters of nedosiran: AUC(0-24) and AUC(0-last) |
|-----------------|--|

End point description:

PK samples taken predose on Day 1, then postdose (h): 0.5, 2, 10, 24, 360 (Day 15), 696 (Day 29)

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 (predose) to Day 29 postdose

| End point values | PK Population - Nedosiran | | | |
|--------------------------------------|---------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: h.ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| AUC(0-24) | 9560 (± 4440) | | | |
| AUC(0-last) | 12700 (± 10700) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: The proportion of participants achieving a > 30% decrease from baseline in 24-hour urinary oxalate on 2 consecutive visits

| | |
|-----------------|--|
| End point title | The proportion of participants achieving a > 30% decrease from baseline in 24-hour urinary oxalate on 2 consecutive visits |
|-----------------|--|

End point description:

24-hour urinary oxalate measurements taken at Study Days 29, 43, 57, and 85 (End of Study).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Screening) to End of Study

| End point values | mITT Population - Nedosiran | mITT Population - Placebo | | |
|-----------------------------|-----------------------------|---------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 2 | | |
| Units: participants | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Signing of the informed consent form (Screening) to End of Study

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Nedosiran |
|-----------------------|-----------|

Reporting group description: -

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events | Nedosiran | Placebo | |
|---|---------------|---------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 2 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Nedosiran | Placebo | |
|---|----------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | 2 / 2 (100.00%) | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis contact | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Scar pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|----------------|----------------|--|
| Renal and urinary disorders | | | |
| Calculus urinary | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 0 | 3 | |
| Renal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 27 April 2020 | v 2.0 (Amendment 1): The 27 February 2020 version of the protocol was updated to incorporate changes to the dosing regimen for 6- to 11-year-old children and to allow for some scheduled study visits to be conducted as telemedicine visits supported by a home health nurse. |
| 13 August 2020 | v 3.0 (Amendment 2): The 27 April 2020 version of the protocol was updated to include the dosing regimen for 6-to-11-year-old children based upon modeling and simulation, to update the total blood volume collected, to perform pregnancy testing at Day 57, to perform urinary creatinine testing at Day 43, to remove the exclusion and concomitant therapy criterion related to routine or chronic use of more than 3 grams of acetaminophen/paracetamol daily, and to update the statistical analyses populations. Other administrative changes were also incorporated. |
| 24 September 2020 | v 4.0 (Amendment 3): The 13 August 2020 version of the protocol was revised to update the exclusion criterion regarding previous IMP administration, add study interruption and stopping rules, remove the drug screen exclusion criterion, add an inclusion criterion requiring participants to be affiliated with or a beneficiary of a health insurance system (if applicable per national regulations), and add text to clarify that the investigator is obligated to anticipate and address injection site pain. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported