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STATISTICAL ANALYSIS PLAN

AN OPEN-LABEL DRUG-DRUG INTERACTION STUDY TO ASSESS THE EFFECTS OF NEMOLIZUMAB ON CYTOCHROME P450 SUBSTRATES IN SUBJECTS WITH MODERATE-TO SEVERE ATOPIC DERMATITIS

SAP Version 3.0
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for

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LIST OF ABBREVIATIONS

Abbreviation	Definition
ACT	Asthma control test
AD	Atopic dermatitis
ADA	Antidrug antibody
AE	Adverse event
AESI	Adverse event of special interest
ANCOVA	Analysis of co-variance
ATC	Anatomical therapeutic chemical system
AUC	Area under the concentration time curve
AUC0-last	Area under the concentration-time curve (AUC) from time 0 to the time of the last quantifiable concentration
AUC0-inf	AUC from time 0 to infinity
BLQ	Below the lower quantification limit
BSA	Body surface area
CI	Confidence interval
CL/F	Apparent total body clearance of the drug from plasma after non-intravenous administration
Cmax	The maximum observed plasma concentration determined by direct inspection of the concentration vs time data
CPK	Creatinine phosphokinase
CRF	Case report form
CRO	Contract research organization
CSR	Clinical study report
CV	Coefficient of variation
CYP/ CYP450	Cytochrome P450
EASI	Eczema area and severity index
ECG	Electrocardiogram
FSH	Follicle-stimulating hormone
HBcAb	Hepatitis B core antibody
HBsAg	Hepatitis B surface antigen
HIV	Human immunodeficiency virus
IAC	Independent adjudication committee
ICH	International Council on Harmonisation
IDMC	Independent data monitoring committee
IGA	Investigator's global assessment
INR	International normalised ratio
LTE	Long-Term Extension
MedDRA	Medical dictionary for regulatory activities
PEF	Peak expiratory flow
PK	Pharmacokinetics
PP NRS/ PP-NRS	Peak pruritus numeric rating scale
PT	Preferred Term
Q4W	Every 4 weeks

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SAE	Serious adverse event
SAP	Statistical analysis plan
SC	Subcutaneous
SD	Standard deviation
SOC	System organ class
t½	The apparent elimination half-life
TB	Tuberculosis
TCI	Topical calcineurin inhibitor
TCS	Topical corticosteroid
TEAE	Treatment-emergent adverse event
Tmax	The time from dosing at which Cmax is apparent determined by direct inspection of the concentration vs time data
ULN	Upper limit of normal
UPT	Urine pregnancy test
WHO	World health organization
λz	Terminal phase (apparent elimination) rate constant

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REVISION HISTORY

Version Number	Effective Date	Changes since previous version
Final 1.0	08 DEC 2020	Original version, Not Applicable
Final 2.0	24 OCT 2023	1) Section 3: The LTE Criteria has been added based latest protocol amendment (Version 5, dated 14 September 2021). 2) Section 3.14.1: For the definition of TEAE the study drug (Nemolizumab) has been specified. 3) Section 7.14: The definition of Prior and Concomitant medication has been modified. 4) Section 7.18: Treatment related ADA definition added. 5) Section 7.19: The definition of Periods has been modified. 6) Section 7.19.2: Normalization criteria added. 7) Section 8: The Table 14.1.1.3, 14.1.7, 14.3.5.1.2, Figure 14.3.4.1.2.5, 14.3.4.1.2.6 and Listing 16.2.1.2 are added. 8) Other edits – typographical or for clarity.
Final 3.0	06 DEC 2023	1) Update in per-protocol population definition 2) Update in caffeine NCA analysis 3) Typographical edits

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1. INTRODUCTION

This statistical analysis plan (SAP) is consistent with the statistical methods section of the final study protocol (Version 5.0, dated 14 SEPT 2021) and includes additional detail of pharmacokinetic (PK), Immunogenicity, efficacy analyses and safety summaries to be included in the clinical study report (CSR).

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2. STUDY OBJECTIVES AND ENDPOINTS

2.1 Objectives

The following are the study objectives.

2.1.1 Primary Objective

To evaluate the effect of nemolizumab (CD14152) on the PK of a drug "cocktail" representative of CYP450 (CYP1A2, CYP2C9, CYP2C19, CYP2D6 and CYP3A4/5 sensitive index substrates) in adult subjects with moderate-to-severe Atopic Dermatitis (AD).

2.1.2 Secondary Objective

To assess the safety of nemolizumab.

2.2 Endpoints

The following are the study endpoints.

2.2.1 Primary Endpoints

Change of PK parameters ($AUC_{0\text{-}inf}$, $AUC_{0\text{-}last}$ and C_{max}) in the 5 probe drugs administered concomitantly (Caffeine, Warfarin Sodium, Omeprazole, Metoprolol Tartrate and Midazolam) derived from the plasma concentration-time profile before and after 9-week of nemolizumab treatment.

2.2.2 Secondary Endpoint

Incidence and severity of adverse events (AEs), including treatment-emergent AEs (TEAEs), AE of special interest (AESIs), and serious AEs (SAEs).

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3. STUDY DESIGN

3.1 General

This is an open-label, single sequence drug-drug interaction study in approximately 25 adult subjects. Two study sites are planned in the United States and Europe.

The expected duration for each subject's participation in the study will be approximately 25 weeks, including up to a 4-week screening period, a 1-week pre-dose period, a 12-week nemolizumab treatment period, and an 8-week follow-up period (12 weeks after the last study drug injection). The 8-week follow-up period is not required for subjects who will continue in the LTE study (SPR.118163), a separate study. Refer to Figure 3-1 below for an overview of the treatment/study design.

Blood samples will be collected at Baseline and at Week 10 before and after each oral dosing up to 120 hours post-dose for warfarin and 24 hours post-dose for rest of the CYP substrates for the determination of the complete plasma PK profile of each CYP probe. A total of 14 blood samples for warfarin and 12 blood samples for the rest of the CYP substrates will be collected at each visit before and after each oral dose making a total of 28 samples for warfarin and 24 samples for rest of the CYP substrates. In addition, blood samples will be collected for the assessment of nemolizumab serum concentrations during the treatment period.

Subjects who complete the Week 13 visit may be eligible to enroll into the long-term extension (LTE) study (SPR.118163). The follow-up period including the follow-up visit is not required for subjects who participate in the LTE study. Subjects who decline or are not eligible to enter into the LTE study will complete a follow-up visit at Week 21 (12 weeks after their last study drug injection). Subjects who discontinue the study prematurely should complete an early termination (ET) visit and a follow-up visit 12 weeks after the last study drug injection.

An independent data monitoring committee (IDMC) will review and monitor subject safety throughout the study, and an independent adjudication committee (IAC) will review all asthma-related events throughout the study.

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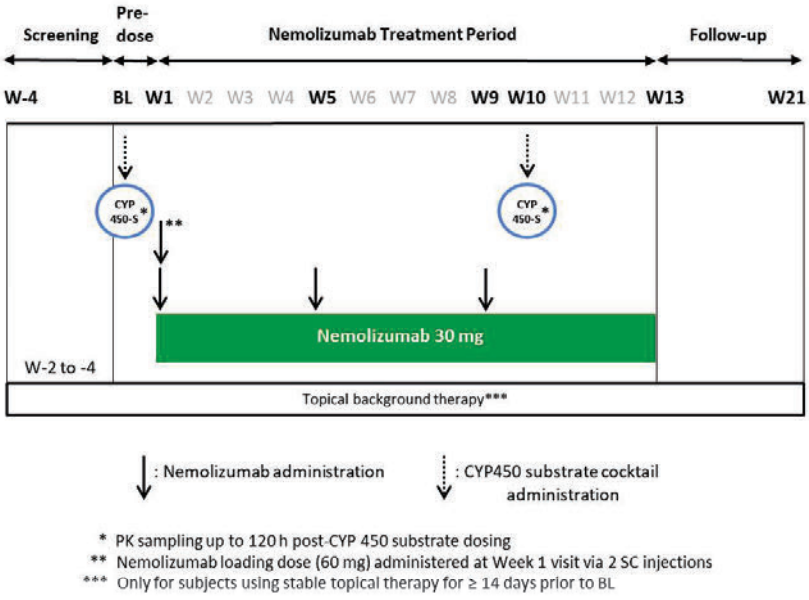
Figure 3-1: Study Design Schematic



Abbreviations: BL=baseline; CYP450-S=cytochrome P450 substrates; SC=subcutaneous; W=week.

Study procedures and assessments with their timing summarized in Table 3-1.

Table 3-1: Study Procedures and Assessments Schedule

Visit	Screening Period	Predose Period					Treatment Period									Follow-up	Early Termination Visit [a] (if applicable)	Unscheduled Visit [b] (if applicable)
	Visit 1	Visit 2/ **Baseline**					Visit 3	Visit 4	Visit 5	Visit 6					Visit 7	Visit 8/ **Final** [a]		
Week	-4 to 0	0					1	5	9	10					13	21		
Day(s)	-28 to -1	-1	1	2	4	6	8	36	64	70	71	72	74	76	92	148		
Window		0	0	0	0	0	+2	±2	±2	0	0	0	0	0	+2	±5		
Inpatient or Outpatient	O	I	I	I[c]	O	O	O	O	O	I	I	I[c]	O	O	O	O		
Informed consent form	X																	
Inclusion/exclusion criteria	X		X															
Demographic data	X																	
Medical history, previous therapy	X																	(X)
EFFICACY ASSESSMENTS																		
[redacted] CCI																		
IGA	X		X															(X)
[redacted] CCI																		
BSA	X		X															(X)
SAFETY ASSESSMENTS [e]																		
ACT [f]	X		X					X	X						X	X	X	(X)
Respiratory exam [g]	X		X					X	X						X	X	X	(X)
PEF testing [h]	X		X					X[h]	X[h]						X	X	X	(X)
Vital signs	X		X					X	X						X	X	X	(X)
Full physical exam	X		X						X						X	X	X	(X)
Height	X																	(X)
Weight	X														X	X	X	(X)
ECG [i]	X		X												X	X	X	(X)

Visit	Screening Period	Predose Period					Treatment Period								Follow-up	Early Termination Visit [a] (if applicable)	Unscheduled Visit [b] (if applicable)
	Visit 1	Visit 2/ **Baseline**					Visit 3	Visit 4	Visit 5	Visit 6					Visit 7	Visit 8/ **Final** [a]	
Week	-4 to 0	0					1	5	9	10					13	21	
Day(s)	-28 to -1	-1	1	2	4	6	8	36	64	70	71	72	74	76	92	148	
Window		0	0	0	0	0	+2	±2	±2	0	0	0	0	0	+2	±5	
Contraceptive counseling	X																(X)
Adverse event reporting [e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)
Concomitant therapies/ procedures [e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)
LABORATORY ASSESSMENTS																	
Blood sample for CYP genotyping	X																	
Blood sample for serology (HIV, Hepatitis B and C test)	X																	(X)
Blood samples for TB test [j]	X																	(X)
Blood samples for hematology and biochemistry [k,l]	X		X [k]												X [k]	X [k]	X [k]	(X)
Urinalysis	X		X												X	X	X	(X)
Drug and alcohol testing [m]	X																	(X)
Pregnancy test [n]	Serum		U				U	U	U		U				U	U	U	(U)
FSH [o]	X																	(X)
PK, ADA ASSESSMENTS																	
Nemolizumab serum samples [p,q,r]			X					X	X		X				X			(X)
CYP substrates plasma samples [s]			X	X	X	X					X	X	X	X				(X)

Visit	Screening Period	Predose Period					Treatment Period									Follow-up	Early Termination Visit [a] (if applicable)	Unscheduled Visit [b] (if applicable)
	Visit 1	Visit 2/ Baseline					Visit 3	Visit 4	Visit 5	Visit 6					Visit 7	Visit 8/ Final [a]		
Week	-4 to 0	0					1	5	9	10					13	21		
Day(s)	-28 to -1	-1	1	2	4	6	8	36	64	70	71	72	74	76	92	148		
Window		0	0	0	0	0	+2	±2	±2	0	0	0	0	0	+2	±5		
INR Sampling	X		X	X	X							X	X					
ADA samples [p]							X		X						X			(X)
STUDY DRUG ADMINISTRATION																		
Study drug injection [t,u]							X [v]	X	X									(X)
CYP substrate administration [w]			X								X							(X)
CONCOMITANT THERAPY																		
Moisturizer use [x]	X----------X																	(X)
Background topical therapy use [y]	X----------X																	(X)

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3.2 Study Population

Approximately 25 adult subjects aged ≥18 years with moderate-to-severe AD. Eligible subjects must have a documented history of inadequate response to topical AD medication(s) within 6 months of screening visit.

3.3 Evaluations at Screening

The study consists of a 2 to 4 week screening period. Subjects will apply a moisturizer at least once daily, beginning at screening and throughout the study. Refer Table 3-1 for screening procedures.

Screen failures may be allowed to rescreen up to 1 time unless the reason for screen failure is related to disease severity inclusion criteria (IGA, EASI, BSA, and PP NRS). The latter subjects are not permitted to rescreen. Subjects who are rescreened must sign a new Informed Consent Form and be assigned a new subject identification number.

3.4 Randomization and Treatment Assignments

Upon confirmation of eligibility for a given subject to participate in the study, a unique SIN for that subject will be assigned via an electronic data capture system. All study treatment will occur with open-label study drug.

This is a single sequence drug-drug interaction study, hence, randomization is not required.

3.5 Determination of Sample Size

Approximately 25 subjects will be enrolled to have 15 completed subjects in the per-protocol population to provide a reliable estimate of the magnitude and variability of the interaction. 15 completed subjects in the per-protocol population is the lower limit of reliability for ANOVA based tests as defined by bioequivalence guidelines.

3.6 Study Drug Administration

Subjects will apply a moisturizer at least once daily, beginning at screening and throughout the study. Subjects using a stable regimen of low- or medium-potency topical corticosteroid (TCS) with or without topical calcineurin inhibitor (TCI) at the screening visit (i.e., ≥ 14 days prior to the baseline visit) should continue their therapy regimen in the study. Subjects not using a stable regimen of TCS with or without TCI at the screening visit should not use these topical therapies during the study unless required as rescue therapy. Moisturizer or background therapies use and any adjustments should be documented in the electronic case report form (eCRF).

Subjects will receive 1 single oral dose of the selected, commercially available, CYP substrates Caffeine100 mg, Warfarin Sodium 10 mg, Midazolam 2 mg (diluted with water, a sugar or sugar substitute may be added), Omeprazole 20 mg, and Metoprolol Tartrate 100 mg] administered 1 at a time in sequence at Baseline/Day 1 under fasted conditions for at least 10 hours.

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After a 1week wash-out period, subjects will receive nemolizumab by subcutaneous (SC) injection every 4 weeks (Q4W) for a treatment period of 12 weeks. Subjects will receive a 60 mg loading dose of nemolizumab (given via 2 consecutive SC 30 mg injections) at Week 1, followed by a single 30 mg dose at Week 5 and Week 9 of the study.

Subjects will receive a second oral dosing of CYP substrates, administered 1 at a time in sequence, 9 weeks after initiation of nemolizumab treatment (at Week 10) under fasted conditions for at least 10 hours at the anticipated peak serum concentration of nemolizumab (i.e., 1 week after the last nemolizumab administration).

Dose modification of the study drug will not be permitted during the clinical trial. Any inadvertent dose modifications should be reported to the sponsor/CRO. In the event of a missed dose (i.e., temporary discontinuation of the study drug), it will be documented in the eCRF that the drug has not been administered at the study visit, together with the reason (eg, for safety). Subjects will be asked to return to the investigational study centers for all remaining visits and complete all study assessments and procedures as described in Table 3-1.

3.7 Prior and Concomitant Therapy

Previous therapies are defined as therapies that have been stopped within the 3 months before the screening visit, unless relevant to the inclusion/exclusion criteria. Whenever possible, previous therapies for AD should be documented.

Concomitant therapies/medications are defined as follows:

- any existing therapies ongoing at the time of the screening visit
- any changes to existing therapies (eg, changes in dose, formulation or application frequency) during the course of the clinical trial
- any new therapies received by the subject since the screening visit

Previous and concomitant therapies for drugs/therapies or for medical/surgical procedures are to be recorded in the appropriate eCRF. Concomitant therapies are to be recorded, reviewed, and updated at each visit. Information recorded will include: start and stop dates and times, dose and route of administration, and indication. Medications taken for a procedure should also be included.

Any new concomitant therapy or modification of an existing therapy may be linked to an AE. In such cases, a corresponding AE form should be completed to account for the new therapy or change in therapy, except in some cases such as dose modification for a chronic condition (Section 3.6), in which case the medication will be linked to an item in the medical history.

Permitted Concomitant Therapy

Unless specified as prohibited therapies, all therapies are authorized including basic skin care (cleansing and bathing), moisturizers, bleach baths, topical anesthetics and antihistamines without a sedative effect.

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Subjects who are not using a stable regimen of topical therapy at the screening visit should not use topical background therapy during the study, unless required as rescue therapy.

Rescue Therapy

Permitted rescue therapies include:

- Topical corticosteroid (higher potency than used at baseline for subjects using TCS background therapy; any potency for subjects not using TCS background therapy)
- Topical Calcineurin inhibitor (only for subjects not using TCI background therapy at baseline)
- Phototherapy

Rescue treatments are only approved and/or standard of care treatments that directly treat AD. Antihistamines, sleep aids, topical and systemic antibiotics, and anti-itch creams are not considered to be rescue therapy because they do not directly treat AD. Rescue treatments can be prescribed to the subjects at any time during the study, except during the screening period.

Prohibited Medication/Therapy

"As needed" (PRN) use of TCS or TCI is not permitted. Treatment with the concomitant medications/therapies listed in Table 4 of the protocol is prohibited during the study unless otherwise specified.

3.8 Drug Compliance

Treatment compliance will be assessed through the treatment records and drug dispensation logs. As study drug is administered in the clinic, treatment compliance will be overseen using the treatment records and drug accountability records. Details of date, time and dose administered will be recorded. Refer to study schedule Table 3-1 for details.

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3.10 Evaluation Pharmacokinetic and Sampling Schedule

CYP probes: Blood samples will be collected according to the schedule of assessments (Table 3-1 and Table 3-2) to determine the PK profile of CYP substrates. CYP substrates PK samples should be collected exactly at the scheduled sampling time points throughout the study, to the extent possible. The actual date and time of the blood sample collection will be recorded in the subject's CRF.

Nemolizumab/ Anti-drug antibody (ADA): Blood samples will be collected according to the schedule of assessments (Table 3-1 and Table 3-2) to determine the PK profile of nemolizumab and ADA. Nemolizumab PK samples should be collected at approximately the same time of day throughout the study, to the extent possible, before study drug injection (predose samples) and at Week 10. The actual date and time of the blood sample collection will be recorded in the subject's CRF.

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3.11 Evaluation of Pharmacodynamics and Sampling Schedule

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3.12 Evaluation of Immunogenicity and Sampling Schedule

According to the schedule of assessments (Table 3-1) and the clinical laboratory manual, blood samples will be collected to assess anti-nemolizumab ADA, which will be determined at these time points by the designated CRO using a validated enzyme-linked immunosorbent assay screening assay. The serum concentration will be assessed using a multi-tiered approach.

The actual date and time of the blood sample collection will be recorded in the subject's CRF.

If serum circulating ADA is detected, presence will be confirmed and characterized (eg, for neutralizing potential) using a validated assay.

3.14 Evaluation of Treatment Safety

3.14.1 Adverse Events

An AE is defined as any untoward medical occurrence in a clinical study subject administered a medicinal product which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not it is related to the medicinal (investigational) product. This includes an exacerbation of pre-existing conditions or events, intercurrent illnesses, drug interaction, or the significant worsening of the indication under investigation that is not recorded elsewhere in the eCRF under specific efficacy assessments.

AEs assessed as related to the treatment or study procedure will be monitored until they have resolved or reached a stable condition. Other AEs will be monitored until the last visit if they have not resolved or reached a stable condition.

If there is a change in severity of an AE, it must be recorded as a separate event.

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A TEAE is defined as an AE that occurs on or after the first date of study drug (Nemolizumab) administration until the date of last study visit.

An SAE is defined as any event that results in death, is immediately life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

Subjects will be monitored throughout the study for AEs, from the time informed consent is obtained through End of Study. The following details will be collected: description of the AE, start date and time, stop date and time, action taken with study drug (dose not changed, drug interrupted, drug withdrawn, and not applicable), outcome (recovered/resolved, not recovered/not resolved, recovered/resolved with sequelae, recovering/resolving, fatal and unknown), severity (mild, moderate, severe, life threatening and fatal), seriousness (yes, no), relationship to study drug (not related, unlikely related, possibly related, probably related, definitely related), additional treatment required.

Adverse Events of Special Interest

An AESI is a noteworthy treatment-emergent event for the study drug that should be monitored closely and reported promptly. An AESI can be either serious or non-serious. AESIs are injection-related reactions, newly diagnosed asthma or worsening of asthma, infections, peripheral edema, facial edema, elevated ALT or AST (> 3 × ULN) in combination with elevated bilirubin (> 2 × ULN).

3.14.2 Clinical Laboratory Assessments

The hematology laboratory analyses, clinical chemistry laboratory analyses, urinalyses, CYP metabolism genotyping, pregnancy testing, virology, and tuberculosis (TB) testing sample will be collected as specified in Table 3-1.

CYP Metabolism Genotyping

Poor metabolizers of CYP2C9, CYP2C19, or CYP2D6 will be identified based on genotype.

Hematology

Testing will include hemoglobin, hematocrit, white blood cell count (with differential including eosinophils), red blood cell count, platelet count, mean cell volume, and INR.

Clinical Chemistry

Testing will include creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyltransferase, alkaline phosphatase, lactate dehydrogenase, total bilirubin, direct bilirubin, albumin, total protein, uric acid, sodium, potassium, calcium, chloride, glucose, urea, total cholesterol, triglycerides, low-density lipoprotein, high-density lipoprotein, and creatinine phosphokinase (CPK). CPK isoenzyme test will be performed only if CPK is elevated to >2.5 × ULN. The investigator should also contact the Medical Monitor in such situations.

The postmenopausal status is defined as no menses for 12 consecutive months, and will be confirmed with a high follicle-stimulating hormone (FSH) level in the postmenopausal range at the screening visit.

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4. CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSIS

All analyses specified in this SAP are consistent with the final study protocol (Version 5.0, dated 14 SEPT 2021). Any changes in this analysis provided or any additional analysis performed will be documented in CSR.

Prior/Concomitant medications is changed from the protocol to:

- Prior medications: defined as therapies that have been started and ended before first dosing of CYP substrate.
- Concomitant medications: defined as medications started or ongoing or ended on or after first dosing of CYP substrate.

Definition of Per-protocol in protocol is 'The per-protocol population (PP population) will consist of all subjects who complete the study without any major protocol deviations or any other event which could render….' But in SAP it is modified to 'The per-protocol population (PP population) will consist of all subjects who complete the treatment period without any major protocol deviations or any other event which could render….' to minimize exclusion of subjects who completed the treatment period and utilize maximum data in summary and analysis.

For Caffeine analyte only, additional NCA calculations for each study periods will be performed using actual sampling times and pre-dose corrected measured concentrations. The pre-dose correction will be performed subtracting, for each subject and each study period, the measured value of caffeine concentration at pre-doses from each correspondent post-dose concentrations.

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5. QUALITY CONTROL AND QUALITY ASSURANCE METHODS FOR DATA ANALYSIS

Case report forms will be monitored and collected by CCI All monitored CRFs will be sent to the Data Management group at CCI and processed according to the CCI Study Specific Procedure SSP DM-02020051.01 Data Management Plan (DMP). The DMP describes CRF data processing, edit checks, data query management, medical dictionary coding, SAE reconciliation, data transfers, and data quality review through database lock or any necessary reopening of the database. After database lock, the data will be retrieved from the database using SAS® (details mentioned in the Section 7.21).

6. PHARMACOKINETIC AND PHARMACODYNAMIC ASSESSMENTS

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6.1 Pharmacokinetic Assessment

No PK parameter for nemolizumab (CD14152) will be calculated. Only trough concentrations will be reported as proof of exposure.

The following individual PK parameters will be measured and/or calculated for each CYP substrates with a Non-Compartmental Analysis (NCA), using Phoenix WinNonlin®, Version 8 or higher, Certara, St. Louis, MO.

Term	Parameter	Description
C_{max}	Maximum observed concentration	Observed maximum plasma concentration
t_{max}	Time to maximum observed concentration	Time to achieve C_{max}
λ_z	Terminal phase (apparent elimination) rate constant	Terminal elimination rate constant, calculated, if feasible, by log-linear regression using at least 3 points excluding C_{max}
$t_{1/2}$	Terminal phase (apparent elimination) half-life	Half-life, calculated, if feasible, as $\ln 2/\lambda_z$
$AUC_{0\text{-last}}$	Area under the concentration-time curve (AUC) from time 0 to the time of the last quantifiable concentration	Area under the concentration-time curve from administration to the last observed concentration-time t, calculated with the linear trapezoidal method
$AUC_{0\text{-inf}}$	AUC from time 0 to infinity	Area under the concentration-time curve extrapolated to infinity, calculated, if feasible, as $AUC_{0\text{-last}} + C_{last}/\lambda_z$, where C_{last} is the last measurable drug concentration
$\%AUC_{extra}$	Percentage of $AUC_{0\text{-inf}}$ extrapolated	Percentage of the residual area (C_{last}/λ_z) extrapolated to infinity in relation to the total $AUC_{0\text{-inf}}$, calculated, if feasible, as $100\times[(C_{last}/\lambda_z)/AUC_{0\text{-inf}}]$
CL/F	Systemic clearance	Systemic clearance, calculated, if feasible, as $DOSE/AUC_{0\text{-inf}}$

The sampling schedule is considered adequate if the ratio $AUC_{0\text{-last}}/AUC_{0\text{-inf}}$ equals or exceeds a factor of 0.8 (i.e., if $\%AUC_{extra}$ is <20%) for more than 80% of the individual PK profiles. This assures that the primary variable $AUC_{0\text{-last}}$ covers a sufficient percentage of the theoretical total extent of exposure. If $\%AUC_{extra}$ is >20%, AUC0-inf will not be reported.

The quality of log-linear regression (and, consequently, the reliability of the extrapolated PK parameters) should be demonstrated by a determination coefficient $R^2 \geq 0.8$.

Individual extrapolated parameters (i.e., λ_z, $t_{1/2}$, $AUC_{0\text{-inf}}$, $\%AUC_{extra}$ and Cl), when considered unreliable, will not be reported.

The calculations of PK parameters will be based on the actual sampling times.

6.1.1 Treatment of Outliers

Individual concentration-time points, if considered anomalous, may be excluded from the analysis at the discretion of the pharmacokinetics following a review of the available documentation. Any such exclusion will be discussed with the sponsor and clearly outlined in the study report.

Entire individual study drug profiles for a subject may be excluded following review of the available documentation and discussion with the sponsor. Examples of reasons for exclusion could be (but are not limited at, see section 7.8.3 and 7.16):

- Subjects experiencing emesis or diarrhea during the course of the study if vomiting or diarrhea occurs at or before two times median T_{max} for CYP substrates.
- the lack of any measurable concentrations or only very low plasma concentrations of the probe drug at visit 2. A subject is considered to have very low plasma concentrations if his/her AUC is less than 5% of the geometric mean AUC of the probe drug at visit 2 (which should be calculated without inclusion of data from the outlying subject).

In case of exclusion concentration and the PK parameter data for the given subject will be listed but excluded from the PK summaries. However, results of analysis with and without the excluded profiles may be presented in the study report as deemed appropriate. Any such exclusion will be clearly listed in the study report along with justification for exclusion.

Any anomalous concentration values observed at predose will be identified and discussed in the CSR. For all analyte except caffeine, pharmacokinetic parameters will be computed if the predose concentration value is not greater than 5% of C_{max} for a given subject. If the predose concentration value is greater than 5% of the subsequent C_{max}, concentration and the PK parameter data for the given subject will be listed but excluded from the PK summaries and statistical analysis.

