



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study to Evaluate the Safety and Efficacy of CCX168 in Subjects with Anti-Neutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis on Background Cyclophosphamide or Rituximab Treatment

Summary

EudraCT number	2011-001222-15
Trial protocol	BE GB CZ SE DE NL HU PL AT IE FR
Global end of trial date	18 January 2016

Results information

Result version number	v1 (current)
This version publication date	12 August 2023
First version publication date	12 August 2023

Trial information

Trial identification

Sponsor protocol code	CL002_168
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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	850 Maude Avenue, Mountain View, California, United States, 94043
Public contact	Clinical trial disclosure, ChemoCentryx, Inc., +1 650-210-2900, clinicaltrials@chemocentryx.com
Scientific contact	Clinical trial disclosure, ChemoCentryx, Inc., +1 650-210-2900, 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	13 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 January 2016
Global end of trial reached?	Yes
Global end of trial date	18 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary safety objective of this study was to evaluate the safety and tolerability of CCX168 in subjects with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) on background cyclophosphamide or rituximab treatment.

The primary efficacy objective was to evaluate the efficacy of CCX168 based on the Birmingham Vasculitis Activity Score (BVAS) version 3.

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. An external data monitoring committee (DMC) reviewed safety data, including rescue glucocorticoid use over the course of the study, and advised the Sponsor regarding progression from each step to the next in the study.

Background therapy:

Standard therapy for AAV includes cyclophosphamide or rituximab and oral glucocorticoids, tapered over a period of time. IV Cyclophosphamide was used throughout the study as background treatment. Subjects with prior rituximab treatment received rituximab throughout.

Evidence for comparator: -

Actual start date of recruitment	27 September 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Sweden: 11
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Czech Republic: 5
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Hungary: 3

Worldwide total number of subjects	67
EEA total number of subjects	67

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)	44
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The Screening period must not have exceeded 14 days prior to Study Day 1 (the first day of dosing).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Placebo BID Plus 60 mg Prednisone
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Arm description:

Placebo plus a full dose of oral glucocorticoids

Arm type	Placebo
Investigational medicinal product name	CCX168 Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Three placebo capsules in the morning and three placebo capsules in the evening.

Duration: Daily for 84 consecutive days.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Prednisone dosage equivalent to 60 mg orally per day if body weight \geq 55 kg, or equivalent to 45 mg orally per day if body weight <55 kg.

Duration: Starting Day 1 with a tapered dose per protocol-specified schedule.

Arm title	CCX168 30 mg BID Plus 20 mg Prednisone
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Arm description:

30 mg CCX168, plus two-thirds reduced dose of oral glucocorticoids.

Arm type	Experimental
Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Prednisone dosage: 20 mg orally per day if body weight >55 kg, or 15 mg orally per day if body weight

<55 kg

Duration: Starting Day 1 with a tapered dose per protocol-specified schedule.

Investigational medicinal product name	CCX168
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Three 10 mg CCX168 capsules in the morning and three 10 mg capsules in the evening, approximately 12 hours following the morning dose.

Duration: Daily for 84 consecutive days.

Investigational medicinal product name	Prednisone-matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Dosage: equivalent to 40 mg orally per day if body weight > 55kg or equivalent to 30 mg orally per day if body weight <55 kg.

Duration: Starting Day 1 with a tapered dose per protocol-specified schedule.

Arm title	CCX168 30 mg BID Without Prednisone
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Arm description:

30 mg of CCX168

Arm type	Experimental
Investigational medicinal product name	CCX168
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Three 10 mg CCX168 capsules in the morning and three 10 mg capsules in the evening, approximately 12 hours following the morning dose.

Duration: Daily for 84 consecutive days.

Investigational medicinal product name	Prednisone-matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Equivalent to 60 mg orally per day if body weight >55 kg, or equivalent to 45 mg orally per day if body weight <55 kg.

Duration: Starting Day 1 with a tapered dose per protocol-specified schedule.

Number of subjects in period 1	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone
Started	23	22	22
Completed	18	19	18
Not completed	5	3	4
Consent withdrawn by subject	3	-	1
Physician decision	-	-	1

Adverse event, non-fatal	2	2	2
Rescue medication	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo BID Plus 60 mg Prednisone
Reporting group description: Placebo plus a full dose of oral glucocorticoids	
Reporting group title	CCX168 30 mg BID Plus 20 mg Prednisone
Reporting group description: 30 mg CCX168, plus two-thirds reduced dose of oral glucocorticoids.	
Reporting group title	CCX168 30 mg BID Without Prednisone
Reporting group description: 30 mg of CCX168	

Reporting group values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone
Number of subjects	23	22	22
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	13	16	15
From 65-84 years	10	6	7
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	59.1	57.0	57.4
standard deviation	± 14.0	± 14.2	± 14.0
Gender categorical Units: Subjects			
Female	6	8	6
Male	17	14	16
Ethnicity (NIH/ OMB) Units: Subjects			
Not Hispanic or Latino	23	22	22
Race (NIH/OMB) Units: Subjects			
White	23	22	22
Smoking Status Units: Subjects			
Current Smoker	3	2	4
Past Smoker	11	6	8
Never Smoked	9	14	10
ANCA disease status			

ANCA = anti-neutrophil cytoplasmic antibody			
Units: Subjects			
Newly diagnosed	18	15	16
Relapsed	5	7	6
Background treatment			
Units: Subjects			
Rituximab	3	5	5
Cyclophosphamide	20	17	17
Type of AAV			
AAV= ANCA-associated vasculitis; GPA = granulomatosis with polyangiitis (Wegener's)			
Units: Subjects			
GPA	10	11	12
Microscopic polyangiitis	10	9	9
Renal-limited vasculitis	2	2	1
Unknown	1	0	0
ANCA status categorical			
ANCA = anti-neutrophil cytoplasmic antibody; MPO=myeloperoxidase; PR3=proteinase 3			
Units: Subjects			
Anti-MPO positive	10	12	13
Anti-PR3 positive	11	10	8
Both anti-MPO positive and anti-PR3 positive	1	0	0
ANCA equivocal	0	0	1
ANCA negative	1	0	0
Urinary red blood cells			
Units of measure: per hpf; HPF= high power field			
Units: Subjects			
30-49	6	4	2
50-75	5	4	3
>75	3	5	3
No data available	9	9	14
BMI			
BMI = Body Mass Index 21 Subjects for CCX168 30 mg BID Plus 20 mg Prednisone and CCX168 30 mg BID Without Prednisone arms.			
Units: kg/m ²			
arithmetic mean	27.3	24.9	26.5
standard deviation	± 7.09	± 4.05	± 4.66
BVAS total score			
BVAS = Birmingham Vasculitis Activity Score			
Units: units on a scale			
arithmetic mean	13.2	14.3	13.8
standard deviation	± 5.80	± 5.98	± 6.38
VDI score			
VDI=Vasculitis Damage Index			
Units: units on a scale			
arithmetic mean	1.2	0.9	0.5
standard deviation	± 1.35	± 1.46	± 1.19
Glomerular filtration rate (MDRD)			
MDRD=Modification of Diet in Renal Disease 22 participants for Placebo BID Plus 60 mg Prednisone arm.			
Units: mL/min/1.73 m ²			
arithmetic mean	47.6	52.5	54.7

standard deviation	± 15.08	± 26.70	± 19.64
Albumin: creatinine ratio			
21 participants for CCX168 30 mg BID Without Prednisone arm. 22 participants for Placebo BID Plus 60 mg Prednisone arm.			
Units: mg/g			
geometric mean	353.9	278.6	283.4
full range (min-max)	28 to 5962	24 to 2459	25 to 3051
Urinary MCP-1: creatinine ratio			
MCP-1 = Monocyte chemoattractant protein 1			
Units: pg/mg creatinine			
geometric mean	825.9	1266.1	846.4
full range (min-max)	171.2 to 2549.2	360.8 to 7290.5	107.2 to 6075.7
ANCA- associated vasculitis disease duration at screening			
ANCA = anti-neutrophil cytoplasmic antibody 21 participants for CCX168 30 mg BID Without Prednisone arm			
Units: months			
median	0.0	0.0	1.0
full range (min-max)	0 to 162	0 to 61	0 to 108

Reporting group values	Total		
Number of subjects	67		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	44		
From 65-84 years	23		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	20		
Male	47		
Ethnicity (NIH/ OMB)			
Units: Subjects			
Not Hispanic or Latino	67		
Race (NIH/OMB)			
Units: Subjects			
White	67		
Smoking Status			
Units: Subjects			
Current Smoker	9		
Past Smoker	25		

Never Smoked	33		
ANCA disease status			
ANCA = anti-neutrophil cytoplasmic antibody			
Units: Subjects			
Newly diagnosed	49		
Relapsed	18		
Background treatment			
Units: Subjects			
Rituximab	13		
Cyclophosphamide	54		
Type of AAV			
AAV= ANCA-associated vasculitis; GPA = granulomatosis with polyangitis (Wegener's)			
Units: Subjects			
GPA	33		
Microscopic polyangiitis	28		
Renal-limited vasculitis	5		
Unknown	1		
ANCA status categorical			
ANCA = anti-neutrophil cytoplasmic antibody; MPO=myeloperoxidase; PR3=proteinase 3			
Units: Subjects			
Anti-MPO positive	35		
Anti-PR3 positive	29		
Both anti-MPO positive and anti-PR3 positive	1		
ANCA equivocal	1		
ANCA negative	1		
Urinary red blood cells			
Units of measure: per hpf; HPF= high power field			
Units: Subjects			
30-49	12		
50-75	12		
>75	11		
No data available	32		
BMI			
BMI = Body Mass Index 21 Subjects for CCX168 30 mg BID Plus 20 mg Prednisone and CCX168 30 mg BID Without Prednisone arms.			
Units: kg/m ²			
arithmetic mean			
standard deviation	-		
BVAS total score			
BVAS = Birmingham Vasculitis Activity Score			
Units: units on a scale			
arithmetic mean			
standard deviation	-		
VDI score			
VDI=Vasculitis Damage Index			
Units: units on a scale			
arithmetic mean			
standard deviation	-		
Glomerular filtration rate (MDRD)			
MDRD=Modification of Diet in Renal Disease			

22 participants for Placebo BID Plus 60 mg Prednisone arm.			
Units: mL/min/1.73 m ² arithmetic mean standard deviation	-		
Albumin: creatinine ratio			
21 participants for CCX168 30 mg BID Without Prednisone arm. 22 participants for Placebo BID Plus 60 mg Prednisone arm.			
Units: mg/g geometric mean full range (min-max)	-		
Urinary MCP-1: creatinine ratio			
MCP-1 = Monocyte chemoattractant protein 1			
Units: pg/mg creatinine geometric mean full range (min-max)	-		
ANCA- associated vasculitis disease duration at screening			
ANCA = anti-neutrophil cytoplasmic antibody 21 participants for CCX168 30 mg BID Without Prednisone arm			
Units: months median full range (min-max)	-		

End points

End points reporting groups

Reporting group title	Placebo BID Plus 60 mg Prednisone
Reporting group description:	Placebo plus a full dose of oral glucocorticoids
Reporting group title	CCX168 30 mg BID Plus 20 mg Prednisone
Reporting group description:	30 mg CCX168, plus two-thirds reduced dose of oral glucocorticoids.
Reporting group title	CCX168 30 mg BID Without Prednisone
Reporting group description:	30 mg of CCX168

Primary: Proportion of subjects achieving disease response at Day 85

End point title	Proportion of subjects achieving disease response at Day 85
End point description:	Disease response is defined as BVAS percentage reduction from baseline of at least 50% plus no worsening in any body system component.
End point type	Primary
End point timeframe:	Baseline to day 85

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	22	21	
Units: Participants	14	19	17	

Statistical analyses

Statistical analysis title	Analysis of Clinical Response Based on BVAS Score
Statistical analysis description:	BVAS = Birmingham Vasculitis Activity Score; ITT = Intent-to-Treat The proportion of subjects with a clinical response, defined as BVAS decrease from baseline of at least 50%, and no worsening in any body system component, after 12 weeks of treatment (at Day 85) for the ITT Population.
Comparison groups	Placebo BID Plus 60 mg Prednisone v CCX168 30 mg BID Plus 20 mg Prednisone

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
P-value	= 0.0019
Method	Noninferiority test for risk difference
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.3
upper limit	37.1

Notes:

[1] - Based on a non-inferiority margin of 20.0%.

Statistical analysis title	Analysis of Clinical Response Based on BVAS Score
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Statistical analysis description:

BVAS = Birmingham Vasculitis Activity Score; ITT = Intent-to-Treat

The proportion of subjects with a clinical response, defined as BVAS decrease from baseline of at least 50%, and no worsening in any body system component, after 12 weeks of treatment (at Day 85) for the ITT Population.

Comparison groups	Placebo BID Plus 60 mg Prednisone v CCX168 30 mg BID Without Prednisone
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[2]
P-value	= 0.0102
Method	Noninferiority test for risk difference
Parameter estimate	Noninferiority test for risk difference
Confidence interval	
level	90 %
sides	2-sided
lower limit	-11
upper limit	32.9

Notes:

[2] - Based on a non-inferiority margin of 20.0%.

Secondary: Proportion of Patients Achieving Renal Response at Day 85

End point title	Proportion of Patients Achieving Renal Response at Day 85
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End point description:

Renal response, assessed in patients with hematuria and albuminuria at baseline, and defined as an improvement in renal parameters, i.e., an increase from baseline to Day 85 in eGFR (Estimated glomerular filtration rate), MDRD (Modification of Diet in Renal Disease), serum creatinine equation, a decrease from baseline to Day 85 in haematuria (central laboratory microscopic count of urinary red blood cells), decrease from baseline to Day 85 in albuminuria count (first morning UACR (urinary albumin:creatinine ratio)).

End point type	Secondary
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End point timeframe:

Baseline to Day 85

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	18	18	
Units: Participants	8	10	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects Achieving Disease Remission at Day 85

End point title	Proportion of Subjects Achieving Disease Remission at Day 85
End point description: Disease remission is defined as BVAS (Birmingham Vasculitis Activity Score) of 0 or 1 plus no worsening in eGFR (Estimated glomerular filtration rate) and urinary RBC (Red Blood cell) count <10/high power field (hpf)	
End point type	Secondary
End point timeframe: Day 85	

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	22	21	
Units: Participants	7	6	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Day 85 in BVAS

End point title	Percent Change From Baseline to Day 85 in BVAS
End point description: Percent change in Birmingham Vasculitis Index Score (BVAS) at week 12, higher percentage change indicates worse outcome	
BVAS = Birmingham Vasculitis Activity Score	
The BVAS form is divided into 9 organ-based systems, with each section including symptoms/signs that are typical of that particular organ involvement in systemic vasculitis. The clinician only scores features believed to be due to active vasculitis. Completion of the form provides a numerical score, which ranges from 0 (best health) to 63 (worst health). A negative percentage change indicated improvement in health.	
End point type	Secondary
End point timeframe: Baseline to Day 85	

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	20	19	
Units: percentage change from baseline				
arithmetic mean (standard deviation)	-56.45 (± 62.100)	-79.05 (± 23.005)	-73.01 (± 29.464)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Day 85 in eGFR

End point title	Change From Baseline to Day 85 in eGFR
End point description: eGFR (Estimated glomerular filtration rate) based on the MDRD (Modification of Diet in Renal Disease) formula using serum creatinine	
End point type	Secondary
End point timeframe: Baseline to Day 85	

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	22	21	
Units: Change in eGFR ml/min/1.73 m ²				
arithmetic mean (standard deviation)	5.55 (± 10.211)	6.00 (± 10.469)	0.79 (± 9.549)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Day 85 in eGFR

End point title	Percent Change From Baseline to Day 85 in eGFR
End point description: eGFR (Estimated glomerular filtration rate) based on the MDRD (Modification of Diet in Renal Disease) formula using serum creatinine	
End point type	Secondary

End point timeframe:

Baseline to Day 85

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	21	19	
Units: Percentage change				
arithmetic mean (standard deviation)	15.36 (± 23.685)	19.91 (± 23.034)	0.92 (± 20.562)	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects Achieving Urinary RBC Count ≤5/Hpf at Any Time During the 84-day Treatment Period

End point title	Proportion of Subjects Achieving Urinary RBC Count ≤5/Hpf at Any Time During the 84-day Treatment Period
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End point description:

In subjects with baseline hematuria >5 RBCs/hpf (Red Blood Cell/High Power Field)

End point type	Secondary
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End point timeframe:

Baseline to Day 85

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	18	18	
Units: Participants	15	11	11	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Achieving Urinary RBC Count ≤5/Hpf at Any Point During the 84-day Treatment Period

End point title	Time to First Achieving Urinary RBC Count ≤5/Hpf at Any Point During the 84-day Treatment Period
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End point description:

In subjects with baseline hematuria ≤5 RBCs/hpf (Red Blood Cell/High Power Field)

*Most of the 75th quantiles were non-estimable due to small sample size. Therefore, the inter-quartile range (IQR) is non-estimable.

Days of first occurrence to urinary RBC ≤ 5 /HPF is as follows:

Placebo: median 69.0, 25th percentile 28.0, 75th percentile 84.0 CCX168 30 mg BID plus 20 mg

prednisone: median 69.0, 25th percentile 28.0, 75th percentile non-estimable CCX168 30 mg BID

without prednisone: median 42.0, 25th percentile 7.0, 75th percentile non-estimable

End point type	Secondary
End point timeframe:	
Baseline to Day 85	

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[3]	0 ^[4]	0 ^[5]	
Units: Participants				

Notes:

[3] - No data displayed because Outcome Measure has zero total participants analysed.

[4] - No data displayed because Outcome Measure has zero total participants analysed.

[5] - No data displayed because Outcome Measure has zero total participants analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects Achieving Urinary RBC Count ≤ 30 /Hpf at Any Time During the 84-day Treatment Period

End point title	Proportion of Subjects Achieving Urinary RBC Count ≤ 30 /Hpf at Any Time During the 84-day Treatment Period
End point description:	
In subjects with baseline hematuria ≥ 30 RBCs/hpf,(Red Blood Cell/High Power Field)	
End point type	Secondary
End point timeframe:	
Baseline to Day 85	

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	13	7	
Units: Participants	11	13	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Achieving Urinary RBC Count ≤ 30 /Hpf at Any Point

During the 84-day Treatment Period

End point title	Time to First Achieving Urinary RBC Count ≤ 30 /Hpf at Any Point During the 84-day Treatment Period
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End point description:

In subjects with baseline hematuria ≤ 30 RBCs/hpf (Red Blood Cell/High Power Field)

Most of the 75th quantiles were non-estimable due to small sample size. Therefore, the inter-quartile range (IQR) is non estimable.

Days of first occurrence to urinary RBC < 30 /HPF is as follows:

Placebo: median 10.5, 25th percentile 1.0, 75th percentile 35.0 CCX168 30 mg BID plus 20 mg

prednisone: median 21.0, 25th percentile 7.0, 75th percentile 42.0 CCX168 30 mg BID without

prednisone: median 42.0, 25th percentile 1.0, 75th percentile non estimable

End point type	Secondary
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End point timeframe:

Baseline to Day 85

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[6]	0 ^[7]	0 ^[8]	
Units: Participants				

Notes:

[6] - No data displayed because Outcome Measure has zero total participants analysed.

[7] - No data displayed because Outcome Measure has zero total participants analysed.

