STATISTICAL ANALYSIS PLAN

Protocol Title	An Open-Label Phase 2 Study to Evaluate the Safety and Efficacy of CCX168 in Subjects with IgA Nephropathy on Stable RAAS Blockade
Protocol Number (Version Date)	CL005_168 Amendment 3.0 (17 July 2015)
Name of Test Drug	Complement 5a Receptor Antagonist CCX168
Indication	IgA nephropathy
Study Phase	2
Methodology	Single arm, open label, change from baseline
IND Number	123187
Sponsor	ChemoCentryx, Inc PPD PPD
Sponsor Representatives	PPD PPD MD, PhD Chief Medical Officer
Document Date	3 October 2016
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SIGNATURE PAGE

Protocol Title: An Open-Label Phase 2 Study to Evaluate the Safety and Efficacy of CCX168 in Subjects with IgA Nephropathy on Stable RAAS Blockade

Sponsor: ChemoCentryx, Inc.
PPD

Protocol Number: CL005_168

Document Date/Version: 3 October 2016 / Final Version 1.0

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SIGNATURE PAGE

Protocol Title: An Open-Label Phase 2 Study to Evaluate the Safety and Efficacy of CCX168 in Subjects with IgA Nephropathy on Stable RAAS Blockade

Sponsor: ChemoCentryx, Inc.
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1. ABBREVIATIONS

Abbreviation	Definition
AE	Adverse events
ATC	Anatomical Therapeutic Chemical
b.i.d.	twice a day
BMI	Body mass index
CFB	Change From Baseline
CTCAE	Common Terminology Criteria for Adverse Events
ECG	Electrocardiogram
eCRF	Electronic case report form
EGF	epidermal growth factor
eGFR	Estimated glomerular filtration rate
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
IgAN	IgA nephropathy
ITT	Intent-to-treat
MCP-1	Monocyte chemoattractant protein-1
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified intent-to-treat
PCR	Urinary protein : creatinine ratio
PD	Pharmacodynamics
PE	Physical Examination
PK	Pharmacokinetics
pP	Per protocol
PT	Preferred Term
RAAS	Renin-angiotensin-aldosterone system
SAE	Serious adverse event
SAP	Statistical analysis plan
SI	International System of Units
SOC	System Organ Class
TEAE	Treatment-emergent adverse event
TESAE	Treatment-emergent serious adverse event
WHODD	World Health Organization Drug Dictionary

2. REVISION HISTORY

This is version 0.2 of the SAP.

3. INTRODUCTION

This statistical analysis plan (SAP) is based on the clinical study protocol CL005_168, Amendment 3.0, dated 17 July 2015 and its associated electronic case report forms (eCRF).

This document describes the rules and conventions to be used in the analysis and presentation of efficacy and safety data as planned for the clinical protocol. It describes, in detail, the data and variables to be summarized and analyzed, including specifications of the analytical methods to be performed.

This SAP does not cover the statistical methods for drug concentration, pharmacokinetic parameters (PK) and pharmacokinetic/pharmacodynamics (PK/PD) analysis. These analyses will be described in a separate plan.

4. STUDY OBJECTIVES

4.1. Primary Objectives

The primary safety objective of this study is to evaluate the safety and tolerability of CCX168 in subjects with IgAN on background supportive therapy with a maximally tolerated dose of RAAS blockade.

The primary efficacy objective is to evaluate the efficacy of CCX168 based on an improvement in proteinuria.

4.2. Secondary Objectives

The secondary objectives of this study include assessment of:

1. Change in albuminuria with CCX168 treatment;
2. Change in renal function based on eGFR with CCX168 treatment;
3. Change in hematuria with CCX168 treatment;
4. Change in renal inflammatory activity based on urinary monocyte chemoattractant protein-1 (MCP 1):creatinine ratio and urinary epidermal growth factor (EGF):MCP-1 ratio with CCX168 treatment;
5. Change in serum IgA:plasma C3 ratio with CCX168 treatment;
6. Changes in pharmacodynamic markers in plasma and urine with CCX168 treatment, e.g., C3a, C5a, properdin, and sC5b-9;
7. Evaluation of the pharmacokinetic profile of CCX168 in subjects with IgAN.

5. STUDY DESIGN

5.1. General Description

This is an open-label, single arm study to test the safety, tolerability, and efficacy of CCX168 in reducing proteinuria in patients with IgAN and persistent proteinuria despite supportive therapy with a maximally tolerated RAAS blocker.

The study includes a ≤14 days screening period, a ≤4 weeks of RAAS dose titration period, a ≤7 days urinary PCR and eGFR eligibility confirmation period, an 8 weeks run-in period, and a 12 weeks treatment period, followed by a 12 weeks of follow-up period.

Patients who meet the inclusion criteria including

- biopsy-proven IgAN
- proteinuria > 1 g/g creatinine (by first morning urinary PCR)

and none of the exclusion criteria will be enrolled for blood pressure/RAAS blockade titration and run-in period. Patients' RAAS blocker(s) dose will be titrated to a maximally tolerated dose (MTD) to achieve a stable blood pressure target of <125/75 mmHg (SBP/DBP). Patients will be maintained on the stable dose of the RAAS blocker(s) for the run-in, treatment and follow-up periods. During the run-in period, patients' urinary protein: creatinine ratio will be collected and the slope over time will be calculated to form the baseline for the primary endpoint analysis. In the treatment period, patients will receive CCX168 b.i.d. The schedule of data collection is found in Study Diagram and Time and Events Table in the sections below.

5.2. Study Treatment

CCX168, 30 mg, will be administered b.i.d. during the treatment period.

5.3. Randomization Methodology

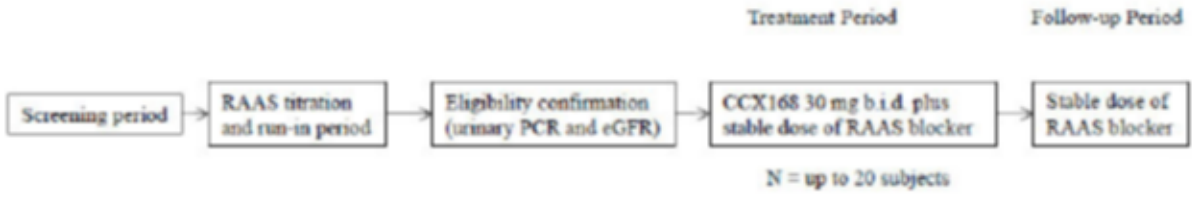
There is only one treatment group in the study. No randomization will be performed.

5.4. Stopping Rules and Unblinding

To safeguard the subject's well-being, the trial stopping criteria are set up as follows.

- If >25% of the patients (N>4) have developed CTCAE (v4.03) study drug-related Grade 3+ leukopenia, neutropenia, or lymphopenia deemed possibly related to CCX168 use, the trial will be stopped.
- The Sponsor will consider stopping the study if at least one subject develops severe liver injury believed to be caused by CCX168. Severe liver injury is based on Hy's law (elevated aminotransferase of >3 x upper limit of normal [ULN], alkaline phosphatase <2 x ULN, and associated with an increase in total bilirubin ≥2 x ULN). If any subject who receives CCX168 develops hepatic aminotransferase or total bilirubin elevations of >3 x ULN, CCX168 use will be stopped in this subject..

5.5. Study Schema



Duration:	≤14 days	Up to 12 weeks; On stable, maximally tolerated dose (MTD) of RAAS blocker for 8 weeks	≤ 7 days	84 days	84 days
Study visits:		RAAS blocker dose titration period: Up to 4 weeks; Once on MTD of RAAS blocker, visits on Day -63 and on Day -35 for U-PCR and eGFR measurements	Two visits in the Day -7 to -2 window for U-PCR and eGFR measurements	Visits: Days 1, 8, 15, 29, 43, 57, 71, and 85	Visits: Days 113, 141, and 169

5.6. Study Procedures

The schedule of events, as outlined in the study protocol, is provided below.

SCHEDULE OF EVENTS

	Study Day[1]														
	Screening[2]	Titration	Run-in			Treatment							Follow-up		
	≤ 14 days	≤ 28 days	-63	-35	-7 to -2	1[3]	8	15	29	43	57	85	113	141	169
Informed consent	X														
Demographics, medical history, prior medications	X														
Physical examination[4]	X					X[5]			X	X	X	X	X		X
Blood pressure[6]	X	X	X	X	X, X	X	X	X	X	X	X	X	X	X	X
RAAS blocker dose titration[7]		(X)													
RAAS blocker stable dosing at MTD			X→	→	→	→	→	→	→	→	→	→	→	→	→
Other vital signs[8]	X					X[5]	X	X	X	X	X	X	X	X	X
Serum pregnancy test for women of childbearing potential	X				X				X	X	X	X	X		X
HIV, HBV, HCV testing	X														
Serum chemistry[9], hematology	X					X[5]	X	X	X	X	X	X	X	X	X
Serum creatinine (not full chemistry)			X	X	X										
Urinalysis[10]	X					X[5]	X	X	X	X	X	X	X	X	X
Urine protein and creatinine assays	X		X	X	X, X	X[5]	X	X	X		X	X	X	X	X
Renal biopsy[11]	X											X			
Urine albumin, MCP-1, EGF, and microscopic RBC count			X	X	X	X[5]	X	X	X		X	X	X	X	X
Serum IgA and plasma C3 samples						X[5]			X		X	X	X	X	X
CCX168 dispensing						X[5]	X	X	X	X	X				
CCX168 dosing 30 mg b.i.d.						X→	→	→	→	→	→	→X			
CCX168 accountability							X	X	X	X	X	X			
PD plasma sample collection[12]						X[5]	X	X	X		X	X	X	X	X
PD urine sample collection						X[5]	X	X	X		X	X	X	X	X
PK plasma sample collection[13]						X[5]	X	X	X	X	X	X			
Concomitant medications	X	X	X	X	X, X	X[5]	X	X	X	X	X	X	X	X	X
Adverse event assessment		X	X	X	X, X	X[5]	X	X	X	X	X	X	X	X	X

[1] Visit Days 1, 8, and 15 must occur on the scheduled study days. Visit Days 29, 43, 57, and 85 may occur within a +/- 2-day window of the scheduled visit. Visit Days 113, 141, and 169 may occur within a +/- 4-day window of the scheduled visit.

[2] Screening must occur within a period not to exceed 14 days.

[3] Start of dosing with CCX168.
[4] Physical examination will include body weight measurement; Height will only be measured at Screening.
[5] These procedures must be done BEFORE taking the first dose of study medication.
[6] Blood pressure needs to be measured in the supine position after 3 minutes of rest.
[7] Four-week dose titration period only needed for patients who are not on a maximum tolerated dose of a RAAS blocker, or stable dose of two RAAS blockers.
[8] Assessment of heart rate and body temperature
[9] Serum chemistry including creatinine measurements
[10] Subjects will be asked to void their bladders completely, and a representative clean catch, midstream urine sample will be collected. Urinalysis includes pH, specific gravity, glucose, nitrite, ketones, bilirubin, urobilinogen, RBCs, and WBCs.
[11] Renal biopsy is an optional procedure for this study, except if necessary for eligibility assessment.
[12] Blood samples will be put in wet ice immediately after collection, centrifuged in a refrigerated centrifuge and plasma put at -70 °C.
[13] PK blood sample (4 mL) will be collected prior to the morning dose on Day 1 and at 0.5, 1, 2, 3, 4, and 6 hours following dosing.

6. DEFINITIONS

Table 1. Terminology and Definition

Terminology	Definition
Age	Age is calculated as the number of full years since date of birth at the time of signing the Informed Consent Form (ICF).
Study Drug	CCX168
Study Day	The number of days relative to the very first day when the subject receives a dose of the study drug. For visits prior to the first dose of the study drug, Study Day is calculated as Visit Date minus the first dose date. For visits after the first dose, Study Day is calculated as Visit Date minus the first dose date plus 1.
Screened	Subject who has signed informed consent.
Enrolled	Subject who has entered the RAAS dose titration/run-in period
Treated	Subject who has received a dose of the study drug.
Treatment Period	From the first dose to the last dose, inclusive, of the study drug
Follow-up Period	After the last dose, exclusive, of the study drug
Completer for the treatment	Subject who has completed the 12 weeks of the treatment period with Day 85 assessment.
Completer for the study	Subject who has completed the 12 weeks of the treatment period and follow-up period.
Baseline	Generally, baseline is defined as the non-missing value collected most recent to and before the time of the very first dose of the study drug unless specified otherwise. For urinary PCR, baseline will be the geometric mean of the two measurements made in the Day -7 to -2 window plus the Day 1 (pre-dose) value. For the eGFR, urinary ACR, MCP-1:creatinine ratio, EGF:MCP-1 ratio, and microscopic RBC count, baseline will be the geometric mean of the one measurement made in the Day -7 to 2 window plus the Day 1 (pre-dose) value.
Pre-treatment Adverse Event	Adverse event starting/worsening prior to the time of the first dose of the study drug administration.
Treatment Emergent Adverse Event	Adverse event starting/worsening between the first and last dose of the study drug administration.
Post-treatment Adverse Event	Adverse event starting/worsening after the last dose of the study drug.
Prior Medication	Medication on the Prior/Concomitant Medication CRF with start date prior to Study Day 1.
Concomitant Medication	Medication collected on the Prior/Concomitant Medication CRF with end date on/after Study Day 1, including missing end date or medication ongoing.

7. EFFICACY AND SAFETY VARIABLES

All efficacy variables are derived from laboratory blood and urine samples, unless indicated otherwise.

7.1. Primary Efficacy Endpoint

- Change in slope of first morning urinary PCR (protein:creatinine ratio) from the 8-week RAAS blocker run-in period to the 12-week treatment period.

7.2. Other Efficacy Endpoints

1. Proportion of subjects achieving renal response, defined as an improvement in proteinuria based on a decrease from baseline to Day 85 in proteinuria to a level <300 mg/g creatinine and maintaining estimated glomerular filtration rate (eGFR) within 15% of baseline
2. Proportion of subjects achieving a partial renal response, defined as an improvement in proteinuria based on a decrease from baseline to Day 85 in proteinuria to a level <1 g/g creatinine and maintaining eGFR within 15% of baseline
3. Change in slope from the run-in period to the treatment period for
    a. urinary ACR,
    b. eGFR,
    c. urinary MCP-1:creatinine ratio,
    d. urinary EGF:MCP-1 ratio, and
    e. urinary microscopic RBC counts
4. Percent change from baseline to Day 85 in
    a. urinary PCR and
    b. urinary ACR
5. Change from baseline (CFB) to Day 85 in eGFR
6. In patients with hematuria at baseline, the percent change from baseline in urinary RBC count
7. Percent change from baseline to Day 85 in urinary MCP-1:creatinine ratio
8. Percent change from baseline to Day 85 in serum IgA:plasma C3 ratio
9. Percent change from baseline to Day 85 in urinary EGF:MCP-1 ratio
10. Percent change from baseline in plasma and urinary biomarkers, e.g., C3a, C5a, properdin, and sC5b-9; if performed, results from these analyses will be presented in a separate report

7.3. Safety Variables

The primary safety endpoint is the subject incidence of adverse events.

Other safety endpoints include:

- Changes from baseline in all safety laboratory parameters;
- Changes from baseline in vital signs.

8. ANALYSIS POPULATIONS

The following subject populations will be evaluated and used for presentation and analysis of the data:

- **Safety Population** includes of all subjects who have received at least one dose of study drug.

- **Modified Intent-to-Treatment (mITT) Population** includes all subjects who have received at least one dose of study drug, and have at least one post baseline urinary PCR assessment.
- **Per-Protocol (pP) Population** includes all MITT subjects who have complied with the protocol for the study drug administration, have been on stable RAAS dose, and not taken protocol-prohibited concomitant medications.

The Safety population will be used for the summaries of disposition, demographics, baseline characteristics, medical history, and prior/concomitant medications. Additionally, the Safety population will be used for the summaries of adverse events, laboratory tests, ECG, and vital signs.

The mITT and pP populations will be used for the summaries of the efficacy endpoints.

9. DATA REVIEW AND PRESENTATION

9.1. Data Screening

In addition to the routine data review for individual subjects, all eCRF data will be periodically reviewed for consistency and accuracy across subjects. The periodic data review may involve ad hoc programming to generate edit checks. When available, tables, figures, and listings (TFL) may be used to identify data issues prior to the database lock.

9.2. Protocol Deviations

All protocol deviations will be classified as major or minor based on the following guidelines:

- Major protocol deviations are those that violate Good Clinical Practice (GCP) guidelines (ICH E6) and impact the ability to analyze the data collected. Examples may include but are not limited to: failure to administer the informed consent prior to initiating study procedures; non-compliance with taking study medication (less than 75% of medication taken based on study records or low plasma CCX168 concentrations indicating non-compliance); violations of inclusion and/or exclusion criteria that could affect the efficacy results.
- Minor deviations may include but are not limited to: out-of-window visits; scheduled assessments omitted or performed in improper sequence.

Protocol deviations will be categorized for data summary purpose.

9.3. Data Presentation

The following rules describe reporting conventions for the study.

- Report output will be provided as Rich Text Format (RTF) or Portable Document Format (PDF) documents generated using SAS.
- Font – Courier New or SAS font with minimum of 9 point font size for tables and 7 point for listings.
- Margins – Minimum of 3/4" bound edge margin and 3/8" other margins on 8.5"x11" paper as per the FDA guidance for e-submission.
- Continuous data will be summarized using n (number of subjects with non-missing observations), mean, median, standard deviation (STD), minimum value, and maximum value. Geometric means and geometric mean ratios (Visit:Baseline) will also be provided for urinary PCR, ACR, RBC count, MCP-1:creatinine, EGF:MCP-1 ratio, EGF:MCP-1 ratio, and serum IgA:plasma C3 ratio. Confidence intervals will also be provided for efficacy parameters.

- Categorical data will be summarized using the frequency count and percentage (n, %) of subjects in each category. Confidence interval for the percentage will be calculated for the efficacy variables.
- Number of subjects with non-missing values or number of subjects with missing values (eg, Not Done) will be presented, where appropriate. Subjects with missing values will not contribute to the denominator of percentage calculations.
- Counts of zero in any category will be presented without percentage.
- Precision of summary statistics:
    - Sample size (n, N) and number of missing responses (if displayed) – Integer.
    - Mean, confidence interval – One additional decimal place than reported/collected.
    - Standard deviation – Two additional decimal places than reported/collected.
    - Median, other percentile, minimum, maximum – Same number of decimal places as reported/collected.
    - Ratios – two decimal places.
    - Percentages – one decimal place generally, or two decimal places for <0.1%.
- Data listings will include pertinent subject information, eg, treatment, age/gender/race, study day. These will be sorted in the order of subject ID, assessment date/time and assessment (in the order collected on CRF, unless specified otherwise).
- Dates will be presented in the ISO-8601 format YYYY-MM-DD. Times will be displayed in 24-hour clock format.
- Numbering for tables, figures and listings will follow ICH E3 Guidelines.

10. STATISTICAL METHODS

10.1. Sample Size Justification

The sample size for the study is based on the slope of the urinary ACR observed in a study in patients with ANCA-associated vasculitis while receiving CCX168. The mean slope was -1.32, with a standard deviation of 1.67 over 12 weeks, and -4.62, with a standard deviation of 4.77 over the initial 4 weeks of the treatment with CCX168 in ANCA-associated vasculitis. Assuming a mean difference in pre-treatment and on-treatment slopes of 4.6, a sample size of 15 subjects will provide approximately 80% power and 20 subjects approximately 90% power to detect a difference in slopes.

10.2. General Statistical Methods and Data Handling

10.2.1. General Methods

Unless specified otherwise, all summary tables will be presented by visit from baseline to end of study (Day 169).

Summary statistics will be presented, as well as 2-sided 95% confidence intervals on selected parameters, as described in the sections below. All data will be included in the subject data listing.

10.2.2. Computing Environment

All statistical summaries and analyses will be performed using SAS software v9.4 or later, unless otherwise noted. Adverse events will be coded using MedDRA version 17.1. Concomitant medications will be coded using World Health Organization Drug Dictionary (WHODD) version March2012.

10.2.3. Grouping of Subjects

This is a single arm study. All subjects will be presented and summarized in the same treatment group.

10.2.4. Definition of Baseline

For all analyses, baseline will be defined as the most recent measurement prior to the date and time of the first administration of CCX168. Baseline can be on the same day as the first dose of study medication, but prior to administration of study drug (typically the Day 1 pre-dose value). For urinary PCR, baseline will be the geometric mean (GM) of the two measurements made in the Day -7 to -2 window plus the Day 1 (pre-dose) value. For the eGFR, urinary ACR, MCP-1:creatinine ratio, EGF:MCP-1 ratio, and microscopic RBC count, baseline will be the geometric mean of the one measurement made in the Day -7 to -2 window plus the Day 1 (pre-dose) value.

10.2.5. Methods of Pooling Data

No pooling of data with other studies is planned.

10.2.6. Adjustments for Covariates

Not applicable.

10.2.7. Multiple Comparisons/Multiplicity

Not applicable.

10.2.8. Subpopulations

Note applicable.

10.2.9. Withdrawals, Dropouts, Loss to Follow-up

Subjects who withdrew from the study will be included in the data listing and summary tables where applicable.

10.2.10. Missing, Unused, and Spurious Data

No imputation will be carried out for missing data points.

10.2.11. Visit Windows

No visit window will be used. All data will be summarized by the evaluation visit recorded on the eCRF. In data listings, all dates will be presented along with the study day relative to the day of the first dose of the study drug.

10.3. Interim Analyses

This is an unblinded single arm study. No formal interim analysis will be performed.

10.4. Subject Disposition

The number of subjects who have signed the informed consent, who entered the titration period, who entered the run-in period, who received study drug, who completed the 12-week treatment period of the study, who discontinued the 12-week period early (with reasons for discontinuation), who completed the

12-week follow-up period, who discontinued the 12-week follow-up period early (with reasons for discontinuation), will be tabulated.

A by-subject data listing of study completion information, including the reason for premature study withdrawal, if applicable, will be presented. If discontinuation is due to an AE, the AE will be specified.

Major and minor protocol deviations will be included in the subject data listing. Subjects with major protocol deviations affecting efficacy evaluation will be excluded from the pP population.

10.5. Demographic and Baseline Characteristics

Demographics (age, sex, race, and ethnicity) as well as height (cm), weight (kg), and BMI at baseline will be summarized for the safety population using descriptive statistics. All demographic data will be provided in a data listing.

IgAN disease duration, calculated from time of first renal biopsy diagnosis to Study Day 1, will be summarized with descriptive statistics.

10.6. Titration and Run-In Periods

The following data collected during the titration (if applicable) and run-in periods will be listed by subject and summarized:

- Blood pressure measurements (supine, after at least 3 minutes of rest);
- RAAS blocker(s) type and dose titration detail;
- Serum creatinine and eGFR measurements;
- Urinary PCR and ACR measurements;
- Urinary MCP-1:creatinine ratio, EGF:MCP-1 ratio, and urinary microscopic RBC count data;
- Changes in concomitant medications, with particular attention to the dose(s) of RAAS blocker(s), and
- Any pre-treatment adverse events reported.

10.7. Efficacy Evaluation

10.7.1. Change in slope of first morning urinary PCR (protein:creatinine ratio) from the 8-week RAAS blocker run-in period to the 12-week treatment period

Slope will be calculated for each subject using the time points as follows.

Time Window for Slope Calculation	Time Points Used for Slope Calculation	Corresponding Time Value Used for Regression*
Weeks -8 to -5	Day -63 and Day -35	-63 and -35
Weeks -4 to -1	Day -35, Day -7 to 02, and Day 1	-35, -5, and 0
Weeks -8 to -1	Day -63, Day -35, Day -7 to 02, and Day 1	-63, -35, -5, and 0
Weeks 1 to 4	Day 1, Day 8, Day 15, and Day 29	0, 7, 14, 28
Weeks 1 to 12	Day 1, Day 8, Day 15, Day 29, Day 57, and Day 85	0, 7, 14, 28, 56, and 85

* For Time Point Day -7 to -2, time value of -5 will be used. For Study Day on/after the first dose, one day is subtracted to return the value to continuous scale such that Day 0 is day of first dose.

For the primary efficacy endpoint analysis, the slope of the urinary PCR during the 8-week run-in period, during the initial 4-week treatment period, as well as the full 12-week treatment period will be calculated for each subject. The mean slope for the 8-week run-in period will be compared to the mean slope for the initial 4-week, as well as the full 12-week treatment period to evaluate the treatment effect of CCX168.

If the slope for the first 4 weeks of the run-in period is steeper than the slope of the last 4 weeks of the run-in period, indicating that steady state has not been achieved over the first 4 weeks, the slope of the last 4 weeks of the run-in period will be used as the baseline slope, instead of the slope over the 8 weeks of the run-in period. This comparison will be performed by the paired t-test. The 95% confidence interval for the difference in the mean slopes will be presented.

10.7.2. Proportion of subjects achieving renal response

Renal response is defined as (1) a decrease in proteinuria from baseline to Day 85 to a level of <300 mg/g creatinine and (2) maintaining the Day 85 estimated glomerular filtration rate (eGFR) within 15% of baseline. The number (%) of subjects achieving renal response will be calculated and presented. Subjects who discontinued prior to Week 12 will be counted as non-responders.

10.7.3. Proportion of subjects achieving partial renal response

Partial renal response is defined as (1) a decrease in proteinuria from baseline to Day 85 to a level of <1 g/g creatinine and (2) maintaining the estimated glomerular filtration rate (eGFR) within 15% of baseline. The number (%) of subjects achieving partial renal response will be calculated and presented. Subjects who discontinued prior to Week 12 will be counted as non-responders.

10.7.4. Change in slope from the run-in period to the treatment period for

a. urinary ACR,
b. eGFR,
c. urinary MCP-1:creatinine,
d. urinary EGF:MCP-1, and
e. urinary microscopic RBC counts

These variables will be summarized similarly to the primary efficacy variable.

10.7.5. Percent change from baseline to Day 85 in

a. urinary PCR and
b. urinary ACR

Urinary PCR and ACR will be summarized with geometric mean, median, minimum, and maximum at each visit. Percent change from baseline will be based on the geometric mean ratios of Visit:Baseline. The 95% confidence interval for the geometric mean ratios will be presented.

10.7.6. Change from baseline to Day 85 in eGFR

Estimated GFR and its change from baseline will be summarized with arithmetic mean, standard deviation, SEM, median, minimum, and maximum at each visit. The 95% confidence interval for the change will be presented.

10.7.7. In patients with hematuria at baseline, the percent change from baseline in urinary RBC count

For the purpose of analysis, urinary RBC count will be recoded as follows. None = 0.1, Occ = 0.5, 1 - 2 = 1, 3 - 5 = 3, 6 - 9 = 6, 10 - 15 = 10, 16 - 29 = 16, 30 - 49 = 30; 50 - 75 = 50, >75 = 75.

The method of summary described in Section 10.6.5 applies here.

10.7.8. Percent change from baseline to Day 85 in urinary MCP-1:creatinine ratio; Percent change from baseline to Day 85 in serum IgA:plasma C3 ratio ; Percent change from baseline to Day 85 in urinary EGF:MCP-1 ratio

The method of summary described in Section 10.6.5 applies here.

10.7.9. Shift in Urinary PCR, ACR, and hematuria

Shift tables will be created for urinary parameters, such as urinary PCR, ACR, and red blood cells, from baseline to each visit. The categories of interest are <300 mg/g, 301-1000 mg/g, ≥1000 mg/g for PCR and ACR, and ≤5 RBCs/hpf, >5 to <30 RBCs/hpf, and ≥30 RBCs/hpf for urinary RBC count.

10.7.10. Percent change from baseline in plasma and urinary biomarkers, e.g., C3a, C5a, properdin, and sC5b-9

If conducted, the results will be presented in a separate report.

10.8. Safety Analyses

Safety analyses will be conducted using the Safety Population.

10.8.1. Drug Exposure

Study drug compliance will be calculated for each patient by dividing the total number of capsules taken (number dispensed – number returned) by the total number prescribed. Duration of subject on CCX168 will be calculated as the time interval (weeks) between first and last dose of the study drug, inclusive. The total number of capsules prescribed is calculated as 6 capsules/day x number of days in the duration. The % compliance and duration of exposure will be summarized with descriptive statistics.

10.8.2. Adverse Events

Adverse events will be coded using MedDRA and displayed in tables using MedDRA SOC and PT.

Treatment emergent adverse event (TEAE) will be summarized using a subject incidence table. In the table, the number and percent (%) are calculated based on the number of unique subjects within each category (eg, PT). A subject reporting multiple events of the same category will be counted only once for the category. For summary purpose, AE relationship to the study drug will be grouped into "possibly related" or "probably not related". For subjects with more than one event coded to the same PT, the subjects will be counted for the categories with the strongest relationship and the greatest severity. On-treatment TEAEs and post-treatment TEAEs will be summarized separately.

An AE overview table summarizing the number (%) subjects meeting each of the following criteria will be presented, where appropriate.

- Treatment-emergent AE (TEAE)
- Possibly related TEAE
- TEAE leading to study drug discontinuation
- CTCAE Grade 3+ TEAE
- Treatment-emergent serious AE (TESAE)
- Related TESAE
- TEAEs with outcome of death

Additionally, the following subject incidence tables will be presented.

- TEAEs by PT sorted by the decreasing order of subject incidence
- TEAEs by SOC and PT sorted by the alphabetic order of the SOC and PT
- TEAEs by SOC and PT, grouped by relationship to study drug (possibly related or probably not related)
- TEAEs by SOC and PT, grouped by CTCAE grade

Data listings will be provided for subjects who died on study, experienced SAEs, or had AEs leading to study drug discontinuation.

A subject data listing will be provided for all adverse events. Included in the listing are the reported term, PT, SOC, TEAE flag, study day and study period (pre-treatment, on-treatment, and post-treatment) when AE starts, duration, relationship, severity, action taken, outcome, and seriousness category.

10.8.3. Laboratory Data

All laboratory reporting units will be converted to International System of Units (SI) units before any calculations. The actual value and change from baseline to scheduled post baseline visit will be summarized for hematology and chemistry. Additionally, subject incidences of shift from baseline classification (with respect to the normal range) to the post-baseline classification will be presented as a shift table. The summary and shift tables will be presented for all visits.

All laboratory data will be included in the by-subject and visit listings. Flags for laboratory values outside of normal limit (L and H) will be applied in the listings.

10.8.4. Vital Signs

Vital signs (body temperature, heart rate, respiration rate, systolic blood pressure, and diastolic blood pressure), and their changes from baseline will be summarized by visit. A subject data listing will be provided.

10.8.5. Physical examination

All physical examination findings will be presented in a data listing.

10.8.6. Concomitant Medications

Prior or concomitant medications will be coded using the WHODD. Subject incidences of the prior and concomitant medications will be tabulated by Anatomic Therapeutic Chemical classification (ATC3) and PT.

The use of concomitant medications will be included in a by-subject data listing.

The total daily dose of RAAS blockers at start of CCX168 dosing will be summarized by the Preferred Term.

11. CHANGES TO PLANNED ANALYSES

None.

12. REFERENCES

None.

APPENDIX A
List of Tables, Listings, and Figures

NUMBER	TITLE	POPULATION
Tables		
14.1.1.1	Disposition	MITT
14.1.1.2	Disposition	Safety
14.1.2.1	Subject Demographics	MITT
14.1.2.2	Subject Demographics	Safety
14.1.3	Baseline IgA Nephropathy Duration	Safety
14.1.4.1	Study Drug Exposure	MITT
14.1.4.2	Study Drug Exposure	Safety
14.1.5	Prior Medications by WHODD Anatomic Therapeutic Chemical Classification and Preferred Term	Safety
14.1.6	Concomitant Medications by WHODD Anatomic Therapeutic Chemical Classification and Preferred Term	Safety
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14.2.2.1	Subjects Achieving Renal Response	MITT
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14.2.3	Change from Baseline in Slope of Urinary Albumin to Creatinine Ration (ACR)	MITT
14.2.4	Change from Baseline in Slope of Urinary Estimated Glomerular Filtration Rate (eGFR)	MITT
14.2.5	Change from Baseline in Slope of Urinary MCP-1 to Creatinine Ratio	MITT
14.2.6	Change from Baseline in Slope of Urinary Epidermal Growth Factor (EGF) to MCP-1 Ratio	MITT
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14.2.8	Percent Change from Baseline in Urinary Protein to Creatinine Ratio	MITT
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16.2.1.5	Prior and Concomitant Medications	Safety
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