For Caffeine analyte only, additional NCA calculations for each study periods will be performed using actual sampling times and pre-dose corrected measured concentrations. The pre-dose correction will be performed subtracting, for each subject and each study period, the measured value of caffeine concentration at pre-doses from each correspondent post-dose concentrations.

6.1.2 Non-Quantifiable Concentrations

All concentration values reported as no results (not collected or not determined) values will be treated as missing.

For the calculation of the PK parameters summary statistics, plotting mean and individual concentration time profiles, concentrations below the lower quantification limit (BLQ) will be treated as follows:

- BLQ plasma concentrations occurring before the first measurable concentration will be treated as zero;

- BLQ plasma concentrations occurring after the first measurable concentration will be omitted from the calculation of PK parameters.

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7. STATISTICAL METHODS

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7.1 General

The statistical analysis will be conducted following the principles specified in the International Council for Harmonisation (ICH) Topic E9 Statistical Principles for Clinical Trials (CPMP/ICH/363/96).

All statistical tabulations and analyses will be done using SAS GRID Linux/SAS Studio (details mentioned in section 7.21). PK parameters will be derived using Phoenix™ WinNonlin®, Version 8 or higher (Certara, St. Louis, MO).

For other than PK data, the default summary statistics for continuous variables includes number of contributing observations (n), mean, standard deviation (SD), median, Q1, Q3, minimum, and maximum.

For categorical variables, the number and percentage (as the percentage of subjects in each category relative to the total number of subjects in each category) will be the default summary presentation.

In the data listings, study day relative to dosing date may be presented. **Study day** relative to dose will be calculated as: event date – first dose date (+ 1 if event date ≥ first dose date). First dose date refers to dosing of CYP substrate administration.

For all the efficacy and safety endpoints/measures, unless otherwise specified except for PP NRS, "**Baseline**" is defined as the last observed value of the parameter of interest prior to first dosing of Nemolizumab, as applicable (this includes unscheduled visits). For PP NRS, "Baseline" is defined as based on the average of daily PP NRS (score ranging from 0 to 10) during the 7 days immediately preceding first dosing of Nemolizumab (rounding to nearest whole number is not permitted). A minimum of 4 daily scores out of the 7 days is required for this calculation. For numerical variables,

- Change from baseline will be calculated as (Post baseline value – Baseline value).
- Percent change from baseline will be calculated as [(Post baseline value – Baseline value) /Baseline value]*100.

There will be no multiple comparison adjustment for various analyses.

Concentrations and PK parameters will be summarized using descriptive statistics to include, as appropriate, n, mean, SD, coefficient of variation (CV), minimum, Q1, median, Q3, maximum, geometric mean (GM), and geometric CV%, 95% CI of mean and number of BLQs (Below Limit of Quantification). BLQ will be considered as missing and excluded from the descriptive summary. For t_{max}, summary statistics will be described by n, minimum, Q1, median, Q3, and maximum only.

Unscheduled and repeat assessment will only be used to derive last post-baseline and maximum post-baseline results and will not be used in rest of the summary tables; however, all results will be included in the data listings.

All data will be summarized by visit for Overall unless otherwise specified.

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7.2 Handling of Dropouts or Missing Data

There will be no imputations for missing data other than that implicit by ignoring missing data when using the trapezoidal rule for the calculation of AUCs. For all variables, only the observed data from the subjects will be used in the by-visit summaries.

If the character result is reported for quantitative laboratory parameter then for summary and analysis it will be changed as follows into numerical value –

a) If less than '<' sign is used then the value will be reduced by 1%.

b) If greater than '>' sign is used then 1% will be added.

Eg: if lab parameter is reported as >40 then it will be considered as 40.4 and if the parameter is reported as <40 then it will be considered as 39.6.

7.2.1 Handling of missing/ incomplete dates for Adverse Event

Imputation rules for missing or partial AE start date are defined below:

If only Day of Adverse Event start date is missing:

If the start date has month and year but day is missing, the first day of the month will be imputed

- If this date is earlier than the first Nemolizumab dose date, then the first Nemolizumab dose date will be used instead.
- If this date is later than the stop date (possibly imputed), then the stop date will be used instead.

If Day and Month of Adverse Event start date are missing:

If the start date has year, but day and month are missing, the 1st of January will be imputed

- If this date is earlier than the first Nemolizumab dose date, then the first Nemolizumab dose date will be used instead.
- If this date is later than the stop date (possibly imputed), then the stop date will be used instead.

If Year of Adverse Event start date is missing:

If the year of AE start is missing or AE start date is completely missing then imputation will not be done.

Missing or partial Adverse Event stop date:

a. If only Day is missing, the earlier between the last date of the month and year reported and the date of the final contact with the subject will be assumed.

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b. If Day and Month are both missing, the earlier between last day of the year reported and the date of the final contact with the subject will be assumed.

c. If Day, Month and year are all missing, 'Ongoing' status to stop date will be assigned.

If the AE end date (full or partial) is before the first dose date then the AE should be considered as a pre-treatment AE. Otherwise, the AE will be considered as TEAE.

7.2.2 Handling missing or partial Prior/Concomitant Medication & Medical and Surgical Procedure Dates

Missing or partial medication start date:

a. If only Day is missing, the first day of the month will be assumed.

b. If Day and Month are both missing, the first day of the year will be assumed.

c. If Day, Month and Year are all missing, the day before the first dose date will be assumed.

Missing or partial medication stop date:

d. If only Day is missing, the earlier between the last date of the month and year reported and the date of the final contact with the subject will be assumed.

e. If Day and Month are both missing, the earlier between last day of the year reported and the date of the final contact with the subject will be assumed .

f. If Day, Month and year are all missing, 'Ongoing' status to stop date will be assigned.

7.3 Multiple Comparisons and Multiplicity

No adjustment will be made for the multiple comparisons.

7.4 Adjustments for covariates

COVID-19, asthma, age or any co-morbidity will be considered as covariate in PK statistical model.

7.5 Multicenter Studies

2 study sites are planned, one in the United States and one in Europe. As the main objective of this study is to evaluate the change of PK parameters ($AUC_{0\text{-}inf}$, $AUC_{0\text{-}last}$, C_{max}) in the 5 probe drugs administered concomitantly, center effect will not be considered for analysis.

7.6 Examination of Subgroups

No subgroup analyses are planned.

7.7 Coding dictionaries

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Medical history and adverse events (AEs) will be coded using the Medical Dictionary for Regulatory Activities (MedDRA, version 23.0 or upper). Medications will be coded using the World Health Organization Drug Reference List (WHO Global B3 format - March 2020 or upper). Medical procedures will not be coded.

7.8 Analysis Populations

7.8.1 Enrolled Population

All subjects who signed the informed consent form and are enrolled in the study.

7.8.2 Safety Population

The safety population will include all subjects who receive at least 1 dose of nemolizumab. All safety and efficacy data will be summarized using the safety population. This set will be used for the safety data summaries, baseline characteristic summaries and pharmacokinetic concentration summaries.

7.8.3 Per Protocol Population

The per-protocol population (PP population) will consist of all subjects who complete the treatment period without any major protocol deviations or any other event which could render the probe drugs plasma concentration-time profiles unreliable, especially (but not limited to):

- Vomiting and diarrhea which could render the plasma concentration-time profiles unreliable i.e., after probe drugs intake and/or before 2 times median t_{max}
- Other AEs which could render the plasma concentration-time profile unreliable
- Intake of concomitant medications which could render the plasma concentration time profile unreliable
- Administration errors which could render the plasma concentration-time profile unreliable

The primary endpoint will be analyzed using the per-protocol population.

7.9 Subject Accountability

Subject disposition will be listed and summarized. It will include all subjects who were screened. Listings will be provided for subject accountability and exclusions from analysis populations. The table will contain following information:

- Number of subjects screened
- Number of screen failure subjects and reason for screen failure
- Number of subjects in Enrolled Population
- Number of subjects received CYP substrate
- Number and percent of subjects who were dosed with at least one dose of Nemolizumab (Safety Population)
- Number and percent of subjects who completed the treatment
- Number and percent of subjects who discontinued early from the treatment and reason for early discontinuation

- Number and percent of subjects who completed the study
- Number and percent of subjects who discontinued early from the study and reason for early discontinuation
- Number and percent of subjects rolled over into LTE study

Percentage will be calculated based on enrolled population.

7.10 Protocol Deviations

Major protocol deviation will be summarized for enrolled population. Separate table for major protocol deviation will be summarized by visit for enrolled population.

All Protocol deviations will be listed.

7.11 Subject Demographics and Baseline Characteristics

Subject demographics and baseline characteristics will be listed and summarized descriptively. The summary will include the subjects' age at informed consent (in years), gender, race, ethnicity, weight at baseline (in kg), height (in cm), Status of Habitual Tobacco Use, EASI (baseline score), PP-NRS (baseline score), IGA at baseline and BSA (%). Demographics will be summarized for enrolled, safety and per-protocol populations.

7.12 Medical and Surgical History

The medical and surgical history data will be coded using the Medical Dictionary for Regulatory Activities (MedDRA Version 23.0 or upper), will be listed and summarized descriptively as number and percent of subjects reporting each system organ class (SOC) and preferred term (PT) and sorted alphabetically by SOC and descending frequency of PT within SOC. Summary tables will be presented for safety population and per-protocol populations.

7.13 Medical and Surgical Procedures

Medical and surgical procedures will be classified as follows:

- Prior procedure: defined as procedures that started and ended before first dosing of CYP substrate.
- Concomitant procedure: defined as procedures started or ongoing or ended on or after first dosing of CYP substrate.

Prior and concomitant medical and surgical procedures will be summarized separately using the number and percent of subjects reporting each SOC and PT and sorted alphabetically by SOC and in descending frequency of PT within SOC. Summary tables will be presented for safety population and per-protocol populations.

Prior and concomitant medical and surgical procedures listings will be provided.

7.14 Prior and Concomitant Medications

Prior/Concomitant medications will be classified as follows:

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- Prior medications: defined as therapies that have been started and ended before first dosing of CYP substrate.
- Concomitant medications: defined as medications started or ongoing or ended on or after first dosing of CYP substrate.
- Rescue Medication will be classified as follows:
- Rescue medication during treatment period is a medication which started from the first Nemolizumab injection to the date of Week 13 (for subject completed the treatment period) or the earliest date between 4 weeks after the last Nemolizumab injection or the date of early termination (for discontinued subject).
- Rescue medication during follow-up period is a medication which started from the date of the post end of treatment period to the date of follow up visit.

Background therapy consists of TCS and TCI with start date prior to study drug administration and that are not classified as rescue therapy.

Table 7-1: ATC code of topical corticosteroid (TCS)

ATC code	Name
D07AC01	betamethasone
D07AC02	fluclorolone
D07AC03	desoximetasone
D07AC04	fluocinolone acetonide
D07AC05	fluocortolone
D07AC06	diflucortolone
D07AC07	fludroxycortide
D07AC08	fluocinonide
D07AC09	budesonide
D07AC10	diflorasone
D07AC11	amcinonide
D07AC12	halometasone
D07AC13	mometasone
D07AC14	methylprednisolone aceponate
D07AC15	beclometasone
D07AC16	hydrocortisone aceponate
D07AC17	fluticasone

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D07AC18	prednicarbate
D07AC19	difluprednate
D07AC21	ulobetasol

Table 7-2: ATC Code of topical calcineurin inhibitor (TCI)

ATC code	Name
D11AH01	tacrolimus
D11AH02	pimecrolimus
D11AH03	cromoglicic acid
D11AH04	alitretinoin
D11AH05	dupilumab
D11AH06	crisaborole

All prior and concomitant medications will be coded using the World Health Organization dictionary of medical codes (WHO Global B3 format - March 2020 or upper), will be listed and summarized descriptively for the safety population and per-protocol populations. Medications will be summarized by ATC level 4, 2 and PT. All rescue medications by period (treatment and follow-up periods) and background therapy will be summarized on safety population only.

7.15 Measurements of Treatment Compliance

The extent of exposure (treatment duration, total dose administered, and treatment compliance percentage, the number of subjects treated with each probe drug at each visit) will be summarized.

Treatment duration (in days) is calculated as follows: [(date of last Nemolizumab injection – date of first Nemolizumab injection) + 1].

Dosing data will be listed for safety population. Compliance will also be presented in the listing. The compliance (%) for Nemolizumab is defined as the cumulative actual dose divided by the cumulative assigned dose to be taken x 100.

7.16 Pharmacokinetic Analysis

The primary endpoints are the PK parameters ($AUC_{0\text{-}inf}$, $AUC_{0\text{-}last}$, and C_{max}) in the 5 probe drugs derived from the plasma concentration-time profile before and after 9-week nemolizumab treatment.

Subjects can be excluded from the analysis of each CYP substrate on the basis of pharmacokinetic reasons only for:

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- Lack of any measurable concentrations or only very low plasma concentrations of the probe drug at visit 2. A subject is considered to have very low plasma concentrations if his/her AUC is less than 5% of the geometric mean AUC of the probe drug at visit 2 (which should be calculated without inclusion of the outlying subject)
- Non-zero baseline concentrations > 5% of C_{max}

Subjects should not be excluded from the statistical test if their individual AUC_{0-t} covers less than 80% of their individual AUC_{0-inf}.

Concentration and PK parameters for the 5 selected CYP substrates (Caffeine, Warfarin Sodium, Omeprazole, Metoprolol Tartrate and Midazolam) will be summarized by timepoint for per-protocol population. These will be listed for Per-protocol Population.

The individual sampling and subject concentration-time for plasma (CYP substrates) concentrations will be displayed graphically on linear and semi-log scales (CYP substrates only). Linear and semi-logarithmic plots of the individual plasma concentration by actual sampling time for each study drug will be provided by subject (one subject per page). For all these figures, each drug in their own figure with all days data presented in the same figure.

Overlay of individual concentration profiles over time will be provided by study drug. Plots of mean (SD) concentration profiles versus time will be presented for each study drug in the separate plot. Each drug in their own figure with all days data presented in the same figure.

Concentration values will be listed and summarized for nemolizumab by condition and timepoints.

For the primary endpoint analysis, a linear mixed-effect model will be used to the log-transformed PK parameters (AUC_{0-inf}, AUC_{0-last} and C_{max}) of each CYP substrate, with treatment (with or without nemolizumab) as a fixed effect and subject as a random effect. The geometric mean ratio between treatments (substrates with [test] or without [reference] nemolizumab) after back-transformation and the corresponding 90% confidence interval (CI) will be provided.

The following example code can be used for statistical analysis. Please note that required modification should be made as necessary as per the data.

```
PROC MIXED DATA=DATASET;
BY ANALYTE;
        CLASS SUBJECT TREATMENT;
        MODEL LOGPK = TREATMENT / S DDFM=KR;
        RANDOM SUBJECT;
        LSMEANS TREATMENT / CL ALPHA=0.1;
        ESTIMATE 'Test VS Reference' TREATMENT -1 1 / ALPHA=0.1 CL;
RUN;
```

Where ANALYTE = CYP substrate

According to the calculated 90% CI for AUC, the following will be claimed:

- If the lower limit of the 90% CI is > 80%, no interaction is present
- If the lower limit of the 90% CI is ≤ 80% and > 50%, a weak interaction is present

- If the lower limit of the 90% CI is ≤ 50% and > 20%, a moderate interaction is present
- If the lower limit of the 90% CI is ≤ 20%, a strong interaction is present

A weak interaction will not be considered clinically meaningful.

An additional sensitivity analysis will be presented with considering COVID-19, asthma, age or any co-morbidity as covariate in PK statistical model. Only effects significant at 5% level of significance will be considered in the analysis.

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7.19 Safety Analyses

7.19.1 Adverse Events

All AEs including those with an onset before the first dosing of study drug will be listed. All AE summaries will include treatment emergent AEs.

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The TEAEs will be summarized and tabulated at both the subject (n [%] of subjects) and event (number of events) level:

- Overall summary of TEAEs
- Summary by SOC and PT
- TEAEs by SOC and PT, maximum severity
  TEAEs Related to Study Drug by SOC and PT, maximum severity
- TEAEs Related to Study Drug by SOC and PT
- TEAEs Related to Protocol Procedure by SOC and PT
- Treatment-emergent AESIs by SOC and PT
- Treatment-emergent SAEs by SOC and PT
- TEAEs resulting in discontinuation of study by SOC and PT
- TEAEs resulting in discontinuation of study drug by SOC and PT
- Most common TEAEs (Occurred in >= 5% of Subjects) by PT

Periods are defined as:

1) Cytochrome only Period: Any AE onset from first dosing of CYP substrate to prior to first dosing of Nemolizumab on Day 8.
2) Nemolizumab only Period: Any AE onset from first dosing of Nemolizumab to prior to drug administration of second CYP substrate.
3) Cytochrome + Nemolizumab Period: Any AE onset after second CYP substrate to end of the study.

The overall incidence of TEAEs (number and percentage of subjects) as well as the number of events will be summarized during Cytochrome only period, severity of TEAE; AESIs; SAE; related TEAE and related SAE; TEAEs leading to study discontinuation, TEAEs leading to study drug discontinuation; and TEAEs leading to death will be tabulated. Adverse events during Cytochrome only period will be summarized by SOC and PT as well.

The frequency of TEAEs (AE burden) will be summarized using descriptive statistics by SOC and PT.

For the incidence at the subject level by SOC and PT, if a subject experiences more than 1 event within the same SOC and PT, only 1 occurrence will be included in the incidence.

For the incidence at the subject level by SOC, PT and severity, if a subject experiences more than 1 event within the same SOC, PT and severity, only the most severe occurrence will be included in the incidence.

For the incidence at the subject level by SOC, PT and relationship to study drug; if a subject experiences more than 1 event within the same SOC, PT and relationship, only the most closely related occurrence will be included in the incidence.

Any SAEs, AEs with outcome of death, AESIs or AEs resulting in discontinuation of study or study drug will be listed separately.

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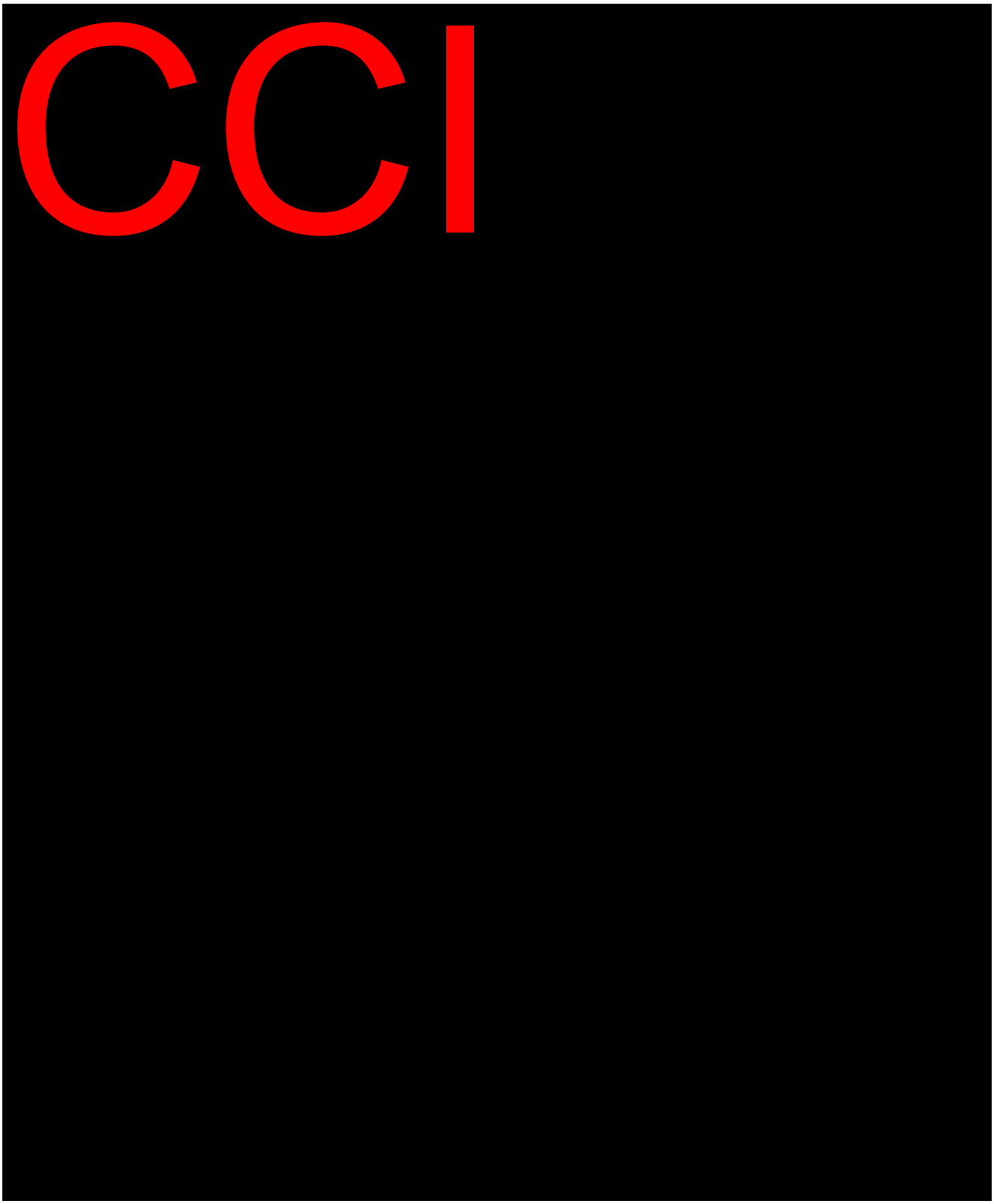

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7.20 Data Monitoring Committee

An IDMC will review and monitor subject safety throughout the study, and an IAC will review all asthma-related events throughout the study. The IDMC and IAC charters provide details on the IDMC and IAC, including the plan of analysis for output, the composition of the committees, procedures, roles, responsibilities, and communications.

7.21 Statistical Software

All data listings, summaries, and statistical analyses will be generated using SAS GRID Linux/SAS Studio.

7.22 General Conventions for Tables, Listings and Figures

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Tables and listings will be presented in landscape mode with minimum of 3/4" bound edge margin and 3/8" other margins on 8.5" x 11" paper.

Times new roman font size of no less than 8 point will be used for tables and listings.

A source line will be included on the bottom of each page of all tables and listings. It will contain the SAS code program name and the run date and time.

Each variable is recorded to a specific number of decimal places. If the raw data is presented with varying precision, then the least precise value will be considered as the data precision.

For summary tables, unless otherwise specified, the number of decimal places provided in the tables and listings will be based on the precision of the least precise value in the raw data as follows:

N	integer
Arithmetic mean	1 decimal place more than the least precise number in the raw data
SD	2 decimal place more than the least precise number in the raw data
CV(%)	2 decimal places
Geometric mean	1 decimal place more than the least precise number in the raw data
Geometric CV	2 decimal places
Median	1 decimal place more than the least precise number in the raw data
Minimum	same number of decimal places as raw data
Maximum	same number of decimal places as raw data
Confidence interval	same number of decimals as the associated statistic
Percentage	1 decimal place

8. LIST OF TABLES, FIGURES, AND LISTINGS

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Table 14.2.1.2	Summary of Cytochrome Probes Plasma Pharmacokinetic Parameters (Per-protocol Population) Note: present for plasma CYP substrates
Table 14.2.1.3	Statistical Analysis of Pharmacokinetic Data (Per-protocol Population) Note: present for plasma CYP substrates
Table 14.2.1.4	Sensitivity Analysis of Pharmacokinetic Data from ANCOVA model (Per-protocol Population)

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	Note: present for plasma CYP substrates
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Table 14.3.5.7	ECG Interpretation Summary (Safety Population)
Table 14.3.5.8	Respiratory Examination Findings Summary (Safety Population)
Table 14.3.5.9	Absolute and Change from Baseline for Asthma Control Test and Peak Expiratory Flow (Safety Population) Note: include Asthma control test and Actual PEF (L/min), and Actual PEF Rate of the predicted value (%)
Table 14.3.5.10	Categorical Summary for Asthma Control Test and Peak Expiratory Flow (Safety Population)
Table 14.3.5.11	Summary of COVID-19 Impact (Safety Population)
Listing Number	**Listing Name**
Section 16.2.1	**Discontinued Subjects**
Listing 16.2.1.1	Subject Disposition (All Screened Subjects)
Listing 16.2.1.2	Visits (Enrolled Population)
Section 16.2.2	**Protocol Deviations**
Listing 16.2.2	Protocol Deviations (Enrolled Population)
Section 16.2.3	**Subjects Excluded from Analysis**
Listing 16.2.3.1	Analysis Populations (Enrolled Population)
Listing 16.2.3.2	Eligibility Criteria (All Screened Subjects)
Section 16.2.4	**Demographic Data**
Listing 16.2.4.1	Demographics and Baseline Characteristics (Enrolled Population) Note: Screening Height, Weight and Smoking History
Listing 16.2.4.2	Medical and Surgical History (Enrolled Population)

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Listing 16.2.4.3	Prior and Concomitant Medications (Enrolled Population)
Listing 16.2.4.4	Prior or Concomitant Medical and Surgical Procedures (Enrolled Population)
Listing 16.2.4.5	Investigator's Global Assessment (Enrolled Population)
Listing 16.2.4.6	Body Surface Area of Atopic Dermatitis Involvement (Enrolled Population)
Section 16.2.5	**Compliance and/or Drug Concentration Data**
Listing 16.2.5.1	Study Drug Dosing Record and Compliance (Safety Population)
Listing 16.2.5.2	Individual Concentrations (Safety Population) Note: present for plasma CYP substrates and serum nemolizumab
Listing 16.2.5.3	Individual Pharmacokinetic Parameters (Safety Population) Note: present for plasma CYP substrates
Figure 16.2.5.1	Plots of Individual Concentration (Safety Population) Note: present for plasma CYP substrates, each analyte separately and all days in one plot
Figure 16.2.5.2	Overlay Plots of Individual Concentration (Safety Population) Note: present for plasma CYP substrates, each analyte separately and all days in one plot
Section 16.2.6	**Individual Efficacy/Pharmacokinetic Response Data**
Section 16.2.6.1	**Individual Efficacy Response Data**
Listing 16.2.6.1.1	Peak Pruritus Numeric Rating Scale Results (Safety population)
Listing 16.2.6.1.2	Eczema Area and Severity Index (Safety population)
Section 16.2.7	**Adverse Event Listings**
Listing 16.2.7	All Adverse Events (Enrolled population)
Section 16.2.8	**Individual Measurements by Subject**
Listing 16.2.8.1	Clinical Laboratory Data (Enrolled population)
Listing 16.2.8.2.1	Pregnancy Test and FSH Results (Enrolled population)
Listing 16.2.8.2.2	Child Bearing Potential (Enrolled population)
Listing 16.2.8.3	International Normalized Ratio Data (Enrolled population)
Listing 16.2.8.4	Vital Signs (Enrolled population) Note: Include weight
Listing 16.2.8.5	Electrocardiogram Results (Enrolled population)
Listing 16.2.8.6	Physical Examination Findings (Enrolled population)
Listing 16.2.8.7	Anti-drug Antibody Results (Safety population)
Listing 16.2.8.8	Asthma Control Test (Enrolled population)
Listing 16.2.8.9	Respiratory Assessment (Enrolled population)
Listing 16.2.8.10	Peak Expiratory Flow Rate (Enrolled population)
Listing 16.2.8.11	Asthma Triggers (Enrolled Population)
Listing 16.2.8.12	QuantiFERON-TB Gold Test Results (Enrolled Population)
Listing 16.2.8.13	Cytochrome P450 Genotyping (Enrolled Population)
Listing 16.2.8.14	Alcohol Urine Test and Urine Drug Screen Results (Enrolled population)
Listing 16.2.8.15	COVID-19 Impact Listing (Enrolled population)

Listing 16.2.8.16 Comments (Enrolled population)

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9. REFERENCES

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