[8] - No data displayed because Outcome Measure has zero total participants analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Day 85 in Urinary RBC Count

End point title	Percent Change From Baseline to Day 85 in Urinary RBC Count
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End point description:

In subjects with hematuria at baseline, RBC (Red Blood Cell)

End point type	Secondary
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End point timeframe:

Baseline to Day 85

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	19	17	
Units: Percentage change				
arithmetic mean (full range (min-max))	-72.37 (-99.4 to 66.7)	1.63 (-99.7 to 1150.0)	-21.26 (-99.4 to 368.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Day 85 in UACR

End point title	Percent Change From Baseline to Day 85 in UACR
End point description: In subjects with albuminuria at baseline UACR (urinary albumin:creatinine ratio)	
End point type	Secondary
End point timeframe: Baseline to Day 85	

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	20	18	
Units: Percentage change				
arithmetic mean (full range (min-max))	-3.10 (-71.1 to 131.7)	-34.18 (-89.2 to 173.1)	-15.21 (-85.9 to 360.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Day 85 in Urinary MCP-1:Creatinine Ratio

End point title	Percent Change From Baseline to Day 85 in Urinary MCP-1:Creatinine Ratio
End point description: Urinary Monocyte Chemoattractant Protein-1 (MCP-1):creatinine ratio	
End point type	Secondary
End point timeframe: Baseline Day 85	

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	20	19	
Units: percentage change from baseline				
arithmetic mean (full range (min-max))	-37.57 (-72.7 to 41.0)	-59.29 (-93.6 to 60.1)	-39.44 (-90.7 to 59.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects Requiring Rescue IV or Oral Glucocorticoid Treatment

End point title	Proportion of Subjects Requiring Rescue IV or Oral Glucocorticoid Treatment
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to Day 85	

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	9	8	
Units: Participants	0	3	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Day 85 in the Vasculitis Damage Index

End point title	Change From Baseline to Day 85 in the Vasculitis Damage Index
End point description:	
VDI=Vasculitis Damage Index; The VDI is comprised of 64 items of damage, grouped into 11 organ-based systems or categorizations. Damage is defined as the presence of non-healing scars and does not give any indication of current disease activity. Damage is also defined as having been present or currently present for at least 3 months. Completion of the form provides a numerical score, which ranges from 0 (best health) to 64 (worst health).	
End point type	Secondary
End point timeframe:	
Baseline to Day 85	

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	20	19	
Units: score on a scale				
arithmetic mean (standard deviation)	0.7 (± 0.81)	0.3 (± 0.57)	0.2 (± 0.54)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Day 85 in Health-related Quality of Life as Measured by the SF-36 v2

End point title	Change From Baseline to Day 85 in Health-related Quality of Life as Measured by the SF-36 v2
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End point description:

SF-36v2: Medical Outcomes Survey Short Form-36 version 2. SF-36v2 measures each of the following eight health domains: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, and Mental Health. Scores on each item are summed and averaged. The SF-36v2 component domain scores range from 0 (worst health) to 100 (best health).

Number of subjects with data at baseline and the specified visit are specified.

*14 subjects for SF-36 Role Physical (Day 29), SF-36 Social Functioning (Day 29), SF-36 Reported Health Transition (Day 29), SF-36 Physical Functioning (Day 29) and SF-36 Role-Emotional (Day 29).
12 Subjects for SF-36 Physical Component Summary (Day 29) and SF-36 Mental Health Summary (Day 29).
13 Subjects for the rest of the categories.

End point type	Secondary
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End point timeframe:

Baseline, Day 29 & Day 85

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10 ^[9]	14 ^[10]	8 ^[11]	
Units: Change from baseline score on a scale				
arithmetic mean (standard error)				
SF-36 Role Physical (Day 29)	9.7 (± 10.73)	13.8 (± 7.61)	8.6 (± 6.02)	
SF-36 Role Physical (Day 85)	13.7 (± 11.06)	36.1 (± 9.28)	16.1 (± 9.24)	
SF-36 Bodily pain (Day 29)	3.1 (± 10.63)	17.3 (± 8.42)	5.1 (± 16.75)	
SF-36 Bodily pain (Day 85)	12.8 (± 7.36)	21.7 (± 9.54)	14.0 (± 9.30)	
SF-36 General Health Perceptions (Day 29)	2.5 (± 8.26)	3.7 (± 4.60)	-13.7 (± 10.21)	

SF-36 General Health Perceptions (Day 85)	5.7 (± 6.05)	2.3 (± 3.93)	-1.5 (± 5.51)	
SF-36 Vitality (Day 29)	7.63 (± 6.403)	12.98 (± 7.400)	-0.78 (± 3.630)	
SF-36 Vitality (Day 85)	4.36 (± 6.457)	22.28 (± 7.541)	10.71 (± 5.893)	
SF-36 Social Functioning (Day 29)	-2.8 (± 11.74)	24.1 (± 6.07)	-7.8 (± 6.22)	
SF-36 Social Functioning (Day 85)	6.3 (± 9.90)	35.6 (± 6.91)	5.4 (± 3.72)	
SF-36 Mental Health (Day 29)	1.7 (± 2.20)	10.8 (± 3.71)	-8.1 (± 6.88)	
SF-36 Mental Health (Day 85)	-1.0 (± 4.88)	16.5 (± 4.65)	2.1 (± 4.86)	
SF-36 Reported Health Transition (Day 29)	0.2 (± 0.22)	-0.6 (± 0.41)	0.3 (± 0.31)	
SF-36 Reported Health Transition (Day 85)	0.0 (± 0.37)	-1.2 (± 0.48)	-0.4 (± 0.48)	
SF-36 Physical Functioning (Day 29)	5.0 (± 6.18)	7.0 (± 6.90)	8.2 (± 11.46)	
SF-36 Physical Functioning (Day 85)	5.2 (± 7.00)	13.5 (± 7.73)	11.4 (± 8.43)	
SF-36 Role-Emotional (Day 29)	1.9 (± 9.08)	20.3 (± 8.04)	-1.1 (± 8.97)	
SF-36 Role-Emotional (Day 85)	0.0 (± 10.98)	21.8 (± 9.42)	10.7 (± 8.27)	
SF-36 Physical Component Summary (Day 29)	2.693 (± 3.436)	4.074 (± 2.601)	2.826 (± 4.526)	
SF-36 Physical Component Summary (Day 85)	5.383 (± 2.694)	6.744 (± 3.132)	4.863 (± 2.415)	
SF-36 Mental Health Summary (Day 29)	0.303 (± 3.120)	10.855 (± 3.244)	-4.760 (± 3.266)	
SF-36 Mental Health Summary (Day 85)	-0.766 (± 3.888)	11.779 (± 3.428)	2.197 (± 1.066)	

Notes:

[9] - 9 Subjects for all categories for Day 29

10 Subjects for all categories for Day 85

[10] - *see description for more details

[11] - 8 Subjects for all categories for Day 29

7 Subjects for all categories for Day 85

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Day 85 in Health-related Quality of Life as Measured by the EQ-5D-5L

End point title	Change From Baseline to Day 85 in Health-related Quality of Life as Measured by the EQ-5D-5L
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End point description:

EQ-5D-5L: EuroQuality of Life-5 Domains-5 Levels. The EQ-5D-5L consists of 2 pages: the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS). The descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems and extreme problems. The answers given can be converted into an Index Score ranging from 0 for death to 1 for perfect health. The EQ-5D questionnaire also includes a Visual Analog Scale (VAS), by which respondents can report their perceived health status with a grade ranging from 0 (the worst imaginable health) to 100 (the best imaginable health).

Number of subjects with data at baseline and the specified visit are specified.

End point type	Secondary
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End point timeframe:

Baseline, Day 29 and Day 85

End point values	Placebo BID Plus 60 mg Prednisone	CCX168 30 mg BID Plus 20 mg Prednisone	CCX168 30 mg BID Without Prednisone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	13	9 ^[12]	
Units: Change from baseline score on a scale				
arithmetic mean (standard deviation)				
VAS Score (Day 29)	-2.4 (± 10.61)	6.5 (± 17.96)	4.5 (± 12.62)	
VAS Score (Day 85)	-3.3 (± 13.23)	11.8 (± 17.61)	4.0 (± 4.69)	
Index Score (Day 29)	-0.044 (± 0.1597)	0.034 (± 0.1111)	-0.057 (± 0.0952)	
Index Score (Day 85)	-0.043 (± 0.1718)	0.067 (± 0.1314)	-0.047 (± 0.0721)	

Notes:

[12] - 8 Subjects for Vas Score and Index Score (Day 29)

7 Subjects for Vas Score and Index Score (Day 85)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

168 Day Treatment Period

Adverse event reporting additional description:

An adverse event is considered treatment-emergent if the start date of the event is on or after administration of the first dose of study medication

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.0
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Reporting groups

Reporting group title	CCX168 + No Prednisone
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Reporting group description:

The Safety Population included all subjects who were randomized and had received at least 1 dose of study medication.

Reporting group title	Placebo + Full Dose Prednisone
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Reporting group description:

The Safety Population included all subjects who were randomized and had received at least 1 dose of study medication.

Reporting group title	CCX168 + Low Dose Prednisone
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Reporting group description:

The Safety Population included all subjects who were randomized and had received at least 1 dose of study medication.

Serious adverse events	CCX168 + No Prednisone	Placebo + Full Dose Prednisone	CCX168 + Low Dose Prednisone
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 22 (45.45%)	5 / 23 (21.74%)	8 / 22 (36.36%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic enzymes increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			

subjects affected / exposed	1 / 22 (4.55%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	0 / 22 (0.00%)	1 / 23 (4.35%)	0 / 22 (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
Vascular disorders			
Vasculitis			
subjects affected / exposed	2 / 22 (9.09%)	1 / 23 (4.35%)	2 / 22 (9.09%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Microscopic polyangiitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 23 (0.00%)	0 / 22 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 23 (4.35%)	0 / 22 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 22 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
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			
Ocular Hyperaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
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			

Pleurisy			
subjects affected / exposed	0 / 22 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
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			
Rash			
subjects affected / exposed	1 / 22 (4.55%)	0 / 23 (0.00%)	0 / 22 (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			
Haematuria			
subjects affected / exposed	0 / 22 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 22 (4.55%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal vasculitis			
subjects affected / exposed	1 / 22 (4.55%)	1 / 23 (4.35%)	0 / 22 (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
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 23 (4.35%)	0 / 22 (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
Infections and infestations			
Respiratory tract infection			

subjects affected / exposed	2 / 22 (9.09%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 23 (4.35%)	0 / 22 (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
Lung infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 23 (0.00%)	0 / 22 (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
Viral infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 23 (4.35%)	0 / 22 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 22 (0.00%)	1 / 23 (4.35%)	0 / 22 (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: 5 %

Non-serious adverse events	CCX168 + No Prednisone	Placebo + Full Dose Prednisone	CCX168 + Low Dose Prednisone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 22 (95.45%)	21 / 23 (91.30%)	21 / 22 (95.45%)
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 22 (27.27%)	2 / 23 (8.70%)	2 / 22 (9.09%)
occurrences (all)	6	2	2

Deep vein thrombosis subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	2 / 23 (8.70%) 2	1 / 22 (4.55%) 1
Vasculitis subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	2 / 23 (8.70%) 2	3 / 22 (13.64%) 3
General disorders and administration site conditions			
Chills subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	0 / 23 (0.00%) 0	1 / 22 (4.55%) 1
Fatigue subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 4	3 / 23 (13.04%) 3	0 / 22 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	5 / 23 (21.74%) 5	1 / 22 (4.55%) 1
Pyrexia subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	3 / 23 (13.04%) 3	0 / 22 (0.00%) 0
Asthenia subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	0 / 23 (0.00%) 0	0 / 22 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	2 / 23 (8.70%) 2	3 / 22 (13.64%) 3
Epistaxis subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	2 / 23 (8.70%) 2	4 / 22 (18.18%) 4
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	2 / 23 (8.70%) 2	2 / 22 (9.09%) 2
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	3 / 23 (13.04%) 3	0 / 22 (0.00%) 0

Insomnia subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	1 / 23 (4.35%) 1	2 / 22 (9.09%) 2
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	1 / 23 (4.35%) 1	1 / 22 (4.55%) 1
Blood creatinine increased subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	2 / 23 (8.70%) 2	1 / 22 (4.55%) 1
Breath sounds abnormal subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	2 / 23 (8.70%) 2	1 / 22 (4.55%) 1
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 4	3 / 23 (13.04%) 3	3 / 22 (13.64%) 3
Paraesthesia subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	3 / 23 (13.04%) 3	3 / 22 (13.64%) 3
Dizziness subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	2 / 23 (8.70%) 2	0 / 22 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	2 / 23 (8.70%) 2	0 / 22 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	2 / 23 (8.70%) 2	1 / 22 (4.55%) 1
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	5 / 22 (22.73%) 5	6 / 23 (26.09%) 6	7 / 22 (31.82%) 7
Vomiting subjects affected / exposed occurrences (all)	5 / 22 (22.73%) 5	1 / 23 (4.35%) 1	4 / 22 (18.18%) 4

Constipation subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	3 / 23 (13.04%) 3	5 / 22 (22.73%) 5
Diarrhoea subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	3 / 23 (13.04%) 3	3 / 22 (13.64%) 3
Abdominal pain upper subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	2 / 23 (8.70%) 2	1 / 22 (4.55%) 1
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 23 (4.35%) 1	2 / 22 (9.09%) 4
Abdominal pain subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	2 / 23 (8.70%) 2	0 / 22 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	2 / 23 (8.70%) 2	2 / 22 (9.09%) 2
Skin and subcutaneous tissue disorders			
Purpura subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	1 / 23 (4.35%) 1	0 / 22 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	1 / 23 (4.35%) 1	1 / 22 (4.55%) 1
Hyperhidrosis subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	2 / 23 (8.70%) 2	0 / 22 (0.00%) 0
Erythema subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	2 / 23 (8.70%) 2	0 / 22 (0.00%) 0
Renal and urinary disorders			
Nocturia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 23 (4.35%) 1	3 / 22 (13.64%) 3
Renal vasculitis			

subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	2 / 23 (8.70%) 2	1 / 22 (4.55%) 1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 22 (22.73%)	2 / 23 (8.70%)	3 / 22 (13.64%)
occurrences (all)	5	2	3
Muscle spasms			
subjects affected / exposed	1 / 22 (4.55%)	5 / 23 (21.74%)	1 / 22 (4.55%)
occurrences (all)	1	5	1
Neck pain			
subjects affected / exposed	2 / 22 (9.09%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Back pain			
subjects affected / exposed	1 / 22 (4.55%)	5 / 23 (21.74%)	1 / 22 (4.55%)
occurrences (all)	1	5	1
Pain in extremity			
subjects affected / exposed	1 / 22 (4.55%)	0 / 23 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Musculoskeletal chest pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 23 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 22 (22.73%)	5 / 23 (21.74%)	4 / 22 (18.18%)
occurrences (all)	5	5	4
Rhinitis			
subjects affected / exposed	2 / 22 (9.09%)	1 / 23 (4.35%)	2 / 22 (9.09%)
occurrences (all)	2	1	2
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 23 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Bronchitis			
subjects affected / exposed	2 / 22 (9.09%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	2	1	0
Oral herpes			

subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	1 / 23 (4.35%) 1	0 / 22 (0.00%) 0
Respiratory tract infection subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	0 / 23 (0.00%) 0	2 / 22 (9.09%) 2
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 23 (0.00%) 0	2 / 22 (9.09%) 2
Viral infection subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	2 / 23 (8.70%) 0	0 / 22 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 23 (0.00%) 0	3 / 22 (13.64%) 3
Hypercholesterolaemia subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	1 / 23 (4.35%) 1	0 / 22 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 April 2012	<p>Changes made to the protocol included the following:</p> <ul style="list-style-type: none">- Laboratory results from the local laboratories obtained within 72 hours of Screening were acceptable in order to avoid unnecessary blood draws- A number of inclusion and exclusion criteria were clarified based on questions from the Investigators- Subjects were permitted to take immunosuppressive treatment, including azathioprine, mycophenolate mofetil, or methotrexate during the 84-day follow-up period, but not during the 84-day treatment period (the rationale was that it was consistent with standard practice at certain study centers)- Data from subjects receiving placebo in all 3 steps could have been combined, irrespective of the study step- A statement was included regarding subject care at the end of the study- A statement was included regarding review of substantial protocol Amendments by the Competent Authorities according to European Directive (CT-1)(2010/C 82/01)- A statement was included regarding archival of clinical study related documents for a period of 10 years according to European Union regulations (LVFS 2003:3)- A statement was included regarding implementation of the study according to Good Clinical Practice as per CPMP/ICH/135/95.
14 March 2013	<p>The main changes that Amendment 2.0 made to the protocol included the following:</p> <ul style="list-style-type: none">- The inclusion criteria for the protocol were amended to change the upper age limit from 75 years to 80 years, and the lower limit of eGFR from 30 mL/min/1.73 m² to 25 mL/min/1.73 m²;- Wording was added to indicate that oral glucocorticoid rescue treatment could be used instead of IV glucocorticoid rescue treatment at the discretion of the Investigator- Wording was added to indicate that data from Steps 1 and 2 could be combined depending on the study course- The study period was changed from 18 months to 30 months to reflect the study duration estimation at the time

30 May 2014	<ul style="list-style-type: none"> -Protocol modified to show that subjects with AAV with or without renal disease were eligible for the study; rituximab allowed instead of cyclophosphamide as background treatment -Study period changed to 60 months -Clinical study objectives revised to indicate the primary efficacy objective and priority order of secondary objectives -Step 3 of the study modified to include the Step 1 CCX168 group in addition to the Step 2 CCX168 group and the standard of care control group -Stratification for MPO and PR3 ANCA and cyclophosphamide or rituximab background treatment were added -Treatment during 84-day follow-up period standardized so that all subjects in the cyclophosphamide stratum received oral azathioprine, starting on Day 99 continuing through Day 168, and all subjects in the rituximab stratum did not receive any additional treatment during the 84-day follow-up period -SF-36 v2 and EQ-5D-5L added to measure changes in health related QoL -Inclusion and exclusion criteria modified to update disease nomenclature (eosinophilic granulomatosis with polyangiitis [Churg Strauss] and IgA vasculitis [Henoch-Schönlein purpura], to be consistent with inclusion of subjects with non-renal AAV, to include elderly subjects, subjects with eGFR ≥ 20 mL/min/1.73 m², hemoglobin ≥ 9 g/dL, liver enzymes not more than 3 x upper limit of normal, to allow up to 3000 mg of IV methylprednisolone prior to Screening, to exclude subjects who had received belimumab or tocilizumab within 12 weeks prior to Screening and subjects with a low lymphocyte count -Plasma sample collection for PD marker and saliva sample for polymorphism assessments added -Safety endpoint added to more precisely evaluate adverse events potentially associated with glucocorticoid use -Efficacy endpoints and statistical analysis methodology sections updated -Sample size estimation section revised -Trough plasma concentration added as a PK parameter -Potential measurements of rituximab plasma added
18 September 2015	<p>Changes made to the protocol included the following:</p> <ul style="list-style-type: none"> - The statistical methodology section was revised to indicate that the difference in proportions of subjects achieving the categorical endpoints were to be used instead of the odds ratio; an MMRM analysis for continuous variables was added - The study schema was corrected to indicate that the Step 3 enrollment target was 36 subjects, not 180 - Wording was revised to consolidate previous country-specific Amendments - Wording was added regarding stopping criteria for CCX168/placebo dosing of the protocol regarding WBC and neutrophil counts: If a subject developed Grade 2 or worse leukopenia or an ANC $< 1 \times 10^9/L$, dosing with CCX168 or placebo was to be ceased in such a subject. Study medication might be resumed only if WBC and absolute neutrophil count both exceeded the lower limit of the respective normal range, the Investigator deemed resumption to be appropriate, and the WBC and ANC were monitored closely thereafter. This recommendation was based on findings of leukopenia/neutropenia in 2 cases in another study in subjects with AAV (study CL003_168).

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.

This study is relatively small and the treatment duration was short.

Notes: