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 Units: Subjects			
Age continuous Units: years			
arithmetic mean	63.3	63.4	62.4
standard deviation	± 7.22	± 7.69	± 7.92
Gender categorical Units: Subjects			
Female	29	24	23
Male	82	86	88
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not hispanic or Latino	111	110	111
Race 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 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 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 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 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 Number of patients with values differs from number of patients in the groups: Placebo: n=63 CCX140-B 5 mg: n=62 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 Number of patients with values differs from number of patients in the groups: Placebo: n=55 CCX140-B 5 mg: n=56 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 Units: years arithmetic mean standard deviation	 -		
Gender categorical Units: Subjects			
Female Male	76 256		
Ethnicity Units: Subjects			
Hispanic or Latino Not hispanic or Latino	0 332		
Race Units: Subjects			
White Asian Black or African American Native Hawaiian or other Pacific Islander Other	322 5 2 1 2		
Smoking status Units: Subjects			
Current smoker Past smoker Never smoked	67 141 124		
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 UACR of 301-800 mg albumin/g creatinine UACR of 801-3000 mg albumin/g creatinine	117 117 98		
eGFR at screening			
eGFR: estimated glomerular filtration rate			
Units: Subjects			
25 to 59 mL/min/1.73 m2 inclusive ≥60 mL/min/1.73 m2	170 162		
Subjects on ACE inhibitors & ARBs			
ACE: angiotensin converting enzyme ARB: angiotensin II receptor blocker			
Units: Subjects			
ACE inhibitors ARBs Both Other	211 116 3 2		
Body mass index Units: kg/m2 arithmetic mean standard deviation	 -		

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

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

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 Units: Subjects			

Age continuous Units: years			
arithmetic mean	62.4	62.5	62.3
standard deviation	± 7.59	± 8.00	± 7.94
Gender categorical Units: Subjects			
Female	15	16	14
Male	49	47	51
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not hispanic or Latino	64	63	65
Race 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 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 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 Units: kg/m2 arithmetic mean standard deviation	 32.7 ± 5.10	 33.2 ± 4.37	 33.2 ± 5.13
Duration of type 2 diabetes Units: month arithmetic mean standard deviation	 178.8 ± 86.39	 179.7 ± 96.78	 195.4 ± 107.91
Duration of diabetic nephropathy Units: month arithmetic mean standard deviation	 44.1 ± 39.37	 54.6 ± 52.24	 47.4 ± 44.30
UACR			
UACR: urinary albumin:creatinin ratio			
Units: mg/g arithmetic mean standard deviation	 650.69 ± 620.143	 562.23 ± 553.516	 694.17 ± 704.568
eGFR (MDRD)			
eGFR: estimated glomerular filtration rate MDRD: Modification of Diet in Renal Disease			
Units: mL/min/1.73 m2 arithmetic mean standard deviation	 64.17 ± 26.069	 62.38 ± 24.215	 61.09 ± 25.065
eGFR (CKD-EPI)			
eGFR: estimated glomerular filtration rate CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration			
Units: mL/min/1.73 m2 arithmetic mean standard deviation	 65.82 ± 25.223	 64.39 ± 24.045	 62.80 ± 24.692
Serum creatinine Units: mg/dL arithmetic mean standard deviation	 1.26 ± 0.481	 1.27 ± 0.475	 1.33 ± 0.535
BUN			
BUN: Blood urea nitrogen			
Units: mg/dL arithmetic mean standard deviation	 23.8 ± 9.47	 25.9 ± 11.37	 25.3 ± 9.97
Serum phosphorus Units: mg/dL arithmetic mean standard deviation	 3.58 ± 0.465	 3.54 ± 0.429	 3.35 ± 0.514
HbA1c			
HbA1c: Hemoglobin A1c			
Units: percentage arithmetic mean standard deviation	 7.66 ± 0.960	 7.54 ± 0.865	 7.76 ± 1.085
Fasting plasma glucose Units: mg/dL arithmetic mean standard deviation	 158.4 ± 42.29	 170.4 ± 39.70	 170.5 ± 47.69

Fasting plasma insulin 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 Number of patients with values differs from number of patients in the groups: Placebo: n=63 CCX140-B 5 mg: n=62 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 Number of patients with values differs from number of patients in the groups: Placebo: n=55 CCX140-B 5 mg: n=56 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 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: 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; 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; 3. The protocol was revised to provide information on the study procedures required at each study visit; 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; 5. Potential reasons for early withdrawal from the study were revised. Rationale: To reflect the study extension; 6. New preclinical results from recently completed studies, including long-term rat and dog toxicology studies, were added; 7. New clinical data from recently completed clinical trials were added; 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 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: 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. 2. Changes to the protocol were made as 332 subjects had finally be enrolled in the study; 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 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: