Statistical Analysis Plan

A Phase 1, Randomized, Double-blind, Three-arm, Parallel Group, Single-dose Study to Compare the Pharmacokinetics and Safety of Three Formulations of Omalizumab (CT-P39, EU-approved Xolair, and US-licensed Xolair) in Healthy Subjects

Protocol No. CT-P39 1.1

[redacted]

Version: 3.0
Date: 01-Jun-2021

[redacted]

Sponsor:
CELLTRION, Inc.

[redacted]

CONFIDENTIAL

SIGNATURES

Sponsor Protocol No.: CT-P39 1.1

[redacted]

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[redacted]

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LIST OF ABBREVIATIONS

$\%AUC_{ext}$	Percentage of $AUC_{0\text{-}inf}$ obtained by extrapolation
AE	Adverse Event
AESI	Adverse Event of Special Interest
ADA	Anti-Drug Antibodies
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
ANCOVA	Analysis of Covariance
AST	Aspartate Aminotransferase
$AUC_{0\text{-}last}$	Area Under the Concentration-Time Curve From Time Zero to the Last Quantifiable Concentration
$AUC_{0\text{-}inf}$	Area Under the Concentration-Time Curve From Time Zero to Infinity
BLQ	Below Lower Limit of Quantification
BMI	Body Mass Index
BP	Blood Pressure
BT	Body Temperature
CI	Confidence Interval
CL/F	Apparent Total Body Clearance
C_{max}	Maximum Serum Concentration
C_{min}	Minimum Serum Concentration
CPK	Creatine Phosphokinase
CRO	Clinical Research Organization
CRP	C-reactive Protein
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
CV	Coefficient of Variation
DRM	Data Review Meeting
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EMA	European Medicines Agency

EOS	End-of-Study
EU	European Union
FDA	Food and Drug Administration
GGT	Gamma Glutamyl Transferase
HBsAg	Hepatitis B Surface Antigen
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HR	Heart Rate
ICF	Informed Consent Form
IgE	Immunoglobulin E
ISR	Injection Site Reaction
ITT	Intent-to-Treat
λ_z	Terminal Elimination Rate Constant
LDH	Lactate Dehydrogenase
LLoQ	Lower Limit of Quantification
Max	Maximum
MedDRA	Medical Dictionary For Regulatory Activities
Min	Minimum
NAb	Neutralizing Antibody
PD	Pharmacodynamic
PFS	Pre-filled syringe
PK	Pharmacokinetic
PT	Preferred Term
RBC	Red Blood Cell
RR	Respiratory Rate
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
[redacted]	[redacted]
SD	Standard Deviation
SI	International System

SOC	System Organ Class
SOPs	Standard Operating Procedures
SUSAR	Suspected Unexpected Serious Adverse Reaction
TEAE	Treatment-Emergent Adverse Event
$t_{1/2}$	Terminal Elimination Half-Life
T_{max}	Time to C_{max}
T_{min}	Time to C_{min}
ULoQ	Upper Limit of Quantification
VAS	Visual Analogue Scale
V_z/F	Apparent Volume of Distribution During the Terminal Phase
WBC	White Blood Cell
WHO DD	World Health Organization Drug Dictionary

1. Introduction

This statistical analysis plan (SAP) is intended to give a detailed description of the summaries and the analyses that will be generated for the present study by [redacted]. Analyses specified in this plan are based on Protocol No. CT-P39 1.1, Version 2.0, dated 20 Apr 2020 [redacted]. Safety, immunogenicity, pharmacokinetic (PK) and pharmacodynamic (PD) analyses will all be described.

Any changes to the SAP will be made with a prior approval of the study Sponsor, and the changes and justification for the changes will be outlined in the planned clinical study reports (CSRs), of which there are two. The first CSR will report the safety, PK and immunogenicity data after the completion of Day 29 of subjects in Part 1. The second CSR will report all safety, PK, PD and immunogenicity data after completion of all visits of all subjects in both Part 1 and Part 2. No revision to the SAP will be required for changes that do not affect the statistical analysis methods, definitions, or rules defined in this document.

When applicable, all methodologies and related processes will be conducted according to [redacted] Standard Operating Procedures (SOPs) as appropriate. Shells for all statistical tables, listings, and figures referred to in this SAP will be displayed in a separate document.

2. Study Objectives

2.1 Primary objective

Part 2:

- To demonstrate PK similarity in terms of area under the concentration-time curve from time zero to infinity ($AUC_{0\text{-inf}}$), area under the concentration-time curve from time zero to the last quantifiable concentration ($AUC_{0\text{-last}}$), and maximum serum concentration (C_{max}) of CT-P39, EU-approved Xolair, and US-licensed Xolair in healthy subjects (CT-P39 to EU-approved Xolair, CT-P39 to US-licensed Xolair, and EU-approved Xolair to US-licensed Xolair).

2.2 Secondary objectives

Data for each part will be independently analyzed and presented.

Part 1:

- To evaluate initial safety up to Day 29 in terms of treatment-emergent adverse events (TEAEs) of CT-P39, compared to that of EU-approved Xolair in healthy subjects.

- To assess additional safety, PK, and immunogenicity of CT-P39 and EU-approved Xolair in healthy subjects up to Day 29.

Both parts:

- To assess additional safety, PK, PD, and immunogenicity of CT-P39, EU-approved Xolair, and US-licensed Xolair in healthy subjects up to Day 127.

3. Study Design

3.1 General Design

This study is a randomized, double-blind, 2-part, parallel, single-dose study, in healthy male and female subjects aged between 18 and 55 years (both inclusive).

This study will be conducted in two parts in approximately 177 subjects. Subjects will be included in either of the parts of the study. Part 1 is a randomized, double-blind, two-arm, parallel group, single-dose study. The first 30 subjects will be enrolled in Part 1 to compare the initial safety and randomized in a 1:1 ratio to receive a single dose (150 mg) of CT-P39 or EU-approved Xolair. The result of Part 1 will not affect the progression into Part 2.

Part 2 is a randomized, double-blind, three-arm, parallel group, single-dose study. Approximately 147 subjects will be subsequently enrolled in Part 2 to demonstrate PK similarity and randomized in a 1:1:1 ratio to receive a single dose (150 mg) of CT-P39, EU-approved Xolair, or US-licensed Xolair. All subjects in Part 1 and Part 2 will undergo the same assessments. However, each part will be conducted independently, and data for each part will be analyzed and presented separately.

A study drug will be administered subcutaneously via pre-filled syringe (PFS) on Day 1 and subjects will be followed up for 127 days for PK, PD, safety, and immunogenicity assessments.

3.2 Study Procedures

The overall schedule of study procedures and assessments is provided in Appendix 1.

3.3 Determination of Sample Size

Overall, a total of approximately 177 subjects will be enrolled in this study.

For Part 1 of the study, approximately 30 healthy subjects will be randomized to receive either CT-P39 or EU-approved Xolair. A sample size justification based on a statistical hypothesis is not relevant for Part 1, hence a formal statistical inference will not be made.

For Part 2 of the study, 126 subjects (42 in each group) with evaluable data in the primary PK Set provide 90% statistical power to show that the 90% confidence interval (CI) for the ratio of geometric means of PK parameters (CT-P39 to EU-approved Xolair, CT-P39 to US-licensed Xolair, and EU-approved Xolair to US-licensed Xolair) lies within equivalence margins of 80% to 125% assuming that the coefficient of variation (CV) is 30% and the expected ratio is 1.03. The sample size is calculated from two one-sided tests with each at 5% significance level. Accounting for 15% of randomized subjects excluded from the PK Set, approximately 147 subjects (49 in each group) will be randomized to achieve the required sample size of 42 per group.

3.4 Definition of Baseline

Unless stated otherwise, baseline will be defined as the last non-missing measurement (including repeated and unscheduled assessments) before the administration of the study drug. Post-baseline will be considered as all measurements collected after the administration of the study drug.

3.5 Randomization, Stratification, and Blinding

Randomization will occur at Day 1 after eligibility for the study has been confirmed. Subjects will be randomly assigned to treatment groups (1:1 ratio of CT-P39 or EU-approved Xolair for Part 1 and 1:1:1 ratio of CT-P39, EU-approved Xolair or US-licensed Xolair for Part 2). The randomization will be stratified by body weight (<70 kg versus ≥70 kg), serum total IgE level (<40 IU/mL versus ≥40 IU/mL), and sex (male versus female) as a part of the randomization for balanced distribution.

The study will be performed in a double-blind manner. The randomization codes will not be revealed to study subjects, investigators, or study center personnel except for the pre-defined unblinded personnel.

As the presentations of the two study drugs are not identical in visual appearance, the trained clinical staff member(s) responsible for drug administration (e.g., nurse/physician, etc.) will be designated as unblinded site personnel and will not be involved in any clinical or safety evaluations that are part of the blinded protocol or have other subject contact. Subjects will be blinded through the use of a blindfold, screen or similar method during the dosing procedure so that the injection syringe will not be visible to subject. Blinded staff will be absent during injection and remain blinded throughout the study.

Under normal circumstances, the blind should not be broken. The blind should be broken if specific emergency treatment would be dictated as knowing the study drug assignment is required for medical management. In such cases, the investigator may, in an emergency, determine the identity of the study drug. If suspected unexpected serious adverse reactions (SUSARs), which are subject to expedited reporting, occur, the blind should be broken before submission to the competent authorities, if required. If the blind is broken, the date, time and reason for the unblinding must be documented in the appropriate field of the electronic Case Report Form (eCRF) and the medical monitor and/or the sponsor will be informed as soon as possible. Any subjects for whom the blind is broken may continue in the study.

The randomization code for each part will be broken separately to report results of the respective part. The first code break will occur for subjects in Part 1 after the database lock for the data up to Day 29 of the last subject in Part 1 to report initial results. The second code break will occur for subjects in Part 2 after completion of the study. To perform the analyses of initial data from Part 1, unblinded personnel will be pre-defined and documented before breaking the study blind for Part 1. Part 1 will remain blinded to the investigators, subjects, pre-defined sponsor and contract research organization (CRO) blinded personnel until all subjects in both parts have completed the study and the database has been finalized for study termination. Regardless of code-breaking for Part 1, the subjects in Part 2 will maintain the blind from the randomization

until all subjects in both parts have completed the study and the database has been finalized for study termination.

4. Changes from the Protocol

Section 8.5 of the protocol states that data up to Day 29 will be analyzed in Part 1 subjects to report the initial safety, PK, PD, and immunogenicity results in first CSR, but due to delay in PD analysis, PD results will not be reported in the first CSR.

Section 3.2.2 of the protocol states that maximum percentage decrease in serum free IgE concentration from screening and maximum percentage increase in serum total IgE concentration from screening will be calculated for pharmacodynamic parameters. However, since free IgE concentration is not collected at screening visit, maximum percentage decrease in serum free IgE concentration will be based on baseline value and in order to harmonize the parameter calculation method, maximum percentage increase in serum total IgE will also be calculated based on baseline value.

Section 7.2.3 of the protocol states that the PD Set is defined as all subjects who receive a complete dose of study drug (CT-P39, EU-approved Xolair, or US-licensed Xolair) and who have at least one post-treatment PD result. To exclude subjects who have unevaluable PD concentration (BLQ throughout the study), a condition of at least one post-treatment free IgE or total IgE concentration above the lower limit of quantification is added for the definition of PD Set.

5. Endpoints

5.1 Primary Endpoints

The primary endpoints will be analyzed for the Part 2 subjects.

Pharmacokinetic parameters will be analyzed based on the concentrations of total omalizumab in the serum samples.

- Area under the concentration-time curve from time zero to infinity ($AUC_{0\text{-}inf}$)
- Area under the concentration-time curve from time zero to the last quantifiable concentration ($AUC_{0\text{-}last}$)
- Maximum serum concentration (C_{max})

5.2 Secondary Endpoints

The secondary endpoints will be analyzed for Part 1 and Part 2, separately. Data for each part will be independently analyzed and presented.

Pharmacokinetics

- Time to C_{max} (T_{max})
- Terminal elimination half-life ($t_{1/2}$)
- Percentage of $AUC_{0\text{-}inf}$ obtained by extrapolation ($\%AUC_{ext}$)
- Terminal elimination rate constant (λ_z)
- Apparent total body clearance (CL/F)
- Apparent volume of distribution during the terminal phase (V_z/F)

For Part 1, the following PK parameters will be analysed as secondary endpoints:

- $AUC_{0\text{-}inf}$
- $AUC_{0\text{-}last}$
- C_{max}

Pharmacodynamics

For free IgE, following parameters will be calculated:

- Minimum serum concentration (C_{min})

• Time to C_{min} (T_{min})

• Maximum percentage decrease in serum free IgE concentration from baseline (max % decrease)

For total IgE, following parameters will be calculated:

• C_{max}

• T_{max}

• Maximum percentage increase in serum total IgE concentration from baseline (max % increase)

Safety

• Adverse events (including serious AEs [SAEs] and AEs of special interest [AESIs])

• Hypersensitivity monitoring (including monitoring for Type III hypersensitivity)

• Injection site reaction monitoring

• Vital sign measurements (blood pressure [BP], heart rate [HR], body temperature [BT], and respiratory rate [RR])

• Physical examination findings

• Clinical laboratory test results including hematology, chemistry, and urinalysis

• Twelve-lead ECG results

• Local injection site pain (using 100 mm visual analogue scale [VAS])

Immunogenicity

• Incidence of anti-drug antibodies (ADAs) and neutralizing antibodies (NAbs).

6. Analysis Sets

The analysis of safety and immunogenicity parameters will be based on the Safety Set detailed in Section 6.2. The analysis of PK parameters will be based on the PK Set detailed in Section 6.3 but for the first CSR, summary of PK concentration and the analysis of available PK parameters (C_{max} and T_{max}) will be based on the Safety Set detailed in Section 6.2 as the PK Set will not be defined at this stage. The analysis of PD parameters will be based on the PD Set detailed in Section 6.4.

6.1 Intent-to-Treat (ITT) Set

The ITT Set is defined as all subjects enrolled and randomly assigned to receive a dose of any study drug, regardless of whether or not any study drug was administered. Subjects will be assigned to treatment arms based on randomization; in an event where there is a discrepancy between the actual treatment received and the randomized treatment, subjects in the ITT Set will be analyzed according to the treatment to which they were randomized.

A summary table presenting the number and percentage of subjects who comprised ITT, Safety, PK and PD Sets will be summarized by treatment group and overall for the ITT Set. Each subject included in the analysis sets will be presented in a listing for the ITT Set.

6.2 Safety Set

The Safety Set is defined as all randomly assigned subjects who receive a full or partial dose of study drug. Subjects will be assigned to treatment groups based on treatment they actually received.

6.3 Pharmacokinetic Set

The PK Set is defined as all randomly assigned subjects who receive a complete dose of study drug and provide at least one post-treatment serum concentration above the lower limit of quantification for omalizumab. A subject will be considered to have received a complete dose of study drug if the subject is recorded as 'Yes' for "Was the total volume administered?" on the "Study Drug Administration" page in the eCRF. Subjects in the PK Set will be analyzed according to the treatment they actually received.

If any subject is found to be non-compliant with respect to dosing or had protocol deviations that could potentially affect the PK profile, a determination of the PK Set will be made at the blinded Data Review Meeting (DRM) before unblinding for final CSR on a case-by-case basis.

There were no subjects found to be non-compliant with respect to dosing or had protocol deviations that could potentially affect the PK profile during the DRM.

6.4 Pharmacodynamic Set

The PD Set is defined as all randomly assigned subjects who receive a complete dose of study drug and have at least one post-treatment free IgE or total IgE concentration above the lower limit of quantification. A subject will be considered to have received a complete dose of study drug if the subject is recorded as 'Yes' for "Was the total volume administered?" on the "Study

Drug Administration" page in the eCRF. Subjects will be analyzed according to the treatment they actually received.

6.5 Outliers

Any outliers that are detected during the blind review of the data will be investigated and discussed during the DRM. In general, outliers will not be excluded unless they are considered to be erroneous values. Sensitivity analyses and exploratory analyses may be conducted excluding outliers to ensure robustness of study conclusions. Details of outliers detected will be presented in the footnotes of the relevant outputs.

One PK sample from the subject, 50510025, Day 57 visit in Part 1 which showed a value deviating from the expected time point of maximum concentration was identified as an outlier during the DRM.

7. Interim Analyses

No formal interim analysis was planned in the protocol. However, this study consists of two parts in which independent statistical analyses will be performed for each CSR. For subjects in Part 1, a planned database unblinding will occur after database lock for data up to Day 29 as described in Section 3.5 to evaluate the preliminary safety, immunogenicity and PK for the first CSR. The specific table/listing/figure lists for this initial analysis are included in Appendix 3-1.

8. Subject Disposition

8.1 Disposition

A summary table reflecting the number of subjects who were screened, who were randomized, who were administered study drug, who completed the study, who discontinued from the study prior to study drug administration, and who discontinued from the study after study drug administration will be summarized for the ITT Set. This table will also present the number of subjects who were screening failures and primary reasons for screening fail and discontinuation from the study and descriptive statistics (n, mean, standard deviation [SD], minimum [Min], median, and maximum [Max]) of time on study prior to discontinuation for subjects who discontinued study after study drug administration. The time on study in days will be calculated as (Last Visit Date – Dose Date + 1).

A listing of subjects reported as screening failures will be provided with a primary reason of screening fail and primary inclusion/exclusion criteria if the criteria was not met. Since the enrollment of subjects is not done separately by part, screening including screening failure for both study parts will be reported in Part 2 table. Screening failure will be presented in a data listing for both parts. Subject randomization and subject disposition will be presented in separate listings for the ITT Set.

8.2 Inclusion and Exclusion Criteria

All recorded inclusion/exclusion criteria status will be presented in a data listing for the ITT Set.

8.3 Protocol Deviations

Protocol deviations occurring during the study will be investigated. The deviations will be defined as “minor” or “major” and assessed during the blinded DRMs before the first and final code breaking.

A major protocol deviation is a subset of protocol deviations defined as follows:

- Protocol deviations that may affect the interpretation of study results or the subject’s rights, safety, or welfare.
- Protocol deviations thought to interfere with the absorption, distribution, metabolism, and excretion of the compound to be measured.

Major protocol deviations leading to exclusion from PK analysis will be summarized and listed for the ITT set.

There were no major protocol deviations leading to exclusion from PK analysis were identified during the DRM.

9. Background Characteristics

9.1 Demographics and Baseline Characteristics

The demographic characteristics will consist of age (years), gender (male, and female), ethnicity (Hispanic or Latino, Not Hispanic or Latino, Not Reported, and Unknown), race (American Indian or Alaska Native, Asian, Black or African American, Australian Aborigine/Torres Strait Islander, Pacific Islander, White, and Other). For female subjects, female fertility status (surgically sterilized, post-menopausal, and potentially able to bear children) will be presented. The baseline characteristics consist of height (cm), weight (kg), body mass index (BMI) (kg/m^2) and serum total immunoglobulin E (IgE) level. Other baseline characteristics (history of alcohol use, smoking history, history of caffeine use [or other stimulating beverages]) will also be presented. The additional information of special diet [e.g., vegetarian], history of whole blood or plasma/platelets donation or loss, and follicle-stimulating hormone (FSH) test results for female subjects whose last period was more than 1 year prior to the date of informed consent will be listed.

Descriptive statistics (n, mean, SD, Min, median, and Max) will be calculated for continuous variables. Frequency counts and percentages will be tabulated for categorical variables and stratification factors in each stratification level. All demographic characteristic will be summarized by treatment group and listed by subject for the ITT Set.

9.2 Medical History

Medical history will be captured at screening and they will be coded using Medical Dictionary for Regulatory Activities (MedDRA Version 22.1 or higher). Medical history will be summarized by treatment group and overall, system organ class (SOC) and preferred term (PT) displaying the number and percentage of subjects for the ITT Set. The total number of medical history and the number and percentage of subjects with at least one medical history will also be presented in the table by treatment group and overall. At each level of subject summarization, a subject is counted once if the subject reported one or more findings.

Medical history will be listed by subject for the ITT Set.

9.3 Urine Drug Screen and Restriction Assessments

The urine test for drugs of abuse will be performed at screening and Day -1 (The urine test can be repeated once at the discretion of investigator). An alcohol breath test will be performed at screening and Day -1. Restriction (alcohol, caffeine, nicotine, meals, activity, medication, contraception) will be monitored throughout the study.

The urine drug screen, alcohol breath test and restriction assessments will be presented in a separate listing for the ITT Set.

9.4 Viral Serology

Serology tests (Hepatitis B Surface Antigen [HBsAg], anti-Hepatitis C Virus [anti-HCV], and Human Immunodeficiency Virus [HIV] antibody tests) will be performed at the screening visit. The results will be presented in a data listing for the ITT Set.

A summary table will be presented for serology test results by treatment arm and overall for the ITT Set.

9.5 Stool and Parasite Evaluation

Stool ova and parasite examination will be performed in subjects with an absolute eosinophil count >2 x ULN and any of risk factors for parasitic disease (travel within 6 months prior to the study drug administration to or living in an endemic area; chronic gastrointestinal symptoms; chronic immunosuppression). The available results will be presented in a listing by subject for the ITT Set.

9.6 General Comments

General Comments collected on eCRF will be presented in a listing for the ITT Set.

10. Treatments and Medications

10.1 Prior and Concomitant Medications

Information (e.g., drug name, date[s] of administration, etc.) about prior medications taken by the subject within 30 days before he or she signs the ICF will be recorded in both the source documents and eCRF.

Concomitant medication use will be recorded from the time the subject signs the ICF until the EOS visit. Concomitant medication use is permitted if indicated by the investigator for premedication or treatment of an AE.

Prior and concomitant medications will be coded using the World Health Organization Drug Dictionary (WHO DD), Version Sep 2019 or later. Medications will be classified as either prior or concomitant. For the purpose of inclusion in prior or concomitant medication tables, incomplete medication start and stop dates on eCRF will be imputed as follows:

- If the stop date is incomplete, the following rules will be applied:
  - Missing day: Assume the last day of the month;
  - Missing day and month: Assume December 31st;
  - Missing day, month, and year: Assume that the medication is continuing;
  - In the case of the death of a subject, the end date will be imputed as the date of death.

- If the start date is incomplete, the following rules will be applied. If the stop date is incomplete, imputed end date will be used instead of reported end date:
  - Missing day: Assume the first day of the month;

However, if the partial date and the date of study drug administration lie within the same month and year and the date of study drug administration is not after the stop date of the medication, set to the date of study drug administration. Otherwise, set to stop date of the medication.

- Missing day and month: Assume January 1st.
  However, if the partial date and the date of study drug administration lie within the same year and the date of study drug administration is not after the stop date of the medication, set to the date of study drug administration. Otherwise, set to stop date of the medication.
- Missing day, month, and year: Assume date of study drug administration if it's not after the stop date for the medication. Otherwise, set to stop date for the medication.

For the missing day imputation, the following examples should be used for reference:

- Example 1:
  Medication start: UNJUN2019
  Medication end: 20OCT2019
  Date of administration: 16OCT2019
  Medication start imputed: 01JUN2019
- Example 2:
  Medication start: UNOCT2019
  Medication end: 20OCT2019
  Date of administration: 16OCT2019
  Medication start imputed: 16OCT2019
- Example 3:
  Medication start: UNOCT2019
  Medication end: 20OCT2019
  Date of administration: 24OCT2019
  Medication start imputed: 20OCT2019

Relative start day or end day with respect to the dose date of study drug will not be calculated if the medication start date or end date is incomplete.

A prior medication is defined as any medication where the start and stop dates or imputed start and stop dates are before the date of study drug administration or checked as 'Yes' for the questionnaire "If end date is unknown, was this drug stopped before the administration of study drug?" on "Prior and Concomitant Medications" page of the eCRF. A concomitant medication is defined as any medication that has an actual or imputed stop date on or after the date of study drug administration, marked as ongoing or checked as 'No' or 'Not Applicable' for the questionnaire "If end date is unknown, was this drug stopped before the administration of study drug?" on the medications page of the eCRF. If the answers are missing for both questionnaires, "Ongoing?" and "If end date is unknown, was this drug stopped before the administration of study drug?" a medication will be considered as a concomitant medication as well.

For each part, the total number of prior or concomitant medications and the number and percentage of subjects with at least one prior or concomitant medication will be summarized for the Safety Set. Prior and concomitant medication data will be presented separately by drug class (using Anatomical Therapeutic Chemical [ATC] Level 2), PT, and treatment arm. At each level of summarization, a subject is counted only once if the subject reported one or more medications at that level. When ATC Level 2 for drug class is not available, Level 1 will be used instead.
All prior and concomitant medications will be presented in data listings for the Safety Set.

10.2 Study Drug Administration

For each study part, the number and percentage of subjects who received study drug will be presented. The number and percentage of subjects who did and did not have a complete dose of study drug administered successfully will be presented for the Safety Set.
Study drug administration data for CT-P39, EU-approved Xolair, or US-licensed Xolair will be presented in a data listing for the Safety Set.

11. Pharmacokinetic Analyses

The initial PK analyses for the first CSR (Day 29 CSR) will be performed on the Safety Set. All PK analyses for the final CSR will be performed on the PK Set unless otherwise specified.

11.1 Handling of the Below the Lower Limit of Quantification (BLQ) and the No Reportable Concentration Values

All concentration BLQ values that occur prior to study drug administration will be treated as zero (0). After study drug administration, all other incidences of BLQs will be treated as missing for serum PK concentrations and PK parameter estimation. Measurable concentrations after consecutive BLQs during the terminal phase will also be set to missing.

Samples with invalid concentration (due to bioanalytical or clinical issue) will be replaced by "0.00" when it occurs prior to dosing. Otherwise they will be set to missing for tabulation, graphical representation and calculation purposes if it occurs after dosing.

11.2 Handling of the Difference between the Scheduled and the Actual Sampling Times

The actual clock time for dosing and each collection time for the PK samples will be recorded. For all sampling times, the actual sampling times relative to dosing will be calculated as the difference between the actual clock time of sampling and the actual clock time of dosing. The actual post-dose sampling times relative to dosing expressed in hours and rounded off to three decimal digits will be used to calculate the PK parameters, except for pre-dose samples occurring prior to dosing, which will always be reported as zero (0.000), regardless of the time difference. Scheduled sampling times will be presented in concentration tables and mean graphs, while actual sampling times will be presented in the individual graphs.

11.3 Serum Concentrations

Blood samples will be collected from each subject during this study for the determination of the PK of omalizumab administered as CT-P39, EU-approved Xolair or US-licensed Xolair. Blood samples for PK analysis of omalizumab will be drawn according to the following schedule (acceptable tolerance window):

- Pre-dose (Day 1, prior to administration of the study drug)
- Day 1, 6 hours after the start of administration of the study drug (±15 minutes)
- Day 1, 12 hours after the start of administration of the study drug (±15 minutes)
- Day 2, 24 hours after the start of administration of the study drug (±15 minutes)
- Day 3, 48 hours after the start of administration of the study drug (±1 hour)
- Day 4, 72 hours after the start of administration of the study drug (±2 hours)
- 120, 168, 240, 336, and 504 hours (Day 6, 8, 11, 15, and 22, respectively) after the start of administration of the study drug (±8 hours)
- 672, 1008, and 1344 hours (Day 29, 43 and 57, respectively) after the start of administration of the study drug (±1 day)

- 1680, 2016, 2520, and 3024 hours (Day 71, 85, 106 and 127, respectively) after the start of administration of the study drug (±3 days).

Serum samples will be analyzed to determine the concentrations of omalizumab using a validated method.

Serum omalizumab concentrations, collection times, and collection time deviations will be listed for the Safety Set by actual treatment arm. Serum omalizumab concentrations will be summarized for the PK Set by treatment and time point, using descriptive statistics (n, arithmetic mean, SD, %CV, geometric mean, minimum, median, and maximum).

The individual, mean (±SD), and overlay of individual serum concentration versus time profiles for omalizumab will be presented graphically on both linear and semi-logarithmic scales by treatment for the PK Set. For ease of presentation, actual and scheduled sampling times will be used to present results for individual and mean figures respectively.

EOS visit of early termination results will not be included in the summaries, but will be presented in data listings. Unscheduled results will not be included in the summary tables except for determining baseline, but will be presented in data listings.

11.4 Serum Pharmacokinetic Parameters

Pharmacokinetic parameters will be presented in data listings and summarized in tables by treatment arm, using descriptive statistics (n, arithmetic mean, SD, %CV, geometric mean, minimum, median, and maximum).

Serum concentrations from omalizumab will be used to calculate the following parameters by standard non-compartmental methods:

$AUC_{0\text{-inf}}$	Area under the concentration-time curve from time zero to infinity (extrapolated)
$AUC_{0\text{-last}}$	Area under the concentration-time curve from time zero to the last measurable concentration
C_{max}	Maximum observed concentration
$\%AUC_{ext}$	Percentage of the area extrapolated for calculation of area under the serum concentration-time curve from time zero to infinity
T_{max}	Time of observed C_{max}
$t_{1/2}$	Terminal half-life, calculated as $\ln 2/\lambda_z$
λ_z	Terminal elimination rate constant
CL/F	Apparent total body clearance, calculated as $Dose/AUC_{0\text{-inf}}$
V_z/F	Apparent volume of distribution, calculated as $Dose/(\lambda_z \times AUC_{0\text{-inf}})$

- $AUC_{0\text{-last}}$ and $AUC_{0\text{-inf}}$ will be calculated using linear-up log-down method which is described below:

- The linear trapezoidal method will be employed for all incremental trapezoids arising from increasing concentrations and the logarithmic trapezoidal method will be used for those arising from decreasing concentrations.

- λ_z will be estimated at terminal phase by linear regression after log-transformation of the concentrations:
  - Only those data points that are judged to describe the terminal log-linear decline will be used in the period after regression.
  - A minimum number of 3 data points in the terminal phase will be used in calculating λ_z with the line of regression starting at any post-C_{max} data point (C_{max} will not be part of the regression slope). The adjusted coefficient of determination (R^2 adjusted) in general should be greater than 0.85. All the derived parameters (e.g., λ_z, $t_{½}$, $AUC_{0\text{-inf}}$, CL/F, V_z/F and $\%AUC_{ext}$) will need to be flagged accordingly in only individual listing.
  - An appropriate number of decimal places will be used for λ_z to enable the reported value of $t_{½}$ to be calculated.

- $\%AUC_{ext}$ will be calculated as $(1 - [AUC_{0\text{-last}}/AUC_{0\text{-inf}}]) \times 100$. The $\%AUC_{ext}$ should not exceed 20% for each individual profile. If the $\%AUC_{ext}$ is more than 20%, the individual result should be flagged as well as all parameters depending on $AUC_{0\text{-inf}}$. All the derived parameters (i.e., $AUC_{0\text{-inf}}$, V_z/F and CL/F) will need to be flagged accordingly in only individual listing.

11.5 Primary Pharmacokinetic Analyses

Statistical analyses will be carried out independently for each part and the primary PK endpoints will be analyzed only for Part 2 subjects.

For Part 2, as primary analysis, Analysis of Covariance (ANCOVA) will be performed on log-transformed $AUC_{0\text{-last}}$, $AUC_{0\text{-inf}}$, and C_{max} at the alpha level of 0.05. Factors incorporated in the model will include treatment as a fixed effect and baseline body weight, total IgE level, and sex as covariates. The ratios of geometric means (CT-P39 to EU-approved Xolair, CT-P39 to US-licensed Xolair, and EU-approved Xolair to US-licensed Xolair) and their 90% CIs will be calculated for $AUC_{0\text{-last}}$, $AUC_{0\text{-inf}}$, and C_{max} based on least-square means from ANCOVA on the log-transformed data. Back transformation will provide the ratios of geometric means and their 90% CIs.

Statistical analyses are to be performed for each comparison. The similarity of PK for each comparison, CT-P39 versus EU-approved Xolair, CT-P39 versus US-licensed Xolair, and EU-approved Xolair versus US-licensed Xolair, will be concluded if all 90% CIs of the ratios of geometric means are entirely contained within 80% to 125% for $AUC_{0\text{-inf}}$, $AUC_{0\text{-last}}$, and C_{max} for Part 2.

Sample code for the procedure in [redacted] for ANCOVA is specified below:

[redacted]

Derived calculations obtained from the ANCOVA analyses will be performed as per the following:

- Ratio = $100 \times e^{DIFFERENCE}$, where DIFFERENCE is the difference in point estimates between the treatments (e.g., A – B, A – C, and B – C) on the log-transformed scale;
- 90% Confidence Limits = $100 \times e^{(DIFFERENCE \pm t_{(dfResidual)} \times SE_{DIFFERENCE})}$.

12. Pharmacodynamic Analysis

All PD analyses will be performed on the PD Set unless otherwise specified.

12.1 Serum Concentrations

Blood samples will be collected from each subject during this study for the determination of the free and total immunoglobulin E (IgE) levels administered as CT-P39, EU-approved Xolair or US-licensed Xolair using a validated immunoassay. Blood samples for PD analysis will be drawn according to the following schedule and acceptable tolerance window:

- Screening (Day -28 to Day -2); sampling for only total IgE analysis
- Pre-dose (Day 1, prior to administration of the study drug)
- 6 hours after the start of administration of the study drug (±15 minutes)
- 12 hours after the start of administration of the study drug (±15 minutes)
- 24 hours after the start of administration of the study drug (±15 minutes)
- 48 hours after the start of administration of the study drug (±1 hour)
- 72 hours after the start of administration of the study drug (±2 hours)
- 120, 168, 240, 336, and 504 hours after the start of administration of the study drug (±8 hours)
- 672, 1,008, and 1,344 hours after the start of administration of the study drug (Day 29, 43 and 57, respectively, ±1 day)
- 1,680, 2,016, 2,520, and 3,024 hours after the start of administration of the study drug (Day 71, 85, 106 and 127, respectively, ±3 days)

Free IgE concentrations that are BLQ (<6.25 ng/mL) will be set to LLoQ (6.25 ng/mL) and above ULoQ values (>400 ng/mL) will be set to ULoQ (400 ng/mL). Total IgE concentrations that were BLQ (<2 IU/mL) will be set to zero. Serum concentrations of free and total IgE, collection times, and collection time deviations will be listed for the Safety Set by actual treatment arm and the concentrations will be summarized for the PD Set by treatment and time point, using descriptive statistics (n, arithmetic mean, SD, %CV, geometric mean, minimum, median, and maximum). Free and total IgE level will be presented using the unit, IU/mL. If raw

concentration values are not reported in this unit, the values will be converted to the unit, IU/mL considering that 1.0 IU/mL IgE corresponds to 2.42 ng/mL IgE.
The individual, mean (±SD), and overlay of individual serum concentration versus time profiles for free and total IgE will be presented graphically on both linear and semi-logarithmic scales by treatment. For ease of presentation, actual and scheduled sampling times will be used to present results for individual and mean figures respectively.

EOS visit of early termination results will not be included in the summaries, but will be presented in data listings. Unscheduled results will not be included in the summary tables except for determining baseline, but will be presented in data listings.

12.2 Serum Pharmacodynamic Parameters

The PD parameters, C_{min}, T_{min}, and maximum percentage decrease from baseline in free IgE; and C_{max}, T_{max}, and maximum percentage increase from baseline in total IgE will be calculated. If concentration of Free IgE at baseline is above ULoQ or that of Total IgE at baseline is BLQ, max % decrease or max % increase will not be calculated, respectively. If free IgE is BLQ at baseline, no PD parameters will be calculated since it would not be appropriate to observe decrease.

Pharmacodynamic parameters will be presented in data listings and summarized in tables for the PD set by treatment, using descriptive statistics (n, arithmetic mean, SD, %CV, geometric mean, minimum, median, and maximum).

13. Safety and Immunogenicity Analyses

All safety and immunogenicity analyses will be based on the Safety Set and they will be presented separately for each study part unless otherwise specified.

13.1 Adverse Events

An AE is defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. Subjects will be instructed to contact the investigator at any time after the ICF was signed if any symptoms develop.

All AEs will be collected from the date the ICF is signed and until the end of the subject's participation in the study, and will be coded by PT and SOC using MedDRA, Version 22.1 or higher.

Relationship to study drug (unrelated, possible, probable, or definite) will be summarized and events will be considered to be related if relationship is possible, probable, or definite. Adverse events with no relationship or intensity will be summarized separately under a missing category. Adverse drug reaction is defined as any treatment-emergent adverse event (TEAE) which has causal relationship with study drug with at least a reasonable possibility, i.e., a TEAE which is considered as related.

All AEs will be graded for intensity according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0.

A TEAE is defined as any event not present before study drug administration or any event already present that worsens in intensity or frequency after study drug administration. TEAEs will be flagged in listings and all AE summaries will be restricted to TEAEs except the overall summary of AEs. All TEAE summary tables will include the number and percentage of subjects experiencing TEAEs by SOC and PT, relationship, and intensity, by treatment arm and overall, and the total number of events overall, unless otherwise specified. Additionally TEAEs, TESAEs, and TEAEs leading to study discontinuation will be summarized by treatment group, SOC, PT and intensity, regardless of relationship, displaying the number and percentage of subjects experiencing at least one TEAE. Summaries that are displayed by SOC and PT will be ordered by alphabetical order of SOC and PT. A subject with 2 or more TEAEs within the same SOC, PT, and relationship will be counted only once using the most severe intensity recorded in that level. Percentages will be based on the number of subjects in the Safety Set in each treatment arm and overall.

For the purpose of inclusion in TEAE tables, the eCRF question "Onset Date" on "Adverse Events" page will be compared to the date of study drug administration, if the answer is not available, the imputed AE onset date will be used. Incomplete AE onset and end dates will be imputed as follows:

- If the stop date of an AE is partial or missing, the following rules will be applied:
    - Missing day (e.g., XXFEB2019): Assume the last day of the month (e.g., 28FEB2019).
    - Missing day and month (e.g., XXXXX2019): Assume December 31st (e.g., 31DEC2019).
    - Missing day, month, and year (e.g., XXXXXXXXX): Leave it as Missing.

- If the start date of an AE is partial or missing, the following rules will be applied. If the stop date of the AE is partial, imputed stop date will be used instead of reported stop date:
    - If the day is missing (e.g., XXFEB2019), the month and year of the partial date will be compared to the date of the study drug administration.
        - If the month and year are equal for both dates, the AE start date will be imputed as the earlier date of: (i) the date of the study drug administration, and (ii) the end date of the AE.
        - If the month and year are not equal, the AE start date will be imputed as the first day of the month (e.g., 01FEB2019).
    - If the day and month are missing (e.g., XXXXX2019), the year of the partial date will be compared to the date of the study drug administration.
        - If the years of both dates are equal, start date will be imputed as the earlier date of: (i) the date of the study drug administration, and (ii) the end date of the AE.

- If the year is not equal, start date will be imputed as the 1st of January of the partial date year (e.g., 01JAN2019).

- If the AE start date is missing (e.g., XXXXXXXXX), start date will be imputed as the earlier date of: (i) the date of the study drug administration, and (ii) the end date of the AE.

Relative start day or end day with respect to the dose date of study drug will not be calculated if the event start date or end date is incomplete.

The duration of the AE will be calculated using the below formula.

- For events with start time and end time collected: duration = AE stop date time – AE start date time

  - Present in minutes if duration is less than (<) 1 hour (60 minutes)
  - Present in hours with 1 decimal place if the duration is more than or equal to (≥) 1 hour (60 minutes) but less than (<) 24 hours (1440 minutes)
  - Present in days with 2 decimal places if duration is more than or equal to (≥) 24 hours (1440 minutes)

- For events without start time or end time collected: duration in days = AE stop date – AE start date + 1

Listings for AEs will include the following information: SOC, PT and Verbatim term; start and stop date/time; TEAE flag, discontinuation flag, Serious Adverse Event (SAE) flag, frequency, outcome, any treatment received, intensity, action taken with study drug, relationship with study drug, AESI flag. All AEs will be presented in a data listing for the Safety Set.

13.1.1 Incidence of Adverse Events

A summary table of overall AEs will be presented by treatment arm and overall for the Safety Set, including total number of AEs, total number of SAEs, total number of TESAEs, total number of TEAEs, number and percentage of subjects with at least one AE, with at least one SAE, with at least one TEAE, with at least one treatment-emergent SAE (TESAE), with at least one TEAE leading to study discontinuation, with at least one TEAE leading to death, with at least one treatment-emergent AE of special interest (AESI). This analysis will be summarized for subjects in each part and for all subjects in both parts.

13.1.2 Serious Adverse Events and Deaths

An SAE is defined as any untoward medical occurrence that at any dose meets any of the following outcomes:

- Results in death
- Is immediately life-threatening

- Requires in-patient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect

Important medical events that may not result in death, be life threatening, or require hospitalization may be considered SAEs when, based upon appropriate medical judgment, they may jeopardize the subject or may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in in-patient hospitalization, or the development of drug dependency or drug abuse.

TESAEs will be summarized by treatment arm, overall and by relationship, intensity, SOC and PT displaying the number and percentage of subjects with at least one TESAE using only the most severe intensity recorded at each level of summarization. The total number of TESAEs will also be displayed.
All SAEs will be listed including a subset of the variables detailed in Section 13.1. Serious criteria with additional SAE description will be presented in an additional information listing. Subjects who have an SAE with serious criteria of "death" will be presented in a separate listing with additional information such as date and cause of death.

13.1.3 Treatment-Emergent Adverse Events Leading to Study Discontinuation

The AE leading to study discontinuation will be determined based on question "Did the adverse event cause the subject to be discontinued from the study?" on "Adverse Events" page of eCRF. TEAEs leading to study discontinuation will be summarized by treatment arm, overall and by relationship, intensity, SOC and PT displaying the number and percentage of subjects with at least one TEAE leading to study discontinuation. The total number of TEAEs leading to study discontinuation will also be displayed. All TEAEs leading to study discontinuations will be listed including a subset of the variables detailed in Section 13.1.

All TEAEs that lead to study discontinuation will be presented in a data listing.

13.1.4 Treatment-Emergent Adverse Events of Special Interest

Treatment-emergent AEs of special interest will be determined as follows:

- **Allergic reactions Type I/anaphylaxis:** Treatment-emergent AEs classified as Allergic reactions Type I/anaphylaxis are determined:
  - if the eCRF question "Is the Adverse event classified as an Allergic reaction Type I or Anaphylaxis or Type III hypersensitivity?" is answered as 'Yes'

  And
  - Treatment-emergent AEs are recorded as Allergic reaction type I or anaphylaxis in the eCRF will be included.

Signs and symptoms of allergic reactions Type I/anaphylaxis will be captured on a separate eCRF page, "Allergic reactions Type I/Anaphylaxis/Type III Hypersensitivity". Signs and

symptoms will be coded using MedDRA Version 22.1 or higher.

- **Serum sickness/serum sickness-like reactions (Type III hypersensitivity):** Treatment-emergent AEs classified as "Type III hypersensitivity" are determined:
  - if the eCRF question "Is the Adverse event classified as an Allergic reaction Type I or Anaphylaxis or Type III hypersensitivity?" is answered as 'Yes'.

  AND
  - Treatment-emergent AEs are recorded as Type III hypersensitivity in the eCRF will be included. Signs and symptoms of Type III hypersensitivity will be captured on a separate eCRF page, "Allergic reactions Type I/Anaphylaxis/Type III Hypersensitivity". Signs and symptoms will be coded using MedDRA Version 22.1 or higher.

- **Injection site reactions (ISRs):** Treatment-emergent AEs classified as ISRs are determined if the eCRF question "Is Adverse event classified as an injection site reaction (ISR)?" is answered as 'Yes'. Signs and symptoms of ISRs will be captured on a separate eCRF page, "Injection Site Evaluation". Signs and symptoms will be coded using MedDRA Version 22.1 or higher.

- **Parasitic (helminth) infections**: Treatment-emergent AEs classified as parasitic (helminth) infections are determined by HLGT if the HLGT is 'Helminthic disorders'.

The treatment-emergent AESIs will be summarized by SOC, PT, relationship and intensity, by treatment arm and overall in separate tables. The total number of events and number of subjects with at least one TEAE classified as AESI will also be displayed in the corresponding table.

Signs and symptoms of allergic reactions Type I/anaphylaxis, ISR, and Type III hypersensitivity will be summarized by SOC, PT and intensity, by treatment arm and overall respectively.
All treatment-emergent AESIs will be presented in separate data listings.

13.2 Clinical Laboratory Parameters

Laboratory analyses of blood and urine samples will be performed by the local laboratories. All planned laboratory test results will be presented in the International System of Units (SI units) for descriptive summary.

The following clinical laboratory assessments will be performed:

Hematology:	Hematocrit, hemoglobin, red blood cell (RBC) count, white blood cell (WBC) count with differential count, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and platelet count.

Clinical Chemistry:	Albumin, alkaline phosphatase (ALP), alanine aminotransferase (ALT), Aspartate aminotransferase (AST), calcium, chloride, total cholesterol, creatine phosphokinase (CPK), creatinine, C-reactive protein (CRP), gamma glutamyl transferase (GGT), glucose, lactate dehydrogenase (LDH), magnesium, potassium, sodium, total bilirubin, total protein, uric acid, direct bilirubin, triglycerides, phosphate, troponin I, urea.
Urinalysis:	pH, specific gravity, ketones, protein, glucose, bilirubin, nitrite, urobilinogen, occult blood, and microscopic examination[1].
Complement tests:	Complement (C3 and C4), hemolytic complement (CH_{50} assay).

[1] Parameters including microscopic examination will be presented in the listing only.

Clinical laboratory testing (hematology, clinical chemistry, and urinalysis) will be performed at screening, on Day -1, 3, 8, 15, 29, 57, 85, and 127 (EOS). Complement (C3 and C4) and total hemolytic complement will be assessed on Day -1 to establish the baseline value. Additional clinical laboratory test samples will be collected and C3, C4, and total hemolytic complement will be assessed in the case of Type III hypersensitivity.

Clinical laboratory values will be flagged as either abnormal, high or low based on the reference ranges provided by the local laboratories for each laboratory parameter.

Clinical laboratory test results will be labelled with a CTCAE term, and grading will be applied to post-baseline values for numeric parameters based on CTCAE v5.0 where applicable. Grades which are part numeric and part clinical input will be assigned based on the numeric portion only; lower grade will be used if different grades share the same criteria. The CTCAE terms and grades are listed in Appendix 2.

Actual values and changes from baseline for quantitative clinical laboratory test results will be summarized by treatment arm and overall at each time point using descriptive statistics (n, mean, SD, minimum, median, and maximum). Any numeric values recorded with inequality signs will be set to the numeric values only without inequality sign for all related summaries. In listings, original results containing inequality sign will be displayed, unless otherwise specified.

Shift tables from baseline to each schedule post-baseline visit will be generated for categorical clinical laboratory test results using normal; abnormal (High or Low if possible), and not done categories as appropriate, by treatment arm and overall for the Safety Set. A subject will be summarized under the not done category if the subject has the relevant data page but no result of interest.

The number and percentage of subjects will be summarized by CTCAE term, CTCAE grade, and treatment arms and overall for the Safety Set, where this summary includes only the most severe case during the overall visits. The CTCAE grades for this analysis will be Grade 1 (Mild), Grade 2 (Moderate), Grade 3 (Severe) and Grade 4 (Life-threatening). The CTCAE Grade 5 (Death)

will not be applied in this analysis since death cannot be determined from a numeric laboratory result. If a subject's most severe result does not satisfy any CTCAE criteria, this subject will be summarized as "No Grade".

Individual clinical laboratory test and complement test results will be presented in data listings.

13.3 Vital Sign Measurements and Body Weight

Vital sign measurements will be performed at screening, on Day -1, on Day 1 prior to the start of study drug administration (within 30 minutes), on Days 2 (at 24 hours after injection), 3, 4, 6, 8, 11, 15, 22, 29, 43, 57, 71, 85, and 106, and at EOS. Body weight will be measured at screening, on Day -1 and at EOS.

Vital signs measurements will include systolic and diastolic blood pressures (BPs), heart rate (HR), respiratory rate (RR), and body temperature (BT). BP, HR, RR, and BT measurements will be performed after the subject has been resting for at least 5 minutes.

Actual values and change from baseline for systolic and diastolic BPs, HR, RR, and BT will be summarized by treatment arm and overall at each time point using descriptive statistics. The body weight data will also be summarized using descriptive statistics. Baseline values for vital sign measurements will be derived utilizing all non-hypersensitivity and hypersensitivity/allergic reactions monitoring data.

Individual vital sign measurements (including repeated and unscheduled measurements) and body weight data will be presented in a data listing.

13.4 Electrocardiogram

Single 12-lead ECGs will be obtained after the subject has been in the supine position for at least 5 minutes. ECG is planned to be performed on screening, Day 3, Day 8, Day 29, Day 57, Day 85, and at EOS.

Findings of 12-lead ECG will be classified as either "normal", "abnormal, not clinically significant", or "abnormal, clinically significant".

Individual ECG measurements (including repeated and unscheduled measurements) will be presented in a data listing. In addition, overall assessment in ECG will be summarized by treatment group and overall in a shift table. Baseline values for ECG measurements will be derived utilizing all non-hypersensitivity and hypersensitivity/allergic reactions monitoring data.

13.5 Hypersensitivity/Allergic Reactions Monitoring

Hypersensitivity/allergic reactions will be assessed by additional ECG and vital sign monitoring (including systolic and diastolic BP, HR, RR, and BT).

Vital sign measurements for hypersensitivity/allergic reactions monitoring will be performed before the start of the study drug administration (pre-dose) [within 30 minutes] and at 30 minutes, 1, 2 [±10 minutes] hours, and 6, 12 [±1 hour] hours after start of administration on Day 1.

Electrocardiograms for hypersensitivity/allergic reactions monitoring will be performed before the start of the study drug administration (pre-dose) [within 30 minutes] and at 2 [±30 minutes] hours after start of administration on Day 1 and additional ECGs can be performed if the subject experiences cardiac symptoms.
In addition, hypersensitivity/allergic reactions will be monitored by routine continuous clinical monitoring. In case of hypersensitivity, emergency medication and equipment, such as adrenaline, antihistamines, corticosteroids, and respiratory support including inhalational therapy, oxygen, and artificial ventilation, will be available and an ECG can be performed.

Actual values and changes from baseline for vital sign measurements to monitor hypersensitivity/allergic reactions will be summarized separately by treatment arm and overall at each time point using descriptive statistics.
The number and percentage of subjects who have clinically notable of vital sign measurements will be summarized in a table by treatment arm and overall, time point, and parameter.
The criteria for clinically notable results are defined as below.

Parameter	Low	High
Systolic blood pressure (mmHg)	≤ 90	≥ 160
Diastolic blood pressure (mmHg)	≤ 50	≥ 90
Respiratory rate (breaths per minute)	≤ 12	≥ 20
Heart rate (beats per minute)	≤ 50	≥ 100
Body temperature (°C)	≤ 35.0	≥ 38.0

Vital sign measurements for hypersensitivity/allergic reactions monitoring (including repeated assessment) will be listed within vital sign listing as described in Section 13.3. High and low flags will be included to show whether a hypersensitivity/allergic reaction result is outside of the clinically notable ranges.

ECG assessments for hypersensitivity/allergic reactions monitoring will be listed and summarized within ECG listing as described in Section 13.4.

13.6 Physical Examination

A standard physical examination will be performed at screening, on Day -1, on Day 3, and at EOS. The examination will include an assessment of general appearance and a review of body systems.

Findings of physical examination will be collected as either ("Normal", "Abnormal, Not Clinically Significant", "Abnormal, Clinically Significant", or "Not done"). The number and percentage of subjects will be summarized in a table by treatment group, visit and body system, in the form of a shift table to detect changes from baseline. The findings of urogenital system

and other will be presented only in the data listing. All physical examination data will be listed for each subject by treatment group, visit and body system.

13.7 Pregnancy Test

A serum pregnancy test will be performed at screening. A urine pregnancy test will be performed in women of childbearing potential on Day -1 and EOS visit. Throughout the study, a urine pregnancy test will be performed when there is any possibility of pregnancy, and a confirmatory serum pregnancy test will be performed if a urine pregnancy test result is positive.

The pregnancy test results will be summarized for female subjects of childbearing potential in the Safety Set. All pregnancy test results will be presented in a data listing.

13.8 Local Site Pain

Local site pain will be assessed immediately (within 15 minutes) after study drug administration (Day 1) using 100 mm VAS. Subjects will be asked to indicate their current level of pain intensity by drawing a single vertical line on the 100 mm VAS labeled “no pain” (0 mm) as the left anchor and “most severe pain” (100 mm) as the right anchor. The length of the line will be measured from the left (in mm) and the value (in mm) will be recorded in the eCRF.

The VAS results will be summarized by treatment arm and overall and they will be presented in a data listing.

13.9 Immunogenicity Testing

Immunogenicity of CT-P39, EU-approved Xolair, and US-licensed Xolair will be assessed prior to study drug administration on Day 1, and on Days 15, 43, and 85, and at EOS.

The ADA assay will follow a three-tiered approach consisting of (i) screening assay, (ii) confirmatory assay, and (iii) titration. Samples that are “Confirmatory” in the screening assay will undergo further testing in the confirmatory assay to determine if subjects are true positive. The overall ADA assay result will be (“Positive” or “Negative”). For further characterization, the antibody level will be assessed by titration in confirmed positive samples. The confirmed positive samples in the ADA assay will be analyzed further to conduct a NAb assessment. The test outcome for NAb assay will be: (“Positive” or “Negative”).

The results of the final ADA assay and the NAb assay will be summarized. The number and percentage of subjects will be provided by treatment group, overall and visit. The descriptive statistics of ADA titration results for each treatment group will be presented by visit. The number and percentage of subjects with at least one positive ADA assay and the number and percentage of subjects with at least one positive NAb assay status after study drug administration (including unscheduled visit and EOS visit) will also be presented in a table.
A listing showing immunogenicity test results from each three-tiered approach will be provided by treatment group and visit.

14. Percentages and Decimal Places

Unless otherwise specified, the following general rules will be used in tables and listings:

- Percentages will be presented to one decimal place.
- Percentages equal to 0 or 100 will be presented as such without a decimal place.
- Minimum and maximum will be presented with the same precision as the values reported in listings.
- Arithmetic mean, median and geometric mean will be presented in tables with one more decimal place or significant figure than the values reported in listings. If minimum value from the data is zero, geometric mean will not be calculated.
- SD and %CV will be presented in tables with two more decimal places or significant figures than the values reported in listings.
- Point estimates and CIs will be presented to two decimal places.

All digits will be used for PK/PD parameter calculations and statistical PK analyses. PK and PD results will be reported to 3 significant figures in listings, except for the following situations:

- $AUC_{0\text{-last}}$ and $AUC_{0\text{-inf}}$ values will be rounded to integers.
- T_{max} and T_{min} values will be rounded to 2 decimal places.

15. Handling of Missing Data

For PK and PD only observed data will be used in the data analysis. PK concentration with BLQ or no reportable values occurring after dosing and measurable concentrations after consecutive BLQs during the terminal phase will be regarded as missing as described in Section 11.1. The assignment of PD concentration BLQ values (e.g. missing, lower limit of quantification) after study drug administration will be determined during the DRM.

The assignment of PD concentration with BLQ or above ULoQ was discussed during the DRM and detail of assignment is specified in Section 12.1.

16. Software to be Used

PK analysis will be performed using [redacted], which is validated for bioequivalence/bioavailability studies by [redacted]. Inferential statistical analyses will be performed using [redacted] according to Food and Drug Administration (FDA) and European Medicines Agency (EMA) guidelines. The tables, listings and figures will be created using [redacted]. The report text will be created using [redacted].

17. Reference List

- Chuang-Stein C. Summarizing laboratory data with different reference ranges in multi-center clinical trials. Drug Information Journal. 1992; 26:77-84.
- Karvanen J. The statistical basis of laboratory data normalization. Drug Information Journal. 2003; 37:101-107.

18. APPENDICES

18.1 Appendix 1: Schedule of Assessments

Table 18-1: Schedule of Assessments

Assessments	Screening	In-House Stay					Outpatient Visit											EOS
Day of Study Period	**-28 to -2**	**-1**	**1**	**2**	**3**	**4**	**6**	**8**	**11**	**15**	**22**	**29**	**43**	**57**	**71**	**85**	**106**	**127**
Visit Window (Day)												**±1**	**±1**	**±1**	**±3**	**±3**	**±3**	**±3**
Informed consent	X																	
Demographics	X																	
Medical history	X	X																
Inclusion and exclusion criteria	X	X																
Body weight & height[1]	X	X																X
Drugs of abuse/alcohol and nicotine check[2]	X	X																
Serum pregnancy test[3]	X																	
Urine pregnancy test[3]		X																X
FSH test[4]	X																	
Stool and parasite evaluation[5]	X																	
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Hematology, clinical chemistry, and urinalysis[7]	X	X			X			X		X		X		X		X		X
Serology[8]	X																	
Physical examination[9]	X	X			X													X
12-lead electrocardiogram	X				X			X				X		X		X		X
Randomization			X[6]															
Study drug administration			X															
Hypersensitivity/allergic reactions and injection site reaction monitoring			X[10]															
C3, C4, and total hemolytic complement[11]		X	(X)															
Local site pain by VAS[12]			X															
Serum total IgE sampling[13]	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Serum free IgE sampling[14]			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PK sampling[15]			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Assessments	Screening	In-House Stay					Outpatient Visit											EOS
Day of Study Period	**-28 to -2**	**-1**	**1**	**2**	**3**	**4**	**6**	**8**	**11**	**15**	**22**	**29**	**43**	**57**	**71**	**85**	**106**	**127**
Visit Window (Day)												**±1**	**±1**	**±1**	**±3**	**±3**	**±3**	**±3**
Immunogenicity sampling[16]			X[6]							X			X			X		X
Restriction assessments	X																	
Prior and/or concomitant medications[17]	X																	
Adverse event monitoring	X																	

Abbreviations: ECG = electrocardiogram; EOS = end-of-study; FSH = follicle-stimulating hormone; HbsAg = hepatitis B surface antigen; HCV = hepatitis C virus; HIV = human immunodeficiency virus; ICF = informed consent form; PD = pharmacodynamics; PK = pharmacokinetic; ULN = upper limit of normal; VAS = visual analog scale.

1. Height will be measured at screening only.
2. Drug abuse testing includes the following: amphetamine class (amphetamines, methamphetamines, methylenedioxymethamphetamines, etc.), methadone, barbiturates, benzodiazepines, cocaine, opiates, phencyclidine, and tetrahydrocannabinol. The urine test for drugs of abuse will be performed at screening and Day -1 (The urine test can be repeated once at the discretion of investigator). An alcohol breath test will also be performed at screening and Day -1. The history of drug abuse, alcohol and nicotine use will be taken by the investigator at screening and Day -1.
3. A serum pregnancy test on women of childbearing potential will be performed at screening visit. A urine pregnancy test will be performed in women of childbearing potential on Day -1 and end-of-study (EOS) visit. Throughout the study, a urine pregnancy test will be performed when there is any possibility of pregnancy, and a confirmatory serum pregnancy test will be performed if a urine pregnancy test result is positive.
4. A follicle-stimulating hormone (FSH) test will be performed on female subjects whose last period was more than 1 year prior to the date of informed consent, to confirm postmenopausal status at screening. A female subject whose last period was more than 1 year prior to the date of informed consent and serum FSH level is ≥40 IU/L will be considered postmenopausal.
5. Stool ova and parasite examination will be performed in subjects with an absolute eosinophil count >2 x ULN AND risk factors for parasitic disease listed at the exclusion criterion 5).
6. Pre-dose on Day 1.
7. The following laboratory variables will be determined: **hematology** (hemoglobin, hematocrit, red blood cell count, white blood cell count with differential count, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and platelet count), **clinical chemistry** (total protein, sodium, potassium, calcium, chloride, magnesium, phosphate, albumin, glucose, total cholesterol, triglycerides, C-reactive protein, urea, creatinine, uric acid, bilirubin [total, direct], alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, lactate dehydrogenase, creatine phosphokinase, and troponin I), and **urinalysis** (pH, specific gravity, glucose, ketones, nitrite, protein, bilirubin, urobilinogen, occult blood, and microscopic examination).
8. Serology tests will be performed at the screening visit for HbsAg, anti-HCV, HIV testing.
9. Physical examination will be done at screening, on Day -1, 3 and at EOS.
10. For hypersensitivity monitoring, vital sign measurements will be performed before the start of the study drug administration (pre-dose) and at 30 minutes, 1, 2, 6, and 12 hours after start of administration on Day 1. Electrocardiogram (ECG) will be performed before the start of the study drug administration (pre-dose) and at 2 hours after start of administration on Day 1. Assessment time points and acceptable tolerance windows for hypersensitivity monitoring are described in Table 6-4 in protocol (CT-P39 1.1). Either 3-lead or 12-lead ECG can be used for hypersensitivity monitoring. Additional ECG will be performed if a subject experiences cardiac symptoms. In addition, hypersensitivity/allergic reactions will be monitored by routine continuous clinical monitoring. If the subject experiences any of hypersensitivity signs and symptoms after discharge, the subject can visit the study center for further assessments. The diagnostic assessment such as serum samples for C3, C4, and total hemolytic complement can be ordered to determine serum sickness based on the investigator's discretion. Injection site examination including but not limited to evaluating erythema, pain, bruising, bleeding, and other signs of discomfort or skin reaction to be completed at least 30 minutes after injection. In the event of significant skin reactions, appropriate informal photographs may be taken. Skin biopsy may also be considered.

11. Complement (C3 and C4) and total hemolytic complement will be assessed on Day -1 to establish the baseline value. Additional serum samples for complement (C3 and C4) and total hemolytic complement will be assessed in the case of Type III hypersensitivity.
12. Local site pain will be observed immediately (within 15 minutes) after the study drug administration on Day 1.
13. Serum total IgE sample will be collected at screening to confirm eligibility. Total IgE samples for PD analysis will be collected on Day 1 before dosing, at 6, 12, 24 (Day 2), 48 (Day 3) and 72 hours (Day 4) from the start of administration and on Days 6, 8, 11, 15, 22, 29, 43, 57, 71, 85, 106 and 127 (EOS). Details of blood sampling time points and acceptable tolerance windows for PD assessments are described in Table 6-2 in protocol (CT-P39 1.1).
14. Free IgE samples for PD analysis will be collected on Day 1 before dosing, at 6, 12, 24 (Day 2), 48 (Day 3) and 72 hours (Day 4) from the start of administration and on Days 6, 8, 11, 15, 22, 29, 43, 57, 71, 85, 106 and 127 (EOS). Details of blood sampling time points and acceptable tolerance windows for PD assessments are described in Table 6-2 in protocol (CT-P39 1.1). Analysis will be performed at the central laboratory.
15. Blood samples for PK analysis will be collected on Day 1 before dosing, at 6, 12, 24 (Day 2), 48 (Day 3) and 72 hours (Day 4) from the start of administration and on Days 6, 8, 11, 15, 22, 29, 43, 57, 71, 85, 106 and 127 (EOS). Details of blood sampling time points and acceptable tolerance windows for PK assessments are described in Table 6-1 in protocol (CT-P39 1.1). Analysis will be performed at the central laboratory.
16. Unscheduled blood sampling will be performed when suspected immunogenicity related adverse event (e.g. hypersensitivity/allergic reactions) occurs. Analysis will be performed at the central laboratory.
17. Prior and/or concomitant medication use will be recorded for the 30 days before the signed date of informed consent form (ICF) until the EOS visit (inclusive of the applicable periods for prohibited medications as defined in Section 4.3 in protocol (CT-P39 1.1).

18.2 Appendix 2: Table of CTCAE Terms and Grades

Table 18-2: CTCAE Terms and Grades.

CTCAE Term	Laboratory Parameter	Level	Grade 1	Grade 2	Grade 3	Grade 4
Alanine aminotransferase increased	Alanine Aminotransferase (ALT)	High	>ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
Alkaline phosphatase increased	Alkaline phosphatase (ALP)	High	>ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal	>2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
Anemia	Hemoglobin	Low	<LLN - 10.0 g/dL; <LLN - 100 g/L; <LLN – 6.2 mmol/L	<10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 – 80 g/L	<8.0 g/dL; <4.9 mmol/L; <80 g/L	-
Aspartate aminotransferase increased	Aspartate Aminotransferase (AST)	High	>ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
Blood bilirubin increased	Total Bilirubin	High	>ULN - 1.5 x ULN if baseline was normal; > 1.0 - 1.5 x baseline if baseline was abnormal	>1.5 - 3.0 x ULN if baseline was normal; >1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 10.0 x ULN if baseline was normal; >3.0 - 10.0 x baseline if baseline was abnormal	>10.0 x ULN if baseline was normal; >10.0 x baseline if baseline was abnormal
Cholesterol high	Total Cholesterol	High	>ULN - 300 mg/dL; >ULN - 7.75 mmol/L	>300 - 400 mg/dL; >7.75 - 10.34 mmol/L	>400 - 500 mg/dL; >10.34 - 12.92 mmol/L	>500 mg/dL; >12.92 mmol/L
CPK increased	Creatine Phosphokinase (CPK)	High	>ULN - 2.5 x ULN	>2.5 x ULN - 5 x ULN	>5 x ULN - 10 x ULN	>10 x ULN
Creatinine increased [1)]	Creatinine	High	>ULN - 1.5 x ULN	>1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	>3.0 x baseline; >3.0 - 6.0 x ULN	>6.0 x ULN
GGT increased	Gamma Glutamyl Transferase (GGT)	High	>ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal	>2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
Hemoglobin increased	Hemoglobin	High	Increase in >0 - 2 g/dL from ULN	Increase in >2 - 4 g/dL from ULN	Increase in >4 g/dL from ULN	-
Hyperkalemia	Potassium	High	>ULN - 5.5 mmol/L	>5.5 - 6.0 mmol/L	>6.0 - 7.0 mmol/L	>7.0 mmol/L

CTCAE Term	Laboratory Parameter	Level	Grade 1	Grade 2	Grade 3	Grade 4
Hypermagnesemia	Magnesium	High	>ULN - 3.0 mg/dL; >ULN - 1.23 mmol/L	-	>3.0 - 8.0 mg/dL; >1.23 - 3.30 mmol/L	>8.0 mg/dL; >3.30 mmol/L;
Hypernatremia	Sodium	High	>ULN - 150 mmol/L	>150 - 155 mmol/L	>155 - 160 mmol/L;	>160 mmol/L
Hypertriglyceridemia	Triglyceride	High	150 mg/dL - 300 mg/dL; 1.71 mmol/L - 3.42 mmol/L	>300 mg/dL - 500 mg/dL; >3.42 mmol/L - 5.7 mmol/L	>500 mg/dL - 1000 mg/dL; >5.7 mmol/L - 11.4 mmol/L	>1000 mg/dL; >11.4 mmol/L
Hypoalbuminemia	Albumin	Low	<LLN - 3 g/dL; <LLN - 30 g/L	<3 - 2 g/dL;<30 - 20 g/L	<2 g/dL;<20 g/L	-
Hypoglycemia	Glucose	Low	<LLN-55mg/dL;<LLN-3.0 mmol / L	< 55 -40mg/dL;< 3.0 – 2.2 mmol / L	< 40 -30mg/dL;< -2.2 – 1.7 mmol / L	<30mg/dL; <1.7mmol/L
Hypokalemia	Potassium	Low	<LLN - 3.0 mmol/L	-	<3.0 - 2.5 mmol/L	<2.5 mmol/L
Hypomagnesemia	Magnesium	Low	<LLN - 1.2 mg/dL; <LLN - 0.5 mmol/L	<1.2 - 0.9 mg/dL; <0.5 - 0.4 mmol/L	<0.9 - 0.7 mg/dL; <0.4 - 0.3 mmol/L	<0.7 mg/dL; <0.3 mmol/L;
Hyponatremia	Sodium	Low	<LLN - 130 mmol/L	125-129 mmol/L	120-124 mmol/L regardless of symptoms	<120 mmol/L
Leukocytosis	White Blood Cells	High	-	-	>100,000/mm^3	-
Lymphocyte count decreased	white blood cell count with differential count	Low	<LLN - 800/mm^3; <LLN – 0.8 x $10e^9$ /L	<800 - 500/mm^3; <0.8 – 0.5 x $10e^9$ /L	<500 - 200/mm^3; <0.5 – 0.2 x $10e^9$ /L	<200/mm^3; <0.2 x $10e^9$ /L
Lymphocyte count increased	white blood cell count with differential count	High	-	>4000/mm^3 - 20000/mm^3	>20000/mm^3	-
Neutrophil count decreased	white blood cell count with differential count	Low	<LLN - 1500/mm^3; <LLN - 1.5 x $10e^9$ /L	<1500 - 1000/mm^3; <1.5 - 1.0 x $10e^9$ /L	<1000 - 500/mm^3; <1.0 - 0.5 x $10e^9$ /L	<500/mm^3; <0.5 x $10e^9$/L
Platelet count decreased	Platelet count	Low	<LLN - 75,000/mm^3;<LLN - 75.0 x $10e^9$ /L	<75,000 - 50,000/mm^3;<75.0 - 50.0 x $10e^9$ /L	<50,000 - 25,000/mm^3;<50.0 - 25.0 x $10e^9$ /L	<25,000/mm3; <25.0 x $10e^9$ /L
White blood cells decreased	White blood cells	Low	<LLN - 3000/mm^3; <LLN – 3.0 x $10e^9$ /L	<3000 - 2000/mm^3; <3.0 - 2.0 x $10e^9$ /L	<2000 - 1000/mm^3; <2.0 - 1.0 x $10e^9$ /L	<1000/mm^3; <1.0 x $10e^9$/L

LLN = lower limit of normal, ULN = upper limit of normal.
1) The most severe grade is counted if the CTCAE grade is discrepant by multiple definitions.

Note: The LLN and ULN values will be the lower and upper limits of the normal ranges as provided by the local laboratories at each relevant transfer. In case numeric value for grading is identical such as Hypokalemia, CTCAE grade which includes numeric value will only be applied, because abnormal lab oratory value with clinical input was reported as an adverse event and graded accordingly.

18.3 Appendix 3-1: Tables, Listings, and Figures (TLFs) List for the first CSR

Table No.	Title
Table 14.1.1.1	Summary of Analysis Set (Intent-to-Treat Set) – Part 1
Table 14.1.2.1	Summary of Subject Disposition (Intent-to-Treat Set) – Part 1
Table 14.1.4.1	Summary of Demographics and baseline Characteristics (Intent-to-Treat Set) – Part 1
Table 14.1.5.1	Study Drug Administration (Safety Set) – Part 1
Table 14.2.1.1	Summary of Serum Concentrations of Omalizumab (μg/mL) by Treatment Arm (Safety Set) – Part 1
Table 14.2.2.1	Summary of Serum Pharmacokinetic Parameters of Omalizumab (C_{max} and T_{max}) by Treatment Arm (Safety Set) – Part 1
Table 14.3.1.1.1	Overall Summary of Adverse Events (Safety Set) – Part 1
Table 14.3.1.2.1	Treatment-Emergent Adverse Events by SOC, PT, Relationship, and Intensity (Safety Set) – Part 1
Table 14.3.1.8.1	Treatment-Emergent Adverse Events Classified as Allergic reactions Type I/anaphylaxis (Safety Set) – Part 1
Table 14.3.1.9.1	Signs and Symptoms of Treatment-Emergent Adverse Events Classified as Allergic reactions Type I/anaphylaxis (Safety Set) – Part 1
Table 14.3.1.10.1	Treatment-Emergent Adverse Events Classified as Injection Site Reaction (Safety Set) – Part 1
Table 14.3.1.11.1	Signs and Symptoms of Treatment-Emergent Adverse Events Classified as Injection Site Reaction (Safety Set) – Part 1
Table 14.3.1.12.1	Treatment-Emergent Adverse Events Classified as Serum Sickness/Serum Sickness-Like Reactions (Safety Set) – Part 1
Table 14.3.1.13.1	Signs and Symptoms of Treatment-Emergent Adverse Events Classified as Serum Sickness/Serum Sickness-Like Reactions (Safety Set) – Part 1
Table 14.3.1.14.1	Treatment-Emergent Adverse Events Classified as Parasitic (helminth) Infections (Safety Set) – Part 1
Table 14.3.5.9.1	Summary of Immunogenicity Assay (Safety Set) – Part 1
Listing No.	**Title**
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Listing 16.2.1.1.1	Subject Disposition (Intent-to-Treat Set) – Part 1
Listing 16.2.1.3.1	Inclusion and Exclusion Criteria (Intent-to-Treat Set)– Part 1
Listing 16.2.1.4.1	Major Protocol Deviations (Intent-to-Treat Set) – Part 1
Listing 16.2.4.1.1	Demographics and baseline Characteristics (Intent-to-Treat Set) – Part 1
Listing 16.2.4.2.1	Medical History (Intent-to-Treat Set) – Part 1
Listing 16.2.4.3.1	Urine Drug Screen (Intent-to-Treat Set) – Part 1
Listing 16.2.4.4.1	Breath Alcohol Assessment (Intent-to-Treat Set) – Part 1
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Listing 16.2.4.6.1	Viral Serology (Intent-to-Treat Set) – Part 1
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Listing 16.2.5.1	Study Drug Administration (Safety Set) – Part 1
Listing 16.2.6.1.1	Individual Serum Collection Times and Concentration (μg/mL) of Omalizumab (Safety Set) – Part 1
Listing 16.2.6.2.1	Individual Serum Pharmacokinetic Parameters of Omalizumab (C_{max} and T_{max}) (Safety Set) – Part 1
Listing 16.2.7.1.1	Adverse Events (Safety Set) – Part 1
Listing 14.3.2.1.1	Adverse Events Leading to Death (Safety Set) – Part 1
Listing 14.3.2.3.1	Treatment-Emergent Adverse Events Leading to Study Discontinuation (Safety Set) – Part 1
Listing 14.3.2.4.1	Treatment-Emergent Adverse Events Classified as Allergic reactions Type I/anaphylaxis (Safety Set) – Part 1
Listing 14.3.2.5.1	Treatment-Emergent Adverse Events Classified as Injection Site Reaction (Safety Set) – Part 1
Listing 14.3.2.6.1	Treatment-Emergent Adverse Events Classified as Serum Sickness/Serum Sickness-Like Reactions (Safety Set) –Part 1
Listing 14.3.2.7.1	Treatment-Emergent Adverse Events Classified as Parasitic (helminth) Infection (Safety Set) – Part 1
Listing 16.2.8.1.1	Clinical Chemistry (Safety Set) – Part 1
Listing 16.2.8.2.1	Hematology (Safety Set) – Part 1

Listing No.	Title
Listing 16.2.8.3.1	Urinalysis (Safety Set) – Part 1
Listing 16.2.9.1.1	Vital signs and Body weights (Safety Set) – Part 1
Listing 16.2.9.2.1	Electrocardiograms (Safety Set) – Part 1
Listing 16.2.9.3.1	Physical Examinations (Safety Set) – Part 1
Listing 16.2.9.7.1	Immunogenicity Testing (Safety Set) – Part 1
Figure No.	**Title**
Figure 14.2.3.1.1	Mean (± SD) Omalizumab Serum Concentrations by Treatment (Safety Set) – Part 1

18.4 Appendix 3-2: Tables, Listings, and Figures (TLFs) List for the Final CSR

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Table 14.1.3.1 Table 14.1.3.2	Summary of Major Protocol Deviations (Intent-to-Treat Set) – Part 1, 2
Table 14.1.4.1 Table 14.1.4.2	Summary of Demographics and baseline Characteristics (Intent-to-Treat Set) – Part 1,2
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Table 14.1.7.1 Table 14.1.7.2	Summary of Viral Serology at baseline (Intent-to-Treat Set) – Part 1,2
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Table 14.1.9.1 Table 14.1.9.2	Summary of Concomitant Medications (Safety Set) – Part 1,2
Table 14.2.1.1 Table 14.2.1.2	Summary of Serum Concentrations of Omalizumab (µg/mL) by Treatment Arm (Pharmacokinetic Set) – Part 1,2
Table 14.2.1.1a	Summary of Serum Concentrations of Omalizumab (µg/mL) by Treatment Arm (Pharmacokinetic Set) – Part 1 (Sensitivity Analysis)
Table 14.2.2.1 Table 14.2.2.2	Summary of Serum Pharmacokinetic Parameters of Omalizumab by Treatment Arm (Pharmacokinetic Set) – Part 1,2
Table 14.2.2.1a	Summary of Serum Pharmacokinetic Parameters of Omalizumab by Treatment Arm (Pharmacokinetic Set) – Part 1 (Sensitivity Analysis)
Table 14.2.3.2	Statistical Analysis of Primary Pharmacokinetic Parameters of Omalizumab (Pharmacokinetic Set) – Part 2
Table 14.2.4.1 Table 14.2.4.2	Summary of Serum Concentrations of Free IgE (IU/mL) by Treatment Arm (Pharmacodynamic Set) – Part 1,2
Table 14.2.5.1 Table 14.2.5.2	Summary of Serum Concentrations of Total IgE (IU/mL) by Treatment Arm (Pharmacodynamic Set) – Part 1,2
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Table 14.3.1.2.1 Table 14.3.1.2.2	Treatment-Emergent Adverse Events by SOC, PT, Relationship, and Intensity (Safety Set) – Part 1,2
Table 14.3.1.3.1 Table 14.3.1.3.2	Treatment-Emergent Adverse Events by SOC, PT, and Intensity (Safety Set) – Part 1,2
Table 14.3.1.4.1 Table 14.3.1.4.2	Treatment-Emergent Serious Adverse Events by SOC, PT, Relationship, and Intensity (Safety Set) – Part 1,2
Table 14.3.1.5.1 Table 14.3.1.5.2	Treatment-Emergent Serious Adverse Events by SOC, PT, and Intensity (Safety Set) – Part 1,2
Table 14.3.1.6.1 Table 14.3.1.6.2	Treatment-Emergent Adverse Events Leading to Study Discontinuation by SOC, PT, Relationship, and Intensity (Safety Set) – Part 1,2
Table 14.3.1.7.1 Table 14.3.1.7.2	Treatment-Emergent Adverse Events Leading to Study Discontinuation by SOC, PT, and Intensity (Safety Set) – Part 1,2

Table No.	Title
Table 14.3.1.8.1 Table 14.3.1.8.2	Treatment-Emergent Adverse Events Classified as Allergic reactions Type I/anaphylaxis (Safety Set) – Part 1,2
Table 14.3.1.9.1 Table 14.3.1.9.2	Signs and Symptoms of Treatment-Emergent Adverse Events Classified as Allergic reactions Type I/ anaphylaxis (Safety Set) – Part 1,2
Table 14.3.1.10.1 Table 14.3.1.10.2	Treatment-Emergent Adverse Events Classified as Injection Site Reaction (Safety Set) – Part 1,2
Table 14.3.1.11.1 Table 14.3.1.11.2	Signs and Symptoms of Treatment-Emergent Adverse Events Classified as Injection Site Reaction (Safety Set) – Part 1,2
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Table 14.3.1.13.1 Table 14.3.1.13.2	Signs and Symptoms of Treatment-Emergent Adverse Events Classified as Serum Sickness/Serum Sickness-Like Reactions (Safety Set) – Part 1,2
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Table 14.3.4.1.1 Table 14.3.4.1.2	Clinical Chemistry Summary Descriptive Statistics (Safety Set) – Part 1,2
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Table 14.3.4.3.1 Table 14.3.4.3.2	Hematology Summary Descriptive Statistics (Safety Set) – Part 1,2
Table 14.3.4.4.1 Table 14.3.4.4.2	Hematology Shifts from baseline (Safety Set) – Part 1,2
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Table 14.3.5.7.1 Table 14.3.5.7.2	Summary of Local Site Pain (Safety Set) – Part 1,2
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Table 14.3.5.9.1 Table 14.3.5.9.2	Summary of Immunogenicity Assay (Safety Set) – Part 1,2

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Listing 16.2.1.2.3	Screen Failure (All subjects) – Part 1 and 2
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Listing 16.2.4.4.1 Listing 16.2.4.4.2	Breath Alcohol Assessment (Intent-to-Treat Set) – Part 1,2
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