Clinical trial results:
An Open Label, Intra-Subject Dose Escalation Study of CCX140-B in Subjects with Primary Focal Segmental Glomerulosclerosis (FSGS) and Nephrotic Syndrome

Summary

EudraCT number	2017-003022-32
Trial protocol	PL
Global end of trial date	24 June 2020

Results information

Result version number	v1
This version publication date	01 November 2022
First version publication date	01 November 2022

Trial information

Trial identification

Sponsor protocol code	CL012_140

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03703908
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 134007

Notes:

Sponsors

Sponsor organisation name	ChemoCentryx, Inc.
Sponsor organisation address	835 Industrial Road, San Carlos, United States, 94070
Public contact	Clinical Trials Disclosure, ChemoCentryx, clinicaltrials@chemocentryx.com
Scientific contact	Clinical Trials Disclosure, ChemoCentryx, 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	27 January 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 June 2020
Global end of trial reached?	Yes
Global end of trial date	24 June 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The Primary Efficacy Objective is to evaluate the effect of CCX140-B on proteinuria in subjects with primary FSGS with nephrotic syndrome.

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	21 September 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	5
EEA total number of subjects	1

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)	5
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

17 subjects were screened and 10 (58.8%) subjects failed screening due to not meeting inclusion/exclusion criteria, and 2 (11.88%) failed due to other reasons (one per sponsor request and one due to the Coronavirus Disease Pandemic).

Pre-assignment

Screening details:

The Screening Period was up to 28 days. Subjects visited the study centre during screening and on Day 1 (baseline), at pre-specified time points throughout Dose Escalation, and through Week 12.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Escalation Study of CCX140 B

Arm description:

All enrolled subjects will initially be treated with the active study medication CCX140-B at a dose of 5 mg twice daily. Dose will increase in a step-wise fashion up to 15 mg twice daily.

Arm type	Sequential
Investigational medicinal product name	CCX140-B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Eligible subjects started treatment with CCX140-B at 5 mg twice daily. CCX140-B was taken orally without food, at least 1 hour before a meal. The dose was increased in a stepwise manner to 15 mg twice daily.

Number of subjects in period 1	Escalation Study of CCX140 B
Started	5
Completed	2
Not completed	3
Consent withdrawn by subject	1
Progression of renal disease	1
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	5	5	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	5	5	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	37.6		
standard deviation	± 18.65	-	
Gender categorical Units: Subjects			
Female	1	1	
Male	4	4	
Race Units: Subjects			
White	4	4	
Other	1	1	
Ethnicity Units: Subjects			
Hispanic or Latino	2	2	
Not Hispanic or Latino	3	3	
Country Units: Subjects			
Poland	1	1	
United States	4	4	
Podocyte effacement			
Based on electron microscopy			
Units: Subjects			
<30%	1	1	
≥30%	4	4	
Glomeruli showing segmental lesions Units: Subjects			
≤1	1	1	

>1	4	4	
Concomitant use of glucocorticoids and/or immunosuppressive medications Units: Subjects			
Yes	4	4	
No	1	1	
Concomitant use of ACE inhibitor or ARB			
ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker			
Units: Subjects			
Yes	5	5	
No	0	0	
All calcineurin inhibitors combined			
Includes cyclosporin or tacrolimus			
Units: Subjects			
Yes	2	2	
No	3	3	
Concomitant use of rituximab or other anti-CD20 Units: Subjects			
Yes	0	0	
No	5	5	
Age at diagnosis of FSGS			
FSGS= focal segmental glomerulosclerosis			
Units: Years			
arithmetic mean	35.2		
standard deviation	± 19.18	-	
Duration of FSGS			
Duration of FSGS was calculated from the time of first diagnosis based on renal biopsy.			
Units: Months			
arithmetic mean	29.4		
standard deviation	± 16.32	-	
Baseline UPCR – morning void			
UPCR= urinary protein:creatinine ratio			
Units: g protein/g creatinine			
arithmetic mean	5.71		
standard deviation	± 1.563	-	
Baseline UPCR – 24-hour Units: g protein/g creatinine			
arithmetic mean	4.80		
standard deviation	± 1.376	-	
Baseline UACR – morning void			
UACR= urinary albumin:creatinine ratio			
Units: g protein/g creatinine			
arithmetic mean	4.12		
standard deviation	± 1.394	-	
Baseline UACR – 24-hour Units: g protein/g creatinine			
arithmetic mean	3.24		
standard deviation	± 1.316	-	
Baseline eGFR (CKD-EPI Creatinine-Cystatin C)			
eGFR= estimated glomerular filtration rate; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration			

Units: CKD-EPI Creatinine-Cystatin C			
arithmetic mean	50.60		
standard deviation	± 23.923	-	
Baseline eGFR (MDRD Creatinine)			
MDRD = Modification of Diet in Renal Disease			
Units: MDRD Creatinine			
arithmetic mean	54.40		
standard deviation	± 26.245	-	

End points

End points reporting groups

Reporting group title	Escalation Study of CCX140 B

Reporting group description:

All enrolled subjects will initially be treated with the active study medication CCX140-B at a dose of 5 mg twice daily. Dose will increase in a step-wise fashion up to 15 mg twice daily.

Primary: Median Reduction from Baseline of Urine Protein to Creatinine Ratio (UPCR) of at least 20%

End point title	Median Reduction from Baseline of Urine Protein to Creatinine Ratio (UPCR) of at least 20%[1]

End point description:

Median reduction from baseline of UPCR of at least 20%, i.e., ≥20%, by Week 12.

End point type	Primary

End point timeframe:

Baseline to week 12

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the small sample size and abbreviated summary of data no per-protocol analyses will be carried out.

End point values	Escalation Study of CCX140 B			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: g protein/g creatinine				
median (standard deviation)	()			

Notes:

[2] - Due to the small sample size and early termination of the study, no data was available

Statistical analyses

No statistical analyses for this end point

Secondary: Achievement of Partial Remission or Complete Remission of UPCR Through Week 12 and Through the End of Treatment

End point title	Achievement of Partial Remission or Complete Remission of UPCR Through Week 12 and Through the End of Treatment

End point description:

Partial and complete remission were defined as follows:
Partial remission (included all of the following):
Reduction from baseline by ≥50% in urine protein:creatinine ratio (UPCR)
Reduction in UPCR to a level that was <3.5 g/g
Subject could not have been a treatment failure

Complete remission (included all of the following):
Reduction in UPCR to <0.3 g/g
Serum albumin within normal range
For subjects with abnormal serum creatinine levels at baseline, return to normal levels
For subjects with normal serum creatinine levels at baseline, final value within 20% of baseline levels

Subject could not have been a treatment failure

End point type	Secondary

End point timeframe:

Baseline to week 12

End point values	Escalation Study of CCX140 B			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants				
Complete remission at Week 12	0			
Complete remission at End of Treatment	0			
Partial remission at Week 12	1			
Partial remission at End of Treatment	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Urine Protein:Creatinine Ratio (UPCR) Over Time

End point title	Change From Baseline in Urine Protein:Creatinine Ratio (UPCR) Over Time

End point description:

Mean change from baseline in urinary protein:creatinine ratio (UPCR) over time

End point type	Secondary

End point timeframe:

Baseline to week 12 and week 52

End point values	Escalation Study of CCX140 B			
Subject group type	Reporting group			
Number of subjects analysed	3[3]			
Units: g protein/g creatinine				
arithmetic mean (standard deviation)				
CCX140-B Week 52	-0.4985 (± 3.37926)			
CCX140-B Week 12	-1.3100 (± 3.76247)			

Notes:

[3] - Week 12 = 3 subjects
Week 52 = 2 subjects

Statistical analyses

No statistical analyses for this end point

Secondary: Time to and Proportion of Subjects With Achievement of Complete Remission during the treatment period

End point title	Time to and Proportion of Subjects With Achievement of Complete Remission during the treatment period

End point description:

Complete remission is defined as reduction in urine protein:creatinine ratio (UPCR) to <0.3 g/g, normal serum albumin, and normal serum creatinine levels or within 20% of baseline levels.

End point type	Secondary

End point timeframe:

Baseline to week 52

End point values	Escalation Study of CCX140 B			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: Participants				

Notes:

[4] - Due to the small sample size and early termination of the study, no data was available

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Time to and Proportion of Subjects With Achievement of Partial Remission during the treatment period

End point title	Assessment of Time to and Proportion of Subjects With Achievement of Partial Remission during the treatment period

End point description:

Partial remission is defined as reduction from baseline by ≥50% in UPCR, reduction in UPCR to a level that was <3.5 g/g.

End point type	Secondary

End point timeframe:

Baseline to week 52

End point values	Escalation Study of CCX140 B			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: Participants				

Notes:

[5] - Due to the small sample size and early termination of the study, no data was available

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Rescue Therapy

End point title	Time to Rescue Therapy

End point description:

Based on Investigator or physician initiation of glucocorticoids or new immunosuppressive agents or new major treatment modalities (e.g. plasmapheresis, dialysis)

End point type	Secondary

End point timeframe:

Baseline to week 52

End point values	Escalation Study of CCX140 B			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: Participants				

Notes:

[6] - Due to the small sample size and early termination of the study, no data was available

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 to week 52	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1
Reporting groups	
Reporting group title	Escalation Study of CCX140 B
Reporting group description:	
All enrolled subjects will initially be treated with the active study medication CCX140-B at a dose of 5 mg twice daily. Dose will increase in a step-wise fashion up to 15 mg twice daily.	

Serious adverse events	Escalation Study of CCX140 B		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Escalation Study of CCX140 B		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)		
Investigations			
Amylase increased			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Blood potassium increased			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Lipase increased			

subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Ophthalmoplegic migraine			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	3		
Tongue discomfort			

subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Renal and urinary disorders			
End stage renal disease			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Renal impairment			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Limb discomfort			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Tendonitis			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Pulpitis dental			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		

Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 2		
Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all) Hyperlipidaemia subjects affected / exposed occurrences (all) Hyperphosphataemia subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 April 2018	Amendment 1.0 Moved partial and complete remission from primary to secondary objectives and redefined them and evaluated median reduction of UPCR as primary efficacy Added several equations to calculate eGFR equations based on FDA recommendation in study CL011_140 The full list of conditions for subjects being allowed to enter the extended treatment was provided Emphasis added on the importance of 24h urine collection Language added in Dose Modification Based on PK Exposure section Changes made to exclusion numbering as well as addition of exclusion Histological FSGS subtype of collapsing variant Addition of History of gastrointestinal conditions, and medications to exclusion criteria Additional information added for concomitant medications Updated guidelines for reporting of pregnancies and special situation reporting and updated contact information (Medpace) for SAE reporting Addition of Clinical Pharmacologist to SRC and Rescue Therapy Clarifications made throughout for: Dose and dose adjustments Dose modification rules for individual subjects Standardization of all titration requirements on day 43 or beyond, and extended treatment period with the initial treatment period. Adjustment from at least 30% to ≥20% reduction in UPCR The acronym ACTG-BPNS was changed to ACTG-BPNST Detail added onto primary FSGS factors Further clarification made on exclusions i.e. intended exclusion/use of calcineurin inhibitors, or other immunotherapy, Glucocorticoids, addition of international normalized ratio (INR) blood-clotting test, change of QTc to QTcF, two separate criteria for drug exclusion and medication exclusion and CYP3A4 inhibitors and inducers excluded. Removed references to the CTCAE in adverse event reporting Clarity added to the time and events table and footnotes As well as additional administrative and grammatical changes throughout.

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 study was terminated early due to data from CL011_140 study showing that CCX140-B didn't demonstrate a meaningful reduction in proteinuria relative to the control group after 12 weeks of blinded treatment.

Notes: