# Clinical trial results:
# A Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study to Evaluate the Safety and Efficacy of CCX140-B in Diabetic Nephropathy

## Summary

| | |
|---|---|
| EudraCT number | 2011-001267-49 |
| Trial protocol | HU BE CZ GB DE |
| Global end of trial date | 04 August 2014 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 15 December 2022 |
| First version publication date | 15 December 2022 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | CL005_140 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | ChemoCentryx, Inc. |
| Sponsor organisation address | 835 Industrial Road Suite 600, San Carlos, United States, 94070 |
| Public contact | Chemocentryx, Inc., Clinical trial disclosure, clinicaltrials@chemocentryx.com |
| Scientific contact | Chemocentryx, Inc., Clinical trial disclosure, clinicaltrials@chemocentryx.com |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| 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 | 04 August 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 04 August 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 August 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Primary safety objective is to evaluate the safety and tolerability of CCX140-B, based on subject incidence of adverse events over 52 weeks of treatment, in subjects with diabetic nephropathy (DN). Primary efficacy objective is to evaluate the efficacy of CCX140-B, compared to placebo, over 52 weeks of placebo-controlled treatment based on changes from baseline in first morning urinary albumin:creatinine ratio (UACR).

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and with all applicable laws and regulations of the locale and country where the study was conducted, and in compliance with Good Clinical Practice Guidelines. Only subjects that met all the study inclusion and none of the exclusion criteria were entered in the study. The rationale of the study, procedural details, and investigational goals were explained to each subject, along with potential risks and benefits. Each subject was assured of his/her right to withdraw from the study at any time.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 17 October 2011 |
| 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 | Poland: 48 |
| Country: Number of subjects enrolled | United Kingdom: 51 |
| Country: Number of subjects enrolled | Belgium: 15 |
| Country: Number of subjects enrolled | Czechia: 60 |
| Country: Number of subjects enrolled | Germany: 81 |
| Country: Number of subjects enrolled | Hungary: 77 |
| Worldwide total number of subjects | 332 |
| EEA total number of subjects | 281 |

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) | 0 |
| Adults (18-64 years) | 172 |
| From 65 to 84 years | 160 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

883 subjects were screened, 332 (37.6%) were randomized, and 551 (62.4%) subjects failed screening. The randomisation was stratified according to the baseline degree of albuminuria and the baseline eGFR.

### Pre-assignment

Screening details:

The Screening Period was up to 21 days and included 2 study visits. Eligible subjects visited the study center on Day 1, after an overnight fast of at least 10 hours, for a physical examination, vital signs measurements, laboratory tests, stratification, and randomization.

### Period 1

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

Blinding implementation details:

1. The study medication kit, bottle, and capsule appearances were identical
2. Limited access to the randomization code: study site personnel, study subjects, personnel responsible for study monitoring, and biostatisticians and data managers
3. Unblinded CCX140 plasma concentration results were not shared with study sites throughout the study
4. Efficacy data were not made available to study team members outlined in (2) unless it was for safety monitoring

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Group A |

Arm description:

Placebo once daily

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo, four placebo capsules once daily

| | |
|---|---|
| **Arm title** | Group B |

Arm description:

CCX140-B 5mg once daily

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | CCX140-B |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Two CCX140-B 2.5 mg capsules and 2 placebo capsules once daily

| | |
|---|---|
| **Arm title** | Group C |

Arm description:

CCX140-B 10 mg once daily

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | CCX140-B |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Four CCX140-B 2.5 mg capsules once daily

| **Number of subjects in period 1** | Group A | Group B | Group C |
|---|---|---|---|
| Started | 111 | 110 | 111 |
| Completed | 101 | 100 | 97 |
| Not completed | 10 | 10 | 14 |
| Consent withdrawn by subject | 6 | 2 | 7 |
| Physician decision | 1 | 1 | 1 |
| Adverse event, non-fatal | 3 | 6 | 6 |
| Patient relocation | - | 1 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Group A |
| Reporting group description: | |
| Placebo once daily | |
| Reporting group title | Group B |
| Reporting group description: | |
| CCX140-B 5mg once daily | |
| Reporting group title | Group C |
| Reporting group description: | |
| CCX140-B 10 mg once daily | |

| Reporting group values | Group A | Group B | Group C |
|---|---|---|---|
| Number of subjects | 111 | 110 | 111 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 63.3 | 63.4 | 62.4 |
| standard deviation | ± 7.22 | ± 7.69 | ± 7.92 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 29 | 24 | 23 |
| Male | 82 | 86 | 88 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 0 |
| Not hispanic or Latino | 111 | 110 | 111 |
| Race<br>Units: Subjects | | | |
| White | 106 | 107 | 109 |
| Asian | 3 | 2 | 0 |
| Black or African American | 0 | 0 | 2 |
| Native Hawaiian or other Pacific Islander | 0 | 1 | 0 |
| Other | 2 | 0 | 0 |
| Smoking status<br>Units: Subjects | | | |
| Current smoker | 18 | 29 | 20 |
| Past smoker | 49 | 38 | 54 |
| Never smoked | 44 | 43 | 37 |
| Degree of albuminuria at screening | | | |
| The UACR values used for stratification were calculated by taking the geometric mean of the 2 screening values and the eGFR used for stratification was calculated by taking the arithmetic mean of the 2 screening values. | | | |
| Units: Subjects | | | |
| UACR of 100-300 mg albumin/g creatinine | 38 | 39 | 40 |

| | | | |
|---|---|---|---|
| UACR of 301-800 mg albumin/g creatinine | 40 | 39 | 38 |
| UACR of 801-3000 mg albumin/g creatinine | 33 | 32 | 33 |
| eGFR at screening | | | |
| eGFR: estimated glomerular filtration rate | | | |
| Units: Subjects | | | |
| 25 to 59 mL/min/1.73 m2 inclusive | 57 | 56 | 57 |
| ≥60 mL/min/1.73 m2 | 54 | 54 | 54 |
| Subjects on ACE inhibitors & ARBs | | | |
| ACE: angiotensin converting enzyme<br>ARB: angiotensin II receptor blocker | | | |
| Units: Subjects | | | |
| ACE inhibitors | 71 | 77 | 63 |
| ARBs | 39 | 33 | 44 |
| Both | 0 | 0 | 3 |
| Other | 1 | 0 | 1 |
| Body mass index | | | |
| Units: kg/m2 | | | |
| arithmetic mean | 32.5 | 33.2 | 33.0 |
| standard deviation | ± 5.05 | ± 4.71 | ± 4.90 |
| Duration of type 2 diabetes | | | |
| Units: month | | | |
| arithmetic mean | 181.5 | 186.7 | 190.4 |
| standard deviation | ± 89.20 | ± 93.05 | ± 102.87 |
| Duration of diabetic nephropathy | | | |
| Units: month | | | |
| arithmetic mean | 46.5 | 56.4 | 56.7 |
| standard deviation | ± 38.15 | ± 50.76 | ± 58.53 |
| UACR | | | |
| UACR: urinary albumin:creatinin ratio | | | |
| Units: mg/g | | | |
| arithmetic mean | 659.28 | 643.98 | 731.49 |
| standard deviation | ± 578.126 | ± 593.498 | ± 668.577 |
| eGFR (MDRD) | | | |
| eGFR: estimated glomerular filtration rate<br>MDRD: Modification of Diet in Renal Disease | | | |
| Units: mL/min/1.73 m2 | | | |
| arithmetic mean | 60.98 | 60.50 | 59.41 |
| standard deviation | ± 24.480 | ± 22.654 | ± 24.670 |
| eGFR (CKD-EPI) | | | |
| eGFR: estimated glomerular filtration rate<br>CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration | | | |
| Units: mL/min/1.73 m2 | | | |
| arithmetic mean | 62.67 | 62.49 | 61.06 |
| standard deviation | ± 24.192 | ± 22.876 | ± 24.416 |
| Serum creatinine | | | |
| Units: mg/dL | | | |
| arithmetic mean | 1.30 | 1.30 | 1.36 |
| standard deviation | ± 0.470 | ± 0.463 | ± 0.506 |
| BUN | | | |
| BUN: Blood urea nitrogen | | | |

| | | | |
|---|---|---|---|
| Units: mg/dL | | | |
| arithmetic mean | 24.5 | 25.3 | 26.0 |
| standard deviation | ± 9.72 | ± 10.40 | ± 11.01 |
| Serum phosphorus | | | |
| Units: mg/dL | | | |
| arithmetic mean | 3.53 | 3.44 | 3.50 |
| standard deviation | ± 0.500 | ± 0.448 | ± 0.524 |
| HbA1c | | | |
| HbA1c: Hemoglobin A1c | | | |
| Units: percentage | | | |
| arithmetic mean | 7.65 | 7.52 | 7.67 |
| standard deviation | ± 0.975 | ± 0.972 | ± 1.048 |
| Fasting plasma glucose | | | |
| Units: mg/dL | | | |
| arithmetic mean | 165.0 | 163.4 | 166.5 |
| standard deviation | ± 44.98 | ± 40.15 | ± 43.62 |
| Fasting plasma insulin | | | |
| Units: µIU/mL | | | |
| arithmetic mean | 24.8 | 21.9 | 25.6 |
| standard deviation | ± 46.59 | ± 27.85 | ± 33.53 |
| HOMA-IR | | | |
| HOMA-IR: Homeostasis model assessment of insulin resistance ( | | | |
| Units: None | | | |
| arithmetic mean | 10.78 | 9.03 | 11.06 |
| standard deviation | ± 25.719 | ± 11.948 | ± 17.337 |
| Urinary MCP-1:creatinine ratio | | | |
| MCP-1: monocyte chemoattractant protein-1<br>Number of patients with values differs from number of patients in the groups:<br>Placebo: n=63<br>CCX140-B 5 mg: n=62<br>CCX140-B 10 mg: n=60 | | | |
| Units: pg/mg creatinine | | | |
| arithmetic mean | 236.75 | 268.90 | 250.01 |
| standard deviation | ± 77.025 | ± 395.939 | ± 246.111 |
| Plasma MCP-1 | | | |
| MCP-1: MCP Monocyte chemoattractant protein 1<br>Number of patients with values differs from number of patients in the groups:<br>Placebo: n=55<br>CCX140-B 5 mg: n=56<br>CCX140-B 10 mg: n=54 | | | |
| Units: pg/mL | | | |
| arithmetic mean | 236.75 | 268.90 | 250.01 |
| standard deviation | ± 77.025 | ± 395.939 | ± 246.111 |
| Mean arterial blood pressure | | | |
| Units: mmHg | | | |
| arithmetic mean | 98.7 | 97.3 | 98.8 |
| standard deviation | ± 9.50 | ± 8.79 | ± 8.16 |

| **Reporting group values** | Total | | |
|---|---|---|---|
| Number of subjects | 332 | | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | <br><br><br>- | | |
| Gender categorical<br>Units: Subjects | | | |
| Female<br>Male | 76<br>256 | | |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino<br>Not hispanic or Latino | 0<br>332 | | |
| Race<br>Units: Subjects | | | |
| White<br>Asian<br>Black or African American<br>Native Hawaiian or other Pacific Islander<br>Other | 322<br>5<br>2<br>1<br>2 | | |
| Smoking status<br>Units: Subjects | | | |
| Current smoker<br>Past smoker<br>Never smoked | 67<br>141<br>124 | | |
| Degree of albuminuria at screening | | | |
| The UACR values used for stratification were calculated by taking the geometric mean of the 2 screening values and the eGFR used for stratification was calculated by taking the arithmetic mean of the 2 screening values. | | | |
| Units: Subjects | | | |
| UACR of 100-300 mg albumin/g creatinine<br>UACR of 301-800 mg albumin/g creatinine<br>UACR of 801-3000 mg albumin/g creatinine | 117<br>117<br>98 | | |
| eGFR at screening | | | |
| eGFR: estimated glomerular filtration rate | | | |
| Units: Subjects | | | |
| 25 to 59 mL/min/1.73 m2 inclusive<br>≥60 mL/min/1.73 m2 | 170<br>162 | | |
| Subjects on ACE inhibitors & ARBs | | | |
| ACE: angiotensin converting enzyme<br>ARB: angiotensin II receptor blocker | | | |
| Units: Subjects | | | |
| ACE inhibitors<br>ARBs<br>Both<br>Other | 211<br>116<br>3<br>2 | | |
| Body mass index<br>Units: kg/m2<br>arithmetic mean<br>standard deviation | <br><br><br>- | | |

| | | | |
|---|---|---|---|
| Duration of type 2 diabetes<br>Units: month<br>arithmetic mean<br>standard deviation | -<br>- | | |
| Duration of diabetic nephropathy<br>Units: month<br>arithmetic mean<br>standard deviation | -<br>- | | |
| UACR | | | |
| UACR: urinary albumin:creatinin ratio | | | |
| Units: mg/g<br>arithmetic mean<br>standard deviation | -<br>- | | |
| eGFR (MDRD) | | | |
| eGFR: estimated glomerular filtration rate<br>MDRD: Modification of Diet in Renal Disease | | | |
| Units: mL/min/1.73 m2<br>arithmetic mean<br>standard deviation | -<br>- | | |
| eGFR (CKD-EPI) | | | |
| eGFR: estimated glomerular filtration rate<br>CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration | | | |
| Units: mL/min/1.73 m2<br>arithmetic mean<br>standard deviation | -<br>- | | |
| Serum creatinine<br>Units: mg/dL<br>arithmetic mean<br>standard deviation | -<br>- | | |
| BUN | | | |
| BUN: Blood urea nitrogen | | | |
| Units: mg/dL<br>arithmetic mean<br>standard deviation | -<br>- | | |
| Serum phosphorus<br>Units: mg/dL<br>arithmetic mean<br>standard deviation | -<br>- | | |
| HbA1c | | | |
| HbA1c: Hemoglobin A1c | | | |
| Units: percentage<br>arithmetic mean<br>standard deviation | -<br>- | | |
| Fasting plasma glucose<br>Units: mg/dL<br>arithmetic mean<br>standard deviation | -<br>- | | |
| Fasting plasma insulin<br>Units: µIU/mL<br>arithmetic mean<br>standard deviation | -<br>- | | |

| | | | |
|---|---|---|---|
| HOMA-IR | | | |
| HOMA-IR: Homeostasis model assessment of insulin resistance ( | | | |
| Units: None<br>arithmetic mean<br>standard deviation | -<br> | | |
| Urinary MCP-1:creatinine ratio | | | |
| MCP-1: monocyte chemoattractant protein-1<br>Number of patients with values differs from number of patients in the groups:<br>Placebo: n=63<br>CCX140-B 5 mg: n=62<br>CCX140-B 10 mg: n=60 | | | |
| Units: pg/mg creatinine<br>arithmetic mean<br>standard deviation | -<br> | | |
| Plasma MCP-1 | | | |
| MCP-1: MCP Monocyte chemoattractant protein 1<br>Number of patients with values differs from number of patients in the groups:<br>Placebo: n=55<br>CCX140-B 5 mg: n=56<br>CCX140-B 10 mg: n=54 | | | |
| Units: pg/mL<br>arithmetic mean<br>standard deviation | -<br> | | |
| Mean arterial blood pressure<br>Units: mmHg<br>arithmetic mean<br>standard deviation | -<br> | | |

**Subject analysis sets**

| | |
|---|---|
| Subject analysis set title | Placebo - uninterrupted dosing after study day 85 |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

Because of the substantial decrease in the number of subjects after Study Day 85, as well as interruptions of study drug dosing in several subjects between Days 85 and 113, the focus of the primary efficacy analysis is on the population with uninterrupted dosing between the Day 85 and Day 113 visits.

| | |
|---|---|
| Subject analysis set title | CCX140-B 5 mg - uninterrupted dosing after study day 85 |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

Because of the substantial decrease in the number of subjects after Study Day 85, as well as interruptions of study drug dosing in several subjects between Days 85 and 113, the focus of the primary efficacy analysis is on the population with uninterrupted dosing between the Day 85 and Day 113 visits.

| | |
|---|---|
| Subject analysis set title | CCX140-B 10 mg - uninterrupted dosing after study day 85 |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

Because of the substantial decrease in the number of subjects after Study Day 85, as well as interruptions of study drug dosing in several subjects between Days 85 and 113, the focus of the primary efficacy analysis is on the population with uninterrupted dosing between the Day 85 and Day 113 visits.

| **Reporting group values** | Placebo - uninterrupted dosing after study day 85 | CCX140-B 5 mg - uninterrupted dosing after study day 85 | CCX140-B 10 mg - uninterrupted dosing after study day 85 |
|---|---|---|---|
| Number of subjects | 64 | 63 | 65 |

| | | | |
|---|---|---|---|
| Age categorical<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age continuous<br>Units: years | | | |
| arithmetic mean | 62.4 | 62.5 | 62.3 |
| standard deviation | ± 7.59 | ± 8.00 | ± 7.94 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 15 | 16 | 14 |
| Male | 49 | 47 | 51 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 0 |
| Not hispanic or Latino | 64 | 63 | 65 |
| Race<br>Units: Subjects | | | |
| White | 61 | 62 | 64 |
| Asian | 3 | 0 | 0 |
| Black or African American | 0 | 0 | 1 |
| Native Hawaiian or other Pacific Islander | 0 | 1 | 0 |
| Other | 0 | 0 | 0 |
| Smoking status<br>Units: Subjects | | | |
| Current smoker | 11 | 18 | 13 |
| Past smoker | 26 | 21 | 32 |
| Never smoked | 27 | 24 | 20 |
| Degree of albuminuria at screening | | | |
| The UACR values used for stratification were calculated by taking the geometric mean of the 2 screening values and the eGFR used for stratification was calculated by taking the arithmetic mean of the 2 screening values. | | | |
| Units: Subjects | | | |
| UACR of 100-300 mg albumin/g creatinine | 27 | 28 | 28 |
| UACR of 301-800 mg albumin/g creatinine | 19 | 19 | 19 |
| UACR of 801-3000 mg albumin/g creatinine | 18 | 16 | 18 |
| eGFR at screening | | | |
| eGFR: estimated glomerular filtration rate | | | |
| Units: Subjects | | | |
| 25 to 59 mL/min/1.73 m2 inclusive | 30 | 29 | 30 |
| ≥60 mL/min/1.73 m2 | 34 | 34 | 35 |
| Subjects on ACE inhibitors & ARBs | | | |
| ACE: angiotensin converting enzyme<br>ARB: angiotensin II receptor blocker | | | |
| Units: Subjects | | | |
| ACE inhibitors | 41 | 45 | 36 |
| ARBs | 23 | 18 | 25 |
| Both | 0 | 0 | 3 |
| Other | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Body mass index<br>Units: kg/m2<br>arithmetic mean<br>standard deviation | <br><br>32.7<br>± 5.10 | <br><br>33.2<br>± 4.37 | <br><br>33.2<br>± 5.13 |
| Duration of type 2 diabetes<br>Units: month<br>arithmetic mean<br>standard deviation | <br><br>178.8<br>± 86.39 | <br><br>179.7<br>± 96.78 | <br><br>195.4<br>± 107.91 |
| Duration of diabetic nephropathy<br>Units: month<br>arithmetic mean<br>standard deviation | <br><br>44.1<br>± 39.37 | <br><br>54.6<br>± 52.24 | <br><br>47.4<br>± 44.30 |
| UACR | | | |
| UACR: urinary albumin:creatinin ratio | | | |
| Units: mg/g<br>arithmetic mean<br>standard deviation | <br>650.69<br>± 620.143 | <br>562.23<br>± 553.516 | <br>694.17<br>± 704.568 |
| eGFR (MDRD) | | | |
| eGFR: estimated glomerular filtration rate<br>MDRD: Modification of Diet in Renal Disease | | | |
| Units: mL/min/1.73 m2<br>arithmetic mean<br>standard deviation | <br>64.17<br>± 26.069 | <br>62.38<br>± 24.215 | <br>61.09<br>± 25.065 |
| eGFR (CKD-EPI) | | | |
| eGFR: estimated glomerular filtration rate<br>CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration | | | |
| Units: mL/min/1.73 m2<br>arithmetic mean<br>standard deviation | <br>65.82<br>± 25.223 | <br>64.39<br>± 24.045 | <br>62.80<br>± 24.692 |
| Serum creatinine<br>Units: mg/dL<br>arithmetic mean<br>standard deviation | <br><br>1.26<br>± 0.481 | <br><br>1.27<br>± 0.475 | <br><br>1.33<br>± 0.535 |
| BUN | | | |
| BUN: Blood urea nitrogen | | | |
| Units: mg/dL<br>arithmetic mean<br>standard deviation | <br>23.8<br>± 9.47 | <br>25.9<br>± 11.37 | <br>25.3<br>± 9.97 |
| Serum phosphorus<br>Units: mg/dL<br>arithmetic mean<br>standard deviation | <br><br>3.58<br>± 0.465 | <br><br>3.54<br>± 0.429 | <br><br>3.35<br>± 0.514 |
| HbA1c | | | |
| HbA1c: Hemoglobin A1c | | | |
| Units: percentage<br>arithmetic mean<br>standard deviation | <br>7.66<br>± 0.960 | <br>7.54<br>± 0.865 | <br>7.76<br>± 1.085 |
| Fasting plasma glucose<br>Units: mg/dL<br>arithmetic mean<br>standard deviation | <br><br>158.4<br>± 42.29 | <br><br>170.4<br>± 39.70 | <br><br>170.5<br>± 47.69 |

| | | | |
|---|---|---|---|
| Fasting plasma insulin<br>Units: µIU/mL | | | |
| arithmetic mean | 30.3 | 21.7 | 26.1 |
| standard deviation | ± 57.78 | ± 20.14 | ± 30.20 |
| HOMA-IR | | | |
| HOMA-IR: Homeostasis model assessment of insulin resistance ( | | | |
| Units: None | | | |
| arithmetic mean | 12.95 | 9.49 | 11.86 |
| standard deviation | ± 31.706 | ± 10.235 | ± 18.488 |
| Urinary MCP-1:creatinine ratio | | | |
| MCP-1: monocyte chemoattractant protein-1<br>Number of patients with values differs from number of patients in the groups:<br>Placebo: n=63<br>CCX140-B 5 mg: n=62<br>CCX140-B 10 mg: n=60 | | | |
| Units: pg/mg creatinine | | | |
| arithmetic mean | 218.30 | 283.04 | 229.28 |
| standard deviation | ± 69.341 | ± 532.838 | ± 81.606 |
| Plasma MCP-1 | | | |
| MCP-1: MCP Monocyte chemoattractant protein 1<br>Number of patients with values differs from number of patients in the groups:<br>Placebo: n=55<br>CCX140-B 5 mg: n=56<br>CCX140-B 10 mg: n=54 | | | |
| Units: pg/mL | | | |
| arithmetic mean | 218.30 | 283.04 | 229.28 |
| standard deviation | ± 69.341 | ± 532.838 | ± 81.606 |
| Mean arterial blood pressure<br>Units: mmHg | | | |
| arithmetic mean | 98.2 | 95.9 | 98.9 |
| standard deviation | ± 9.31 | ± 8.56 | ± 8.55 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Group A |
| Reporting group description: Placebo once daily | |
| Reporting group title | Group B |
| Reporting group description: CCX140-B 5mg once daily | |
| Reporting group title | Group C |
| Reporting group description: CCX140-B 10 mg once daily | |
| Subject analysis set title | Placebo - uninterrupted dosing after study day 85 |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: Because of the substantial decrease in the number of subjects after Study Day 85, as well as interruptions of study drug dosing in several subjects between Days 85 and 113, the focus of the primary efficacy analysis is on the population with uninterrupted dosing between the Day 85 and Day 113 visits. | |
| Subject analysis set title | CCX140-B 5 mg - uninterrupted dosing after study day 85 |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: Because of the substantial decrease in the number of subjects after Study Day 85, as well as interruptions of study drug dosing in several subjects between Days 85 and 113, the focus of the primary efficacy analysis is on the population with uninterrupted dosing between the Day 85 and Day 113 visits. | |
| Subject analysis set title | CCX140-B 10 mg - uninterrupted dosing after study day 85 |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: Because of the substantial decrease in the number of subjects after Study Day 85, as well as interruptions of study drug dosing in several subjects between Days 85 and 113, the focus of the primary efficacy analysis is on the population with uninterrupted dosing between the Day 85 and Day 113 visits. | |

### Primary: Percent change from baseline to Day 365 in the first morning UACR

| | |
|---|---|
| End point title | Percent change from baseline to Day 365 in the first morning UACR |
| End point description: UACR: urinary albumin:creatinine ratio | |
| End point type | Primary |
| End point timeframe: Baseline to Day 365 | |

| End point values | Placebo - uninterrupted dosing after study day 85 | CCX140-B 5 mg - uninterrupted dosing after study day 85 | CCX140-B 10 mg - uninterrupted dosing after study day 85 | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 64[1] | 63[2] | 65[3] | |
| Units: percentage of baseline | | | | |

| | | | | |
|---|---|---|---|---|
| least squares mean (confidence interval 95%) | -2 (-11 to 9) | -18 (-26 to -8) | -11 (-20 to -1) | |

Notes:

[1] - primary efficacy analysis on the population with uninterrupted dosing between the Day 85 and Day 113
[2] - primary efficacy analysis on the population with uninterrupted dosing between the Day 85 and Day 113
[3] - primary efficacy analysis on the population with uninterrupted dosing between the Day 85 and Day 113

## Statistical analyses

| **Statistical analysis title** | Mixed-effects model of repeated measures (MMRM) |
|---|---|

Statistical analysis description:

Factors: treatment group, visit, and treatment-by-visit
Covariates: baseline UACR, eGFR, HbA1c, and MAP.
Repeated measure units from the same subjects: visits.
Variance-covariance matrix assumed to be unstructured.
Treatment group difference at Week 52 estimated with the simple contrast and the overall between-group difference over the course of the study.
Ho: Neither CCX group differs from placebo
Ha: At least one of the CCX140-B groups differs from placebo.

| Comparison groups | Placebo - uninterrupted dosing after study day 85 v CCX140-B 5 mg - uninterrupted dosing after study day 85 v CCX140-B 10 mg - uninterrupted dosing after study day 85 |
|---|---|
| Number of subjects included in analysis | 192 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[4] |
| P-value | ≤ 0.05 |
| Method | t-test, 2-sided |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11 |
| upper limit | 9 |

Notes:

[4] - Gatekeeping procedure to control overall type 1 error rate at the α=0.05 level:
1. Test the 10 mg group vs the placebo group at a 2-sided α=0.05 level. If p≤0.05, accept Ha for the 10 mg group and proceed to Step 2.
Otherwise, accept Ho for the 10 mg and 5 mg groups.
2. Test the 5 mg group vs the placebo at a 2-sided α=0.05 level. If
p≤0.05, accept Ha for the 5 mg group. Otherwise, accept the Ho for the 5 mg group.

## Primary: Incidence of adverse events

| End point title | Incidence of adverse events[5] |
|---|---|

End point description:

TEAE: Treatment-emergent adverse event

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

End point timeframe:

Overall 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: No formal hypothesis testing was performed to compare safety parameters.

| End point values | Group A | Group B | Group C | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 111 | 110 | 111 | |
| Units: subjects | | | | |
| TEAEs | 81 | 71 | 68 | |
| Serious TEAEs | 13 | 13 | 25 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Changes from baseline to Day 365 in eGFR (determined by the Modification of Diet in Renal Disease equation).

| End point title | Changes from baseline to Day 365 in eGFR (determined by the Modification of Diet in Renal Disease equation). |
|---|---|

End point description:

Because of the substantial decrease in the number of subjects after Study Day 85, as well as interruptions of study drug dosing in several subjects between Days 85 and 113, the focus of the primary efficacy analysis is on the population with uninterrupted dosing between the Day 85 and Day 113 visits.

eGFR: estimated glomerular filtration rate

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

End point timeframe:

From baseline to Day 365

| End point values | Placebo - uninterrupted dosing after study day 85 | CCX140-B 5 mg - uninterrupted dosing after study day 85 | CCX140-B 10 mg - uninterrupted dosing after study day 85 | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 64[6] | 63[7] | 64[8] | |
| Units: mL/min/1.73 m2 | | | | |
| least squares mean (confidence interval 95%) | -0.71 (-1.87 to 0.45) | -1.27 (-2.45 to -0.09) | -1.60 (-2.78 to -0.42) | |

Notes:

[6] - Population with uninterrupted dosing between the Day 85 and Day 113 & with a value at Day 365

[7] - Population with uninterrupted dosing between the Day 85 and Day 113 & with a value at Day 365

[8] - Population with uninterrupted dosing between the Day 85 and Day 113 & with a value at Day 365

### Statistical analyses

No statistical analyses for this end point

## Secondary: Changes from baseline to Day 365 in HbA1c.

| End point title | Changes from baseline to Day 365 in HbA1c. |
|---|---|

End point description:

Because of the substantial decrease in the number of subjects after Study Day 85, as well as interruptions of study drug dosing in several subjects between Days 85 and 113, the focus of the

primary efficacy analysis is on the population with uninterrupted dosing between the Day 85 and Day 113 visits.

HbA1c: Hemoglobin A1c

| End point type | Secondary |
|---|---|
| End point timeframe: | |
| From baseline to Day 365 | |

| **End point values** | Placebo - uninterrupted dosing after study day 85 | CCX140-B 5 mg - uninterrupted dosing after study day 85 | CCX140-B 10 mg - uninterrupted dosing after study day 85 | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 64 | 63 | 63 | |
| Units: Percentage change | | | | |
| least squares mean (confidence interval 95%) | 0.03 (-0.10 to 0.17) | 0.04 (-0.09 to 0.18) | -0.07 (-0.20 to 0.07) | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

393 days

Adverse event reporting additional description:

An adverse event was considered treatment-emergent if the start date of the event was on or after the date of first dose of study medication and up to and including 14 days after the date of last dose of study medication.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 14.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | CCX140-B 10mg |
| Reporting group description: - | |
| Reporting group title | CCX140-B 5mg |
| Reporting group description: - | |
| Reporting group title | Placebo |

Reporting group description: -

| Serious adverse events | CCX140-B 10mg | CCX140-B 5mg | Placebo |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 25 / 111 (22.52%) | 13 / 110 (11.82%) | 13 / 111 (11.71%) |
| number of deaths (all causes) | 1 | 1 | 0 |
| number of deaths resulting from adverse events | 1 | 1 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Renal cancer | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Prostate cancer | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Rectal cancer stage IV | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 110 (0.91%) | 0 / 111 (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 |

| | | | |
|---|---|---|---|
| Bladder transitional cell carcinoma | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningioma | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Femoral arterial stenosis | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 110 (0.91%) | 0 / 111 (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 |
| Peripheral vascular disorder | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subclavian steal syndrome | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 110 (0.91%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tendon rupture | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Angina unstable | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 2 / 110 (1.82%) | 0 / 111 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 110 (0.91%) | 0 / 111 (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 |

| | | | |
|---|---|---|---|
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Nervous system disorders | | | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 1 / 110 (0.91%) | 0 / 111 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Balance disorder | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 110 (0.91%) | 0 / 111 (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 |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |

| | | | |
|---|---|---|---|
| Eye haemorrhage | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Duodenal ulcer | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Nausea | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Reflux oesophagitis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 110 (0.91%) | 0 / 111 (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 |
| Constipation | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|---|---|---|
| Angioedema | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Purpura senile | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 1 / 110 (0.91%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Meniscal degeneration | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 1 / 110 (0.91%) | 2 / 111 (1.80%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Gangrene | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Lobar Pneumonia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Localised infection | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 110 (0.91%) | 0 / 111 (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 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Septic shock | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 110 (0.91%) | 0 / 111 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 110 (0.91%) | 0 / 111 (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 |
| Lung infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 110 (0.00%) | 1 / 111 (0.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 1 / 110 (0.91%) | 0 / 111 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 110 (0.00%) | 0 / 111 (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 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 110 (0.91%) | 0 / 111 (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: 2 %

| **Non-serious adverse events** | CCX140-B 10mg | CCX140-B 5mg | Placebo |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 68 / 111 (61.26%) | 71 / 110 (64.55%) | 81 / 111 (72.97%) |
| Investigations | | | |
| Blood creatinine phosphokinase increased | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 3 / 110 (2.73%) | 2 / 111 (1.80%) |
| occurrences (all) | 2 | 3 | 2 |
| Blood uric acid increased | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 3 / 110 (2.73%) | 1 / 111 (0.90%) |
| occurrences (all) | 1 | 3 | 1 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 3 / 111 (2.70%) | 0 / 110 (0.00%) | 0 / 111 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Blood creatinine increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 111 (0.00%) | 3 / 110 (2.73%) | 0 / 111 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 1 / 110 (0.91%) | 3 / 111 (2.70%) |
| occurrences (all) | 1 | 1 | 3 |
| Contusion | | | |
| subjects affected / exposed | 3 / 111 (2.70%) | 2 / 110 (1.82%) | 0 / 111 (0.00%) |
| occurrences (all) | 4 | 2 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 9 / 110 (8.18%) | 8 / 111 (7.21%) |
| occurrences (all) | 3 | 9 | 8 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 111 (3.60%) | 6 / 110 (5.45%) | 3 / 111 (2.70%) |
| occurrences (all) | 5 | 6 | 3 |
| Dizziness | | | |
| subjects affected / exposed | 4 / 111 (3.60%) | 2 / 110 (1.82%) | 1 / 111 (0.90%) |
| occurrences (all) | 5 | 2 | 1 |
| General disorders and administration site conditions | | | |
| Edema peripheral | | | |
| subjects affected / exposed | 8 / 111 (7.21%) | 9 / 110 (8.18%) | 12 / 111 (10.81%) |
| occurrences (all) | 11 | 10 | 14 |
| Fatigue | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 4 / 110 (3.64%) | 2 / 111 (1.80%) |
| occurrences (all) | 3 | 4 | 2 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 4 / 110 (3.64%) | 0 / 111 (0.00%) |
| occurrences (all) | 2 | 4 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 111 (3.60%) | 4 / 110 (3.64%) | 5 / 111 (4.50%) |
| occurrences (all) | 4 | 5 | 7 |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 111 (3.60%) | 2 / 110 (1.82%) | 0 / 111 (0.00%) |
| occurrences (all) | 5 | 2 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 3 / 110 (2.73%) | 0 / 111 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 3 / 110 (2.73%) | 3 / 111 (2.70%) |
| occurrences (all) | 3 | 4 | 4 |
| Constipation | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 3 / 110 (2.73%) | 2 / 111 (1.80%) |
| occurrences (all) | 1 | 3 | 3 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 3 / 111 (2.70%) | 1 / 110 (0.91%) | 1 / 111 (0.90%) |
| occurrences (all) | 3 | 1 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 4 / 111 (3.60%) | 4 / 110 (3.64%) | 3 / 111 (2.70%) |
| occurrences (all) | 5 | 5 | 3 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 4 / 111 (3.60%) | 4 / 110 (3.64%) | 6 / 111 (5.41%) |
| occurrences (all) | 4 | 6 | 9 |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 3 / 110 (2.73%) | 2 / 111 (1.80%) |
| occurrences (all) | 1 | 3 | 2 |
| Pain in extremity | | | |
| subjects affected / exposed | 3 / 111 (2.70%) | 1 / 110 (0.91%) | 2 / 111 (1.80%) |
| occurrences (all) | 3 | 2 | 2 |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 2 / 110 (1.82%) | 3 / 111 (2.70%) |
| occurrences (all) | 1 | 2 | 3 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 1 / 110 (0.91%) | 3 / 111 (2.70%) |
| occurrences (all) | 2 | 1 | 3 |

| | | | |
|---|---|---|---|
| Arthralgia | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 0 / 110 (0.00%) | 3 / 111 (2.70%) |
| occurrences (all) | 2 | 0 | 4 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 10 / 111 (9.01%) | 9 / 110 (8.18%) | 6 / 111 (5.41%) |
| occurrences (all) | 11 | 10 | 6 |
| Bronchitis | | | |
| subjects affected / exposed | 3 / 111 (2.70%) | 3 / 110 (2.73%) | 5 / 111 (4.50%) |
| occurrences (all) | 3 | 3 | 5 |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 111 (2.70%) | 3 / 110 (2.73%) | 3 / 111 (2.70%) |
| occurrences (all) | 3 | 4 | 3 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 4 / 110 (3.64%) | 1 / 111 (0.90%) |
| occurrences (all) | 0 | 4 | 1 |
| Rhinitis | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 1 / 110 (0.91%) | 3 / 111 (2.70%) |
| occurrences (all) | 2 | 1 | 3 |
| Metabolism and nutrition disorders | | | |
| Hyperglycemia | | | |
| subjects affected / exposed | 4 / 111 (3.60%) | 2 / 110 (1.82%) | 1 / 111 (0.90%) |
| occurrences (all) | 4 | 3 | 1 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 3 / 110 (2.73%) | 3 / 111 (2.70%) |
| occurrences (all) | 1 | 3 | 3 |
| Hypoglycemia | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 3 / 110 (2.73%) | 5 / 111 (4.50%) |
| occurrences (all) | 1 | 3 | 6 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 05 April 2012 | The lower limit of the UACR eligibility criterion was changed from 200 mg/g creatinine to 100 mg/g creatinine and the lowest UACR stratum subject enrollment limit was changed from not more than 25% to not more than 40% of subjects enrolled. Rationale: To increase the number of subjects to be recruited in the lowest UACR stratum because this stratum was not well represented in the study population. Subjects who previously were found ineligible during screening because of urinary UACR 100 to 199 mg/g creatinine were allowed to be re-screened for the study. |
| 14 November 2012 | The following changes to the study conduct were made and the protocol was amended accordingly:<br><br>1. The Treatment Period was extended from 12 weeks to 52 weeks. Rationale: To evaluate the longer term safety and efficacy profile of CCX140-B in subjects with DN;<br>2. The Follow-up Period was changed from starting at the end of the 12-week period to starting at the end of the 52 week period. Rationale: To facilitate uninterrupted dosing from the end of 12 weeks through 52 weeks;<br>3. The protocol was revised to provide information on the study procedures required at each study visit;<br>4. As an option contemplated when the clinical study was designed, the sample size of the study was increased from 135 to up to 270 subjects. Rationale: To provide an adequate number of subjects for the study extension and to increase the statistical power of the study to detect a treatment effect on albuminuria, the primary efficacy parameter of the study, and on other efficacy parameters;<br>5. Potential reasons for early withdrawal from the study were revised. Rationale: To reflect the study extension;<br>6. New preclinical results from recently completed studies, including long-term rat and dog toxicology studies, were added;<br>7. New clinical data from recently completed clinical trials were added;<br>8. Provision was made for a formal interim analysis of efficacy and safety data when at least the first 135 subjects enrolled had completed at least their Day 85 Visit. Rationale: To plan for future clinical trials; and<br>9. The exploratory markers (PAI-1 and NT-proBNP) were added. Rationale: To evaluate the effect of CCX140-B on cardiovascular markers. |
| 15 November 2013 | The following changes to the study conduct were made and the protocol was amended accordingly:<br>1. Two additional urine and serum samples were collected on 2 days after the Day 365 Visit. Rationale: To reduce variability by having triplicate measurements instead of single measurements for the key efficacy parameters, particularly UACR and eGFR.<br>2. Changes to the protocol were made as 332 subjects had finally be enrolled in the study;<br>3. The Day 365 allowable visit window was changed from plus or minus 4 days of the scheduled Day 365 Visit to within 4 days prior to the scheduled Day 365 Visit. Rationale: In order to collect the 2 additional urine and serum samples after the Day 365 Visit as close as possible to the end of the study medication treatment period; and<br>4. Language was added to indicate that a CDF would be calculated for the percent change from baseline in eGFR. |

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.

| |
|---|
| The efficacy analysis was made on the subset of the ITT population whose treatment was not interrupted between day 85 and day 113 as it was the most relevant population from an efficacy evaluation perspective. |

Notes: