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Statistical Analysis Plan

Sponsor Name: Galderma S.A./Galderma R&D, LLC

Protocol Number: RD.06.SPR.118380
Protocol Title: A Randomized, Double-Blind, Placebo-Controlled Study to Assess Immunization Responses in Adult and Adolescent Subjects with Moderate-to-Severe Atopic Dermatitis Treated with Nemolizumab

Protocol Version and Date: 4.0 (06-Jul-2022)

PPD

Authors: PPD

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Revision History

Version #	Date (DD-Mmm-YYYY)	Document Owner	Revision Summary
V1.0	PPD		Finalized first version
V2.0	PPD		Finalized second version and included the following changes: - Updated visit windows for dairy data (See Section 6.4) - Updated derivation of CCI [redacted] at baseline and post-baseline visits. - Updated approach used for analysis of the secondary efficacy endpoints (See Section 9.2) - Added imputation of the worst-case value for efficacy data for subjects who received rescue medication
V3.0	PPD		Finalized third version and included the following changes: - Updated efficacy visit windows (See Section 6.4) - Updated Last-post baseline results derivation for the laboratory evaluations, vital signs, weight and height to include unscheduled visits in the derivation (See Section 10.4, 10.5)
V4.0	PPD		Finalized fourth version and included the following changes: - MI under missing not at random with control-based pattern mixture approaches replaced by MI under missing at random. - The "Background therapy" subgroup analyses were added for CCI [redacted] using MI.
V5.0	PPD		Finalized fifth version and included the following changes: - Additional continuous vaccine endpoints (See Sections 4.2.1 and 8.2) - Details about imputation of concentration/titers below LLOQ and above ULOQ for vaccine data were provided - Subgroup analysis based on weight: threshold changed from 110kg to 90kg

I confirm that I have reviewed this document and agree with the content.

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1. Glossary of Abbreviations

Abbreviation	Description
ACT	Asthma Control Test
AD	Atopic Dermatitis
CCI	CCI [redacted]
AE	Adverse Event
AESI	Adverse Event of Special Interest
ANCOVA	Analysis of Covariance
CCI [redacted]	[redacted]
ATC	Anatomical Therapeutic Chemical
CCI	[redacted]
BMI	Body Mass Index
CI	Confidence Interval
CMH	Cochran-Mantel-Haenszel
COVID-19	Coronavirus Disease-19
CRF	Case Report Form
CRO	Clinical Research Organization
CV	Coefficient of Variation
DCS	Dual-chamber, single-use Syringe
CCI	[redacted]
ECG	Electrocardiogram
ELISA	Enzyme-linked Immunosorbent Screening Assay
GMC	Geometric mean concentrations
GMT	Geometric mean of titers
IAC	Independent Adjudication Committee
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IDMC	Independent Data Monitoring Committee
CCI	[redacted]
IgG	Immunoglobulin G

Abbreviation	Description
IMP	Investigational Medicine Product
IRR	Injection-related Reaction
IRT	Interactive Response Technology
ITT	Intent-to-treat
LLOQ	Lower Limit of Quantification
LTE	Long-term Extension
MAR	Missing at Random
Max	Maximum
MedDRA	Medical Dictionary for Regulatory Activities
MenC	Meningococcal Serogroup C
MI	Multiple Imputation
Min	Minimum
mITT	modified Intent-to-treat
MMRM	Mixed-effect Model for Repeated Measures
MNAR	Missing Not at Random
N/A	Not Applicable
NA	Not Applicable
NCA	Non-compartmental Analysis
OC	Observed Case
PE	Physical Examination
PEF	Peak Expiratory Flow
PK	Pharmacokinetics
PKAP	Pharmacokinetic Analysis Population
CCI	[redacted]
PT	Preferred Term
Q4W	Every 4 Weeks
QC	Quality Control
SAE	Serious Adverse Event
SAF	Safety Population
SAP	Statistical Analysis Plan
SBA	Serum Bactericidal Assay

Abbreviation	Description
SD	Standard Deviation
CCI [redacted]	[redacted]
SE	Standard Error
SOC	System Organ Class
SOP	Standard Operating Procedure
TB	Tuberculosis
TCI	Topical Calcineurin Inhibitor
TCS	Topical Corticosteroid
TEAE	Treatment Emergent Adverse Event
TFL	Table, Figure and Figure
ULOQ	Upper Limit of Quantification
WHO DD	World Health Organization's Drug Dictionary
WOCBP	Women of Childbearing Potential

2. Purpose

The purpose of this statistical analysis plan (SAP) is to ensure that the data listings, summary tables and figures which will be produced, and the statistical methodologies that will be used, are complete and appropriate to allow valid conclusions regarding the study objectives.

2.1. Responsibilities

PPD will perform the statistical analyses and are responsible for the production and quality control of all tables, figures and listings. Descriptive summary will be provided for pharmacokinetics parameters. The derivation of Pharmacokinetics parameters and the statistical modelling will be specified in a separate Modeling Analysis Plan and PK Analysis Plan, respectively.

3. Study Objectives

3.1. Primary Objective

The primary objective is to assess the effect of nemolizumab (CD14152) on humoral immune responses to tetanus and meningococcal vaccination in adult and adolescent subjects with moderate-to-severe atopic dermatitis (AD).

The main estimand for primary objective is listed as below:

Primary Endpoint	The proportion of subjects with a positive serum IgG response to tetanus toxoid at Week 16 (4 weeks post-vaccination) defined as: ≥ 4-fold increase in anti-tetanus IgG concentrations from baseline in subjects with pre-vaccination anti-tetanus IgG concentrations ≥ 0.1 IU/mL OR ≥ 0.2 IU/mL anti-tetanus IgG concentrations in subjects with pre-vaccination anti-tetanus IgG concentrations < 0.1 IU/mL
Population	Of all defined by the study inclusion / exclusion criteria, the analysis population will include all randomized subjects who received at least one dose of study drug and vaccine injection, have an evaluable vaccine response and did not receive any systemic rescue therapy prior to the post-vaccination vaccine response assessment (mITT population).
Population-level Summary	Primary endpoint will be analyzed by the Cochran-Mantel-Haenszel (CMH) estimate of the risk difference and corresponding 2-sided 90% CI, adjusted for the randomization stratum baseline CCI [redacted] using weighted average of stratum-specific proportion.
Intercurrent Event	None

3.2. Secondary Objective(s)

The secondary objectives are to assess the safety and efficacy of nemolizumab (CD14152) after a 16-week treatment period in adult and adolescent subjects with moderate-to-severe AD.

3.3. Brief Description

This is a randomized, double-blind, placebo-controlled, multi-center, parallel-group study in adult and adolescent subjects (≥ 12 to 54 years) with moderate-to-severe AD. Eligible subjects must have a documented history of inadequate response to topical AD medication(s).

Approximately 245 subjects will be randomized 1:1 to receive either 30 mg nemolizumab (with a 60 mg loading dose) or placebo, stratified by baseline disease severity CCI [redacted]

The study consists of a 2- to 4-week screening period, a 16-week treatment period, and an 8-week follow-up period (12 weeks after the last study drug injection).

The screening period will evaluate subject eligibility. Subjects will apply a moisturizer at least once daily, beginning at screening. Subjects using a stable regimen of low- or medium-potency topical corticosteroid (TCS) with or without topical calcineurin inhibitor (TCI) at the screening visit (ie, ≥ 14 days prior to the baseline visit) should continue their therapy regimen. 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.

At the baseline visit, subjects will receive a loading dose of nemolizumab (60 mg) or placebo via 2 subcutaneous injections. Nemolizumab (30 mg) or placebo will then be administered via a single subcutaneous injection every 4 weeks (Q4W) at Week 4, 8, and 12. At the Week 12 visit, subjects will also receive single doses of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (PPD and quadrivalent meningococcal conjugate PPD vaccines. Clinical assessments will occur according to the schedule of assessments. Refer to Figure 1 for an overview of the study design.

Subjects will continue to apply a moisturizer at least once daily throughout the study. Subjects using background topical therapy (TCS with or without TCI) from the screening visit will continue use in the treatment period, which should be adjusted according to the disease activity and tolerability, based on investigator clinical judgment. (Subjects not using background topical therapy from the screening visit should not apply background topical therapy in the study.) If deemed to be medically necessary by the investigator (eg, to control intolerable AD signs/symptoms), topical and/or phototherapy rescue therapies can be prescribed to any subject at any time during the study, except during the screening period.

Subjects who complete the Week 16 treatment period may be eligible to enroll into a long-term extension (LTE) study (Protocol 118163). 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 24 (12 weeks after their last study drug injection).

Subjects who discontinue the study prematurely should complete an early termination visit and a follow-up visit 12 weeks after their 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 adverse events (AEs).

An overview of the study design is present in the Figure 1.

Figure 1. Study Design

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3.4. Subject Selection

Subjects will be selected based on the inclusion and exclusion criteria in Protocol Sections 8.1 and 8.2.

3.5. Determination of Sample Size

Approximately 245 subjects will be randomized (123 per arm) to show that the 90% confidence interval of the proportion difference between treatment groups will exclude a difference of more than 10%.

3.6. Treatment Assignment & Blinding

At the baseline visit, a unique randomization number will be assigned to an eligible subject via interactive response technology (IRT). Subjects will be randomized in a 1:1 ratio to receive either nemolizumab or placebo. The randomization scheme will be stratified by baseline disease severity CCI [redacted] to ensure appropriate distribution of assignment to the 2 treatment groups.

All attempts will be made to keep the study center staff and subjects blinded throughout the study. Members of the study center staff, including those responsible for dual-chamber, single-use syringe [DCS] preparation, will not have access to the randomized treatment assignment.

To ensure double-blind administration of study drug, the study center pharmacist(s) or other qualified personnel will prepare all nemolizumab or placebo treatments, according to the current version of the pharmacy manual, the instructions for use, and assigned DCS provided by the IRT system.

As there may be detectable differences between nemolizumab and placebo during the reconstitution

process, the DCS is delivered for injection after the reconstitution is complete. The pharmacist (or other qualified personnel) preparing study medication should not be involved with any study assessments and should not discuss any aspects of study drug reconstitution with the subject/caregiver or study staff involved in subject interviews or study assessments.

To maintain the integrity of the study blinding, the bioanalytical laboratory staff who process/analyze the CCI and the central laboratory staff who will analyze sample for vaccines response (immunogenicity) will not provide any information to sponsor, clinical research organization (CRO), or investigational study center personnel directly involved with the ongoing conduct of the study that may lead to unblinding during the ongoing study.

Unblinding of a subject's individual treatment code should occur only in case of a medical emergency or in the event of a serious medical condition that necessitates identification of the study drug for the welfare of that subject, as judged by the investigator. The emergency unblinding process utilizes IRT to allow the investigator to have unrestricted, immediate, and direct access to the subject's individual study treatment. When possible (ie, when the health of the subject is not immediately at risk), the investigator or sub-investigator is encouraged to consult with the medical monitor and the sponsor before breaking the blind.

When the blinding code is broken, the reason must be fully documented. If the code is broken by the investigator, the subject must be withdrawn from the study and must also be appropriately followed for a minimum of 12 weeks after the last dose of study drug.

The reporting requirements for unblinding are the same for reporting a serious adverse event (SAE).

The randomization code will remain blinded to all study sites and study team members until completion of the study and after the study database has been locked. Although initial treatment period results will be analyzed after all subjects have either completed the Week 16 visit, or have withdrawn or been discontinued from the study before Week 16, personnel from sponsor, CRO, and investigational sites directly involved with the ongoing conduct of the study will not have access to any information that may lead to unblinding for the ongoing maintenance evaluation.

The IDMC will review data at periodic intervals throughout the study as defined in the IDMC charter. The IDMC charter will specify the procedures for unblinding to ensure that treatment assignment remains undisclosed to all individuals involved in the direct execution and management of the study until the final database is locked.

3.7. Administration of Study Medication

At the baseline visit, subjects will receive a loading dose of nemolizumab (60 mg) or placebo via 2 subcutaneous injections. Nemolizumab (30 mg) or placebo will then be administered via a single subcutaneous injection every 4 weeks (Q4W) at Week 4, 8, and 12. At the Week 12 visit, Tdap and MCV4 vaccines will be administered separately each as a 0.5 mL intramuscular injection.

3.8. Study Procedures and Flowchart

Provision of a written, signed informed consent form (ICF) is required before any study-related procedures are performed.

The planned study assessments are in **Table 1**. At each visit, assessments/procedures should be performed in the following order:

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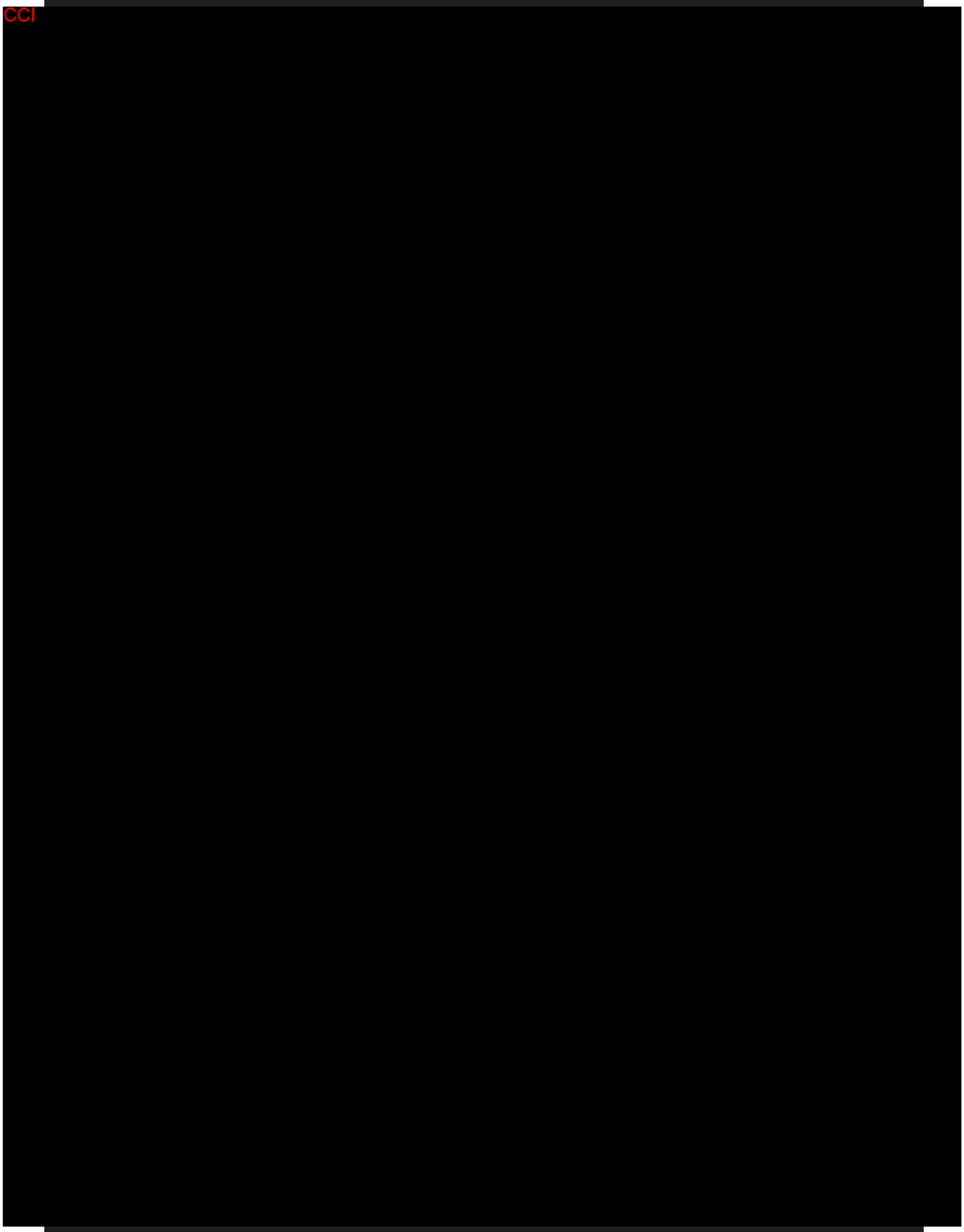
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4. Endpoints

4.1. Primary Vaccine Response Endpoint

The primary endpoint of this study is the proportion of subjects with a positive serum immunoglobulin G (IgG) response to tetanus toxoid at Week 16 (4 weeks post-vaccination) defined as:

- ≥ 4-fold increase in anti-tetanus IgG concentrations from baseline in subjects with pre-vaccination anti-tetanus IgG concentrations ≥ 0.1 IU/mL, OR
- ≥ 0.2 IU/mL anti-tetanus IgG concentrations in subjects with pre-vaccination anti-tetanus IgG concentrations < 0.1 IU/mL

4.2. Secondary Endpoints

4.2.1. Secondary Vaccine Response Endpoints

The secondary vaccine response endpoints are as follows:

- Proportion of subjects with a positive serum IgG response to tetanus toxoid at Week 16 defined as:
  - ≥ 2-fold increase in anti-tetanus IgG concentrations from baseline in subjects with pre-vaccination anti-tetanus IgG concentrations ≥ 0.1 IU/mL, OR
  - ≥ 0.2 IU/mL anti-tetanus IgG concentrations in subjects with pre-vaccination anti-tetanus IgG concentrations < 0.1 IU/mL
- Proportion of subjects with serum anti-tetanus IgG concentrations of ≥ 0.1 IU/mL at Week 16
- Proportion of subjects with serum anti-tetanus IgG concentrations of ≥ 1.0 IU/mL at Week 16
- Proportion of subjects with a positive serum bactericidal antibody response to meningococcal serogroup C polysaccharide at Week 16 (4 weeks post-vaccination) defined as ≥ 4-fold increase in serum bactericidal assay (SBA) reciprocal titer from baseline
- Proportion of subjects with a positive serum bactericidal antibody response to meningococcal serogroup C polysaccharide at Week 16 defined as SBA reciprocal titer ≥ 8

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[redacted]

4.2.3. Safety Endpoints

The safety endpoint of this study is as follows:

- Incidence and severity of AEs, including AEs of special interest (AESI) [defined in protocol Section 13.1.1], treatment-emergent AE (TEAE), and SAE.
- Clinical laboratory tests
- Physical examination and vital signs
- Respiratory examination and assessments (ie, asthma control test [ACT], peak expiratory flow [PEF])
- 12-lead electrocardiogram (ECG)

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[redacted]

5. Analysis Population

5.1. Screened Population

The Screened population comprises all subjects who signed the informed consent. This population includes screen failures, and randomized subjects. For clarity, screen failed subjects are defined as those subjects who fail to meet inclusion criteria or meet exclusion criteria and discontinued the study prior to randomization. Subjects that are re-screened will only be counted once, under the subject ID assigned for the repeat screening.

5.2. Safety Population (SAF)

The SAF will consist of all randomized subjects who received at least one administration of study drug. The treatment group assignment in this population will be defined by the treatment actually received. This population will be used for all the analyses of safety endpoints.

5.3. Intent-to-Treat Population (ITT)

The ITT population will consist of all randomized subjects. The ITT population will be the primary population for efficacy analyses. All analyses under the ITT population will be analyzed under the treatment group as randomized.

5.4. Modified Intent-to-Treat Population (mITT)

The mITT population will consist of all randomized subjects who received at least one dose of study drug and vaccine injection, have an evaluable vaccine response and did not receive any systemic rescue therapy prior to the post-vaccination vaccine response assessment.

An evaluable vaccine response is defined as measured responses to the tetanus toxoid vaccine, i.e. an evaluable serum IgG response to tetanus toxoid as per the protocol section 16.4.1. The mITT will be the primary population for vaccine response. All analyses under the mITT will be analyzed under the treatment group actually received.

5.5. Pharmacokinetic Analysis Population (PKAP)

The PK analysis population (PKAP) will consist of all subjects included in the SAF, with at least one measurable post-baseline PK concentration assessment. Similar to SAF, the treatment group assignment in this population will be defined by the treatment actually received. This population will be used for the analyses of PK.

6. General Aspects for Statistical Analysis

6.1. General Methods

The statistical evaluation will be performed using SAS® software version 9.4 or higher (SAS Institute, Cary, NC). All data will be listed, and summary tables will be provided. Summary statistics will be presented by treatment group. Summaries will be presented for each treatment and overall for Demographic, Other Baseline Characteristics and Medication. For all other analyses, summaries will be presented for each treatment.

Continuous variables will be summarized using the number of observations (n), mean, standard deviation (SD), median, minimum, and maximum by treatment group. Categorical variables will be summarized using number of observations (n), frequency and percentages of subjects for each category by treatment group.

All statistical tests on the vaccine response endpoints will be conducted at the 2-sided 10% level and the 90% CI will be estimated. For all other endpoints, the statistical tests will be conducted at the 2-sided 5% level and the 95% CI will be estimated.

6.2. Key Definitions

6.2.1. Baseline

Unless otherwise stated, the baseline value for any variable will be the last non-missing value taken prior to the receipt of study treatment at the Baseline visit (Day 1). The receipt of study treatment is defined as the 1st injection of study drug if it exists. Otherwise, baseline is defined as the last value taken prior to the randomization.

For diary data (CCI [redacted]), the baseline values will be derived from data collected during the 7 days prior to the first administration of study drug, if it exists. Otherwise, the data collected during 7 days prior to randomization will be used. Baseline score will be the weekly prorated average of non-missing subject diary scores reported during the 7 days. A minimum of 4 daily scores out of the 7 days is required to calculate the weekly prorated average score.

6.2.2. Study Day

Study Day is the number of days since the first dose date. If the assessment date is after the randomization, the study day is calculated as (date of assessment - first dose date + 1). If the assessment date is prior to the first dose date, the study day is calculated as (date of assessment - first dose date).

6.2.3. Study period

First treatment date is defined as the date of 1st study drug (Nemolizumab or Placebo) injection.

Last treatment date is defined as the date of last study drug (Nemolizumab or Placebo) injection.

Treatment period is defined as follow:

- Subject completed the treatment: first dose date up to Week 16
- Subject who discontinued the treatment: first dose date up to earliest among:

- 4 weeks after the last study drug administration
- the early study termination date if available

Screening period is defined the period before the treatment period.

Follow-up period is defined the period after the treatment period.

6.3. Missing Data

Adverse events and concomitant medications with missing assessment times will have imputed times for the purposes of assessing treatment emergence for AEs or classifying medications into prior/concomitant. However, the assessment times (start date, stop date) without imputation will be presented in the listings.

For the start of a concomitant medication or AE:

- Only the year is reported: If the subject received the first study drug dose in the year reported, then the date of the first dose of study drug will be used as the start date; otherwise, January 1 of the year reported will be used as the start date.
- The month and year are reported: If the subject received the first study drug in the month and year reported, then the date of the first dose of study drug will be used as the start date; otherwise, the first day of the month and year will be used as the start date.
- The time is missing: If the start date is the same as the date the subject started receiving study drug, then the time of the first dose of study drug will be used as the start time; otherwise, 00:00 will be used as the start time.

For the end of a concomitant medication or AE:

- Only the year is reported: The earlier between December 31 of the year reported and the date of the last study contact with the subject will be used as the stop date.
- The month and year are reported: The earlier between the last date of the month and year reported and the date of the final contact with the subject will be used as the stop date.

If an AE has the start date completely missing and the stop date on/after the first dose date of study drug, this AE will be considered as treatment emergent.

If a medication has the stop date completely missing and ongoing tick box in CRF is checked, this medication will be considered as concomitant.

Imputations or calculations for specific efficacy endpoints will be included in the section that describes the analysis of that endpoint.

6.4. Visit Windows

Efficacy by-visit summaries will use the analysis visit. Unscheduled and early termination visits will be windowed based on the following analysis visit window which is based on study day. If multiple measurements are taken within the same window, the one taken closest to the target study day will be

used for the analysis. If there are multiple measurements with same difference from target day, the later assessment should be used for the analysis.

Analysis Visit	Target Study Day (relative to first treatment date)	Analysis Visit Window
Baseline	1	<=1
Week 4	29	2 to 42
Week 8	57	43 to 71
Week 12	85	72 to 99
Week 16	113	100 to 141
Week 24 Follow-up	169	> 141

Safety and pharmacokinetics data will not be windowed for by-visit summary. i.e., scheduled visit (including Early Termination visit) data will be used for analysis. For clinical laboratory assessments, if repeated measurements are taken for either time point (scheduled visit), then the last measurement will be used for the value for that time point.

Daily diary efficacy data (CCI [redacted]) will be classified into analysis visits as follows.

Analysis Visit	Target Study Day of Analysis Visit (relative to first treatment date)
Baseline	1
Week 1	8
Week 2	15
Week 3	22
Week 4	29
Week 5	36
Week 6	43
Week 7	50
Week 8	57
Week 9	64
Week 10	71
Week 11	78
Week 12	85
Week 13	92
Week 14	99
Week 15	106
Week 16*	113

CCI [redacted]

*CCI [redacted]

These analysis visits will be used in the calculations for all week-based parameters collected on subject's diary data. Other non-diary data, such as, CCI vital signs, body weight, clinical laboratory assessments, respiratory assessment/PEF, will be analyzed according to actual scheduled visits.

Unscheduled labs will be included in listings and considered in the derivation of last, worst post-baseline values, but not summaries of the data by visit.

6.5. Pooling of Centers

No center pooling is planned.

6.6. Subgroups

Subgroup analysis will be performed in an exploratory manner to investigate the treatment effect across various subgroup. The following subgroup analyses will be performed for the primary and secondary vaccine response endpoints:

- By age (<18 years; >=18 years)
- By sex (Male, Female)
- By race (White, Black or African American, Asian, Other)
- CCI
- [redacted]
- Baseline Weight (≤Q1, <Q1 - median, <median - Q3, > Q3)
- Baseline Weight (≤90 kg, > 90 kg)
- Coronavirus disease-19 (COVID-19) Infection (Subjects infected by COVID-19, Subjects not infected)
- Background therapy (subjects with background therapy, subject without background therapy)

In addition, analyses will be performed on the last subgroup (background therapy) for selected secondary efficacy endpoints.

7. Demographic, Other Baseline Characteristics and Medication

7.1. Subject Disposition and Withdrawals

The screened subjects, screen failures and reasons for screen failures will be summarized in the disposition table.

In addition, the following frequencies (subject number and percent) will be summarized based on ITT Population by treatment group and overall for:

- Randomized subjects
- Subjects treated with at least one dose of study drug
- Subjects who completed treatment (until Week 16)
- Subject who discontinued the treatment and Primary reason for early treatment discontinuation
    - Subject who discontinued from treatment with COVID-19 related reason [This will be identified using Other specify field in CRF]
- Subjects who completed study
- Subject who discontinued the study and Reason for study discontinuation
    - Subject who discontinued from study with COVID-19 related reason [This will be identified using Other specify field in CRF]
- ITT Population (subject number only)
- mITT Population
- SAF Population
- PKAP

The number and frequency will be summarized by site and by treatment group and overall for:

- Subjects screened,
- Screen failure, percentage calculated based on number of screened
- Subjects randomized, percentage calculated based on number of screened
- Subjects treated, percentage calculated based on ITT

Summary of subjects at each visit will be provided by treatment group and overall on ITT population.

The individual time (days) to Permanent Discontinuation of Study Drug by Reason will be presented graphically by treatment group using ITT population. Time to permanent discontinuation is defined as (date of last study drug administration – date of 1st study drug administration + 1).

By-subject listings of eligibility details, randomization details, and withdrawal/study completion details (including reason for discontinuation and duration of treatment prior to discontinuation) will be provided.

A listing of subjects in different analysis population (ITT, mITT, SAF, PKAP) will also be produced.

7.2. Protocol Deviations

All protocol deviations will be identified, evaluated, and finalized before the respective database lock (final analysis) and will be discussed in the clinical study report. Protocol deviations will be categorized by type, and whether major or minor based on clinical review and will be determined before database lock. Individual deviations (major and minor) will be presented in a data listing. A summary table for number and percentage of subjects with major protocol deviation and with COVID-19 related deviation will be summarized by type of deviation and treatment group.

7.3. Demographic and Other Baseline Characteristics

The following demographic and baseline characteristics will be summarized by treatment group and overall using descriptive statistics for ITT, mITT and safety population:

- Demographics data: Age (years) at screening as continuous and as categorical (12-17 years, >= 18 years), sex, ethnicity, race, height (cm) at screening, body weight (kg) at baseline (overall and by age group), body mass index (overall and by age group).
- Baseline disease characteristics: smoking status, CCI [redacted] CCI [redacted] CCI [redacted] and disease severity based on CCI [redacted]

The stratification factor will also be summarized on ITT and mITT population to show if any discrepancies between what was reported through Interactive Voice Response System (IVRS)/Interactive Web Response System (IWRS) versus baseline value derived using eCRF data.

By-subject listings of demographic data and other baseline characteristics (as summarized above) will be provided.

7.4. Medical History

Medical history will be coded using Medical Dictionary for Regulatory Activities (MedDRA Version 25.0).

Medical history will be summarized by treatment group using the number and percent of subjects reporting each system organ class (SOC) and preferred term (PT) and sorted by descending overall total of SOC and PT. Summary tables will be presented for ITT, mITT, and SAF populations.

Medical history data listings will also be provided.

7.5. Medical and Surgical Procedures

Medical and surgical procedures will be coded using MedDRA Version 25.0.

Prior procedures are defined as procedures which stop before 1st injection of study drug. Concomitant procedures are defined as procedures which start or stop on or after the 1st injection of study drug.

Prior and concomitant medical and surgical procedures will be summarized separately by treatment group using the number and percent of subjects reporting each SOC and PT and sorted by descending overall total of SOC and PT. Summary tables will be presented for ITT population.

Medical and surgical procedures will also be listed.

7.6. Medications/Therapies

Prior medications/therapies are defined as medications/therapies which stop before 1st injection of study drug. Concomitant medications/therapies are defined as medications/therapies which start or stop on or after the 1st injection of study drug.

If start and/or stop dates of medications and therapies are missing or partial, the dates will be compared as far as possible with the date of first dose of study drug. Medications and therapies will be assumed to be Concomitant, unless there is clear evidence (through comparison of partial dates) to suggest that they started and stopped prior to the first dose of study treatment. If there is clear evidence to suggest that the medication or medical and surgical procedure started and stopped prior to the first dose of study drug, they will be assumed to be Prior.

For prior and concomitant medications, incomplete (i.e., partial missing) start dates and/or stop dates will be imputed using the algorithm described in Section 6.3.

Medications will be coded using the World Health Organization's Drug Dictionary (WHO DD) Version Global B3 SEP 2019 using the Preferred Anatomical Therapeutic Chemical (ATC) terms. TCI and TCS will be automatically identified using the following rule:

- TCS will be identified by ATC code "D07A".
- TCI will be identified by ATC code "D11AH" and with standardized medication name "TACROLIMUS" and "PIMECROLIMUS".

Prior and Concomitant medications will be summarized separately by Anatomical Therapeutic Chemical (ATC) level 2, level 4, and preferred name in frequency tables using ITT, mITT and safety population. Subjects with more than one medication in a given ATC level and preferred name will be counted only once in that category. It will be sorted in descending frequency of ATC level and of PT within ATC level term.

The following summaries will be produced:

- Prior medication
- Concomitant medication
- Rescue medication during treatment period (ITT Population only)
- Rescue medication during follow-up period (ITT Population only)

- Background therapy (ITT Population only) consisting of TCS and TCI with start date prior to study drug administration and that are not classified as rescue therapy

All medications will be listed. The background TCS dispensation/receipt will also be listed.

8. Vaccine Response Analysis

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8.1. Primary Vaccine Response Endpoint and Analysis

8.1.1. Primary Analysis of Primary Endpoint

The primary endpoint of this study is the proportion of subjects with a positive serum IgG response to tetanus toxoid at Week 16 (4 weeks post-vaccination), defined as:

- ≥ 4-fold increase in anti-tetanus IgG concentrations from baseline in subjects with pre-vaccination anti-tetanus IgG concentrations ≥ 0.1 IU/mL, OR
- ≥ 0.2 IU/mL anti-tetanus IgG concentrations in subjects with pre-vaccination anti-tetanus IgG concentrations < 0.1 IU/mL

Anti-tetanus IgG concentrations and the ratio from baseline will be summarized by treatment group and by visit using descriptive statistics.

The analysis for primary endpoint will be using the Cochran-Mantel-Haenszel (CMH) estimate of the risk difference and corresponding 2-sided 90% CI. It will be adjusted for the randomization stratum baseline CCI [redacted] using weighted average of stratum-specific proportion using CMH. The example SAS code for CMH model is included in Section 20.1. The primary analysis will be conducted on the mITT population.

Subjects in receipt of systemic rescue medication will not be vaccinated. As the primary analysis will be conducted on the mITT, no imputation is required.

8.1.2. Sensitivity Analysis of Primary Endpoint

Three sensitivity analyses will be performed on ITT population and the same statistical testing as the primary analysis will be performed:

- **Non-responder Imputation**: any subjects without an evaluable vaccine response will be regarded as a Non-Responder. Non-evaluable vaccine response: defined as a response that cannot be classified as positive or negative due to missing assessment for the endpoint.

- **Observed Case**: No data will be imputed. All data as observed will be included in the analysis and the percentage will be calculated based on the number of observation available.

- **COVID-19 Affected Case**: Removal of subjects with COVID-19 (i.e. exclusion of subjects who had COVID-19).

8.1.3. Subgroup Analysis of Primary Endpoint

The subgroup analyses as specified in section 6.6 will be performed for the primary endpoints on mITT population:

The results from the analysis will be presented as forest plot summarizing frequencies in each treatment group, risk difference and the corresponding 2-sided 90% CI on each subgroup.

8.2. Secondary Vaccine Response Endpoints and Analyses

The following secondary vaccine response endpoints are to be analysed:

- Proportion of subjects with a positive serum IgG response to tetanus toxoid at Week 16 (≥ 2-fold increase in anti-tetanus IgG concentration from baseline in subjects with pre-vaccination anti-tetanus IgG concentration ≥ 0.1 IU/mL OR ≥ 0.2 IU/mL anti-tetanus IgG concentrations in subjects with pre-vaccination anti-tetanus IgG concentrations < 0.1 IU/mL)

- Proportion of subjects with serum anti-tetanus IgG concentrations of ≥ 0.1 IU/mL at Week 16

- Proportion of subjects with serum anti-tetanus IgG concentrations of ≥ 1.0 IU/mL at Week 16

- Proportion of subjects with a positive serum bactericidal antibody response to meningococcal serogroup C polysaccharide at Week 16 (4 weeks post-vaccination) defined as ≥ 4-fold increase in SBA reciprocal titer from baseline

- Proportion of subjects with a positive serum bactericidal antibody response to meningococcal serogroup C polysaccharide at Week 16 defined as SBA reciprocal titer ≥ 8

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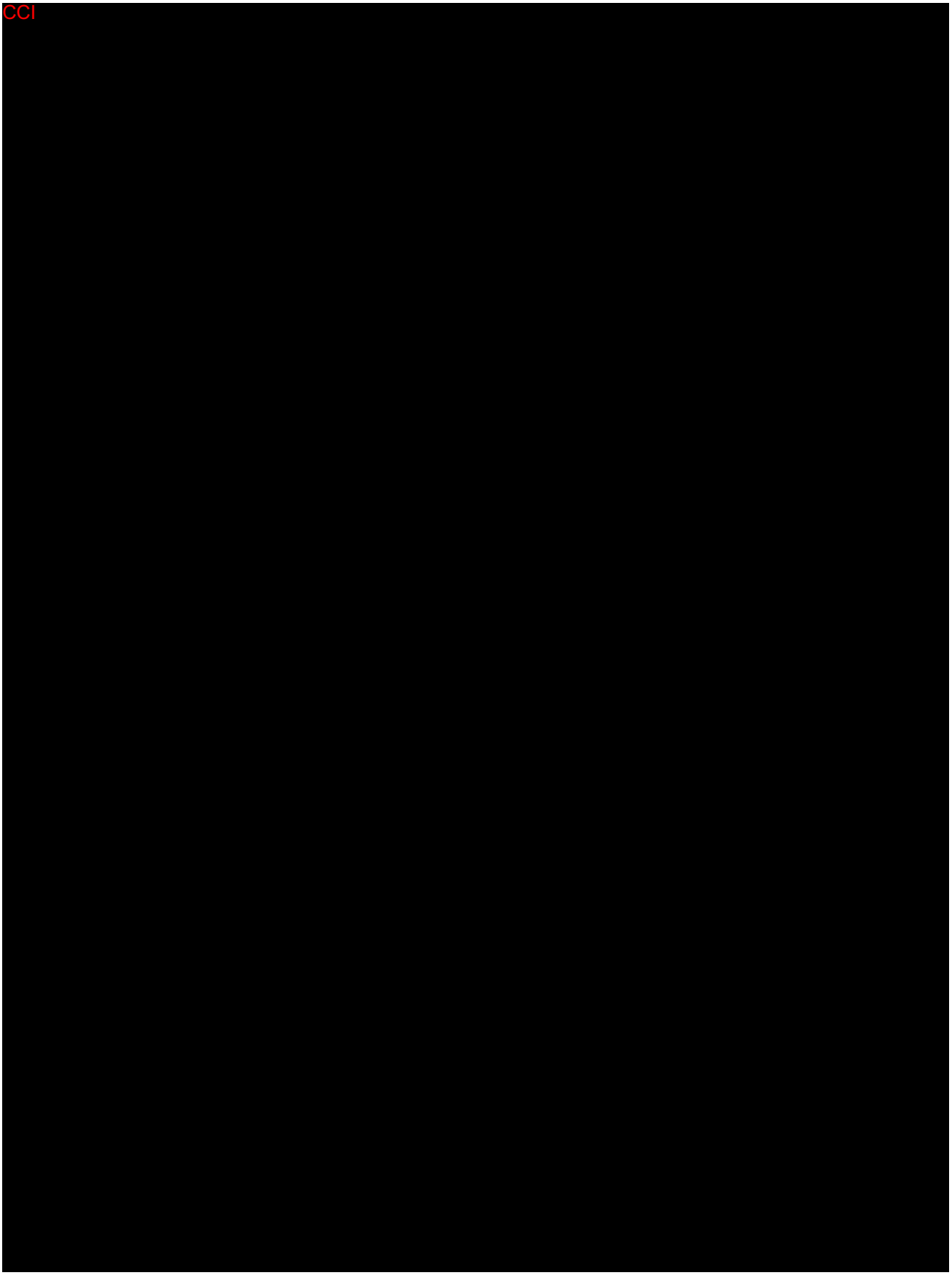

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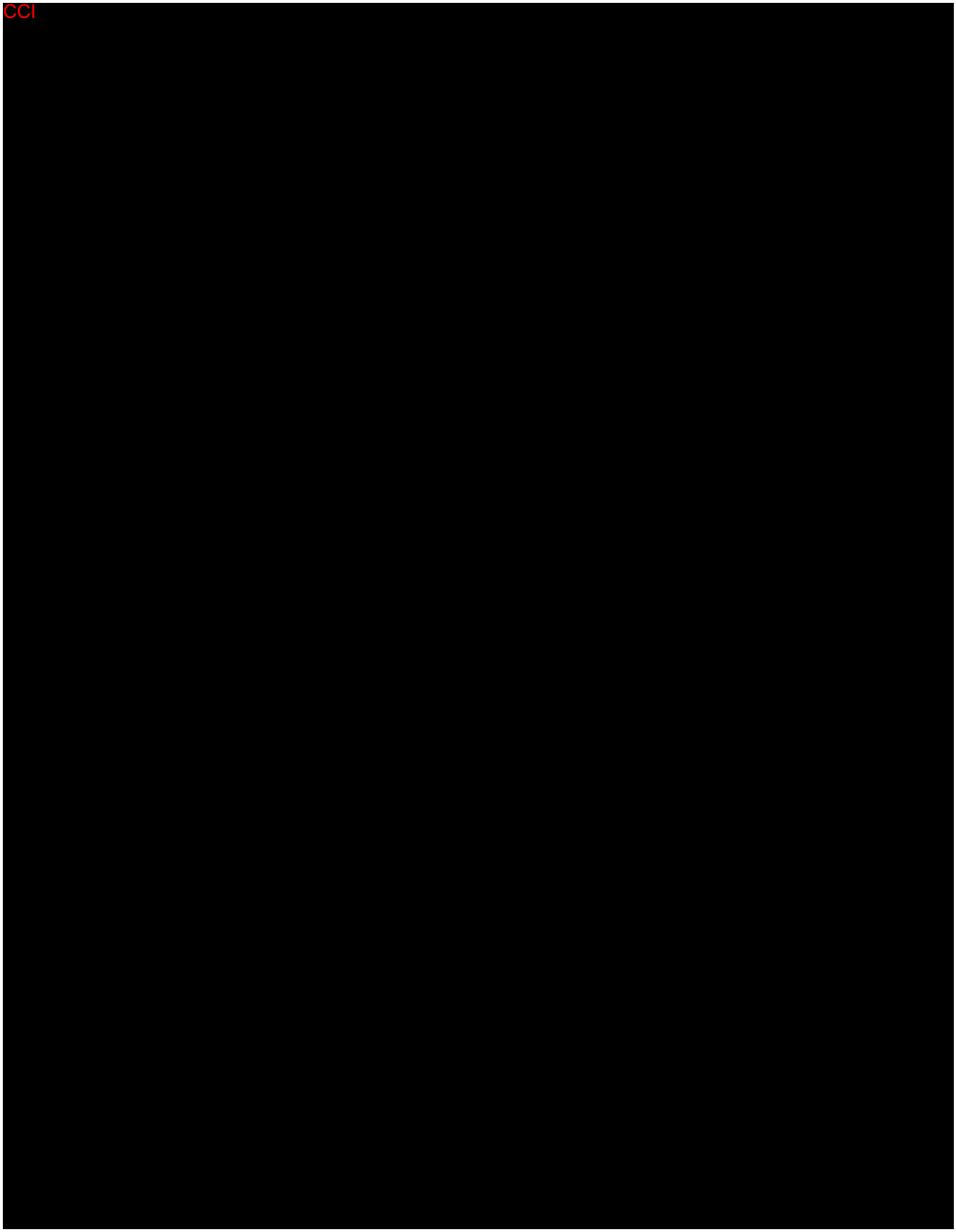

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10. Safety Analysis

The population used for safety analyses will be the SAF.

10.1. Extent of Exposure

The extent of exposure will be summarized by treatment group as follows:

- Treatment duration (in days): calculated as [(date of last treatment - date of first treatment) + 1],
- the number of subjects exposed to study drug at visit Baseline, Week 4, Week 8 and Week 12,
- Cumulative dose received (mg): calculated as sum of all dose of study drug administered
- The number of subjects who received vaccines (Tdap and MCV4 and overall) at Week 12.
- The number of subjects missed at least one dose and the number of doses missed due to COVID-19, i.e. the reason for dose not administered reported in eCRF is related to COVID-19
- The subject with Vaccine injection missed due to COVID-19, i.e. the reason for dose not administered reported in eCRF is related to COVID-19

Extent of exposure information, study drug administration and vaccine administration will be listed, separately.

10.2. Treatment Compliance

Dose modification of the study drug (nemolizumab 30 mg or Placebo) will not be permitted during the clinical study.

Treatment compliance of study drug will be calculated as the ratio (expressed as percentage) between the total number of actual injections and the total number of expected injections.

The total number of actual injections will be counted based on collected study drug administration data. The total number of expected injections will be counted based on the following dosage schedule.

Table 2: Treatment Period Dosing By Treatment Group

Treatment Group	Dose/route	Week(s)	Schedule
Nemolizumab (CD14152)	30 mg × 2 SC injections	Baseline	Baseline
	30 mg × 1 SC injections	4, 8, 12	Q4W
Placebo	Placebo× 2 SC injections	Baseline	Baseline
	Placebo× 1 SC injections	4, 8, 12	Q4W

Abbreviation(s): Q4W=every 4 weeks; SC=subcutaneous.

The compliance data will be listed and summarized by treatment group.

10.3. Adverse Events / Adverse Drug Reactions

Adverse events (AEs) will be coded using MedDRA Version 25.0.

Treatment-emergent AEs (TEAEs) is defined as AEs with an onset date on or after the first dose date of study treatment. Partially missing date will be handled using the algorithm described in Section 6.3. AE

related to study drug is defined as AE with a relationship to study drug reported as 'Reasonable Possibility' or missing.

Summary table for adverse events will include the number and percent of subjects and the numbers of events by treatment group and by System Organ Class (SOC) and Preferred Term (PT). SOC and PT within each SOC will be sorted by descending overall frequency. Subjects who have multiple events in the same SOC and the same PT within each SOC will be counted only once in the subject counts, but all events will be considered and presented (if applicable). For summary by maximum severity, subjects who experience multiple occurrences of an AE, the most severe category for each SOC and for each PT within each SOC will be considered in the summary.

The summary tables for following TEAEs will be presented:

- Overall Summary: summary of the number and percentage of subjects reporting TEAEs, TEAEs by maximum severity, serious TEAEs, study drug-related TEAEs, drug-related serious TEAE, study drug-related TEAEs by maximum severity, treatment-emergent AESI, Confirmed or suspected COVID-19 infection, TEAEs leading to study drug withdrawal, TEAEs leading to study drug interruption, TEAEs leading to study discontinuation, and TEAEs leading to death
- The total number and incidence of TEAEs by SOC and PT
- The total number and incidence of Serious TEAEs by SOC and PT
- The total number and incidence of TEAEs related to study drug by SOC and PT
- The total number and incidence of serious TEAEs related to study drug by SOC and PT
- The total number and incidence of TEAEs by SOC, PT, and maximum severity
- The total number and incidence of drug-related TEAEs by SOC, PT, and maximum severity
- The total number and incidence of TEAEs leading to temporary interruption of study drug by SOC and PT
- The total number and incidence of TEAEs leading to permanent discontinuation of study drug by SOC and PT
- The total number and incidence of TEAEs leading to study discontinuation by SOC and PT
- The total number and incidence of TEAEs of special interest by SOC and PT
- Most common TEAEs (frequency > 5%) by PT. All TEAEs with a frequency >5% in any treatment group will be presented.

Subject listings will be presented for all AEs, all SAEs, AEs leading to study drug withdrawal, AEs of special interest (AESIs). All AEs will be listed by subject, along with information regarding onset, duration, relationship and severity to study drug, action taken with study drug, treatment of event, and outcome.

10.4. Laboratory Evaluations

Clinical laboratory tests are performed at Screening, Baseline, Week 8, Week 16, Follow-up Visit, and Early Termination Visit. All laboratory values will be reported in SI units.

For statistical and graphical summaries of the laboratory tests, values below or above the limit of detection (e.g. '< 3' or '>500') are substituted with the lower limit of detection minus 1% for values below the lower limit and are substituted with the upper limit of detection plus 1% for values above the upper limit (e.g. '< 3' is substituted by '2.97', '> 500' is substituted by '505'). In data listings, the values are shown including the < or > sign.

Results from the central laboratory (hematology, blood chemistry and urinalysis) will be summarized by treatment group and visit using descriptive statistics, including observed values and change from baseline values (for numeric laboratory parameters), distribution of categories (for categorical laboratory parameters). By visit summaries will be performed at all visits (scheduled and ET visits) and for the last post-baseline results during treatment period. Last-post baseline results will include unscheduled visits in the derivation.

In addition, the number and percentage of subjects who met criteria of Potentially Clinically Significant Values (PCSV) will be summarized by treatment group and by visit. Criteria for PCSV are included in Section 20.2.

Shift tables from baseline will be generated by treatment group using the reference ranges at each visit, last post-baseline during treatment period, the worst post-baseline. Hematology, chemistry and applicable urinalysis results will be classified as low (L), normal (N), and high (H) by the laboratory parameter's normal range. Worst post-baseline value is defined the value farthest from the reference range (lower and higher limit). If all post-baseline values are "Normal", the subject is classified as Normal. If any post-baseline value is "Abnormal" ("High" or "Low"), select the farthest one from Lower or Higher limit of reference range.

Distribution of Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP), Total bilirubin and Creatinine Phosphokinase (CPK) will be displayed graphically as boxplot by treatment group for each scheduled visit and the maximum post-baseline values.

Listings for laboratory test satisfying PCSV criteria and all laboratory tests (hematology, blood chemistry, urinalysis, pregnancy test, virology, tuberculosis test) will be provided.

10.5. Vital Signs, Weight and Height

Weight, Height and Vital signs including systolic blood pressure, diastolic blood pressure, pulse rate and temperature will be summarized using descriptive statistics by treatment group and visit, including observed values and change from baseline values. By visit summaries will be performed at all visits (scheduled and ET visits) and for the last post-baseline results during treatment period. Last-post baseline results will include unscheduled visits in the derivation.

In addition, the number and percentage of subjects who met criteria of Potentially Clinically Significant Values (PCSV) will be summarized by treatment group and by visit. Criteria for PCSV are included in Section 20.2.

Shift tables from baseline will be generated by treatment group using the reference ranges at each visit, last post-baseline during treatment period, the worst post-baseline. Weight, Height and Vital signs results will be classified as normal, abnormal CS (clinically significant), and abnormal NCS (not clinically significant). Worst post-baseline value is defined the value farthest from the reference range (lower and higher limit). If all post-baseline values are "Normal", the subject is classified as Normal. If any post-baseline value is "Abnormal" ("High" or "Low"), select the farthest one from Lower or Higher limit of reference range.

Vital signs data and data satisfying PCSV criteria will also be listed.

10.6. ECG

A standard 12-lead ECG will be performed at Screening, Week 16, and Early Termination Visit. ECGs will be performed in the supine position. Subjects will be monitored for potentially clinically significant ECG results. Tests with abnormal results that are deemed clinically significant will be repeated to ensure reproducibility of the abnormality.

The overall ECG interpretations will be collected as "Normal", "Abnormal, not clinically significant" and "Abnormal, clinically significant". Summary of overall interpretation will be tabulated by treatment group and visit.

Listings for all ECG data will be provided.

10.7. Physical Examination

Complete physical examination (PE) will be performed at the Screening, Week 8, Week 16, and Early Termination Visit. A complete physical examination will include assessments of the head, ears, eyes, nose, throat, neck (including thyroid), skin/integumentary system, cardiovascular system, respiratory system (for additional respiratory assessments), gastrointestinal system, musculoskeletal system, lymph nodes, and nervous system.

The PE results will be categorized as "Normal", "Abnormal, not clinically significant" and "Abnormal, clinically significant". Summary table of PE results will be provided by treatment group, visit and body system. Listing will also be provided.

10.8. Respiratory Assessments

All data will be listed. A separate listing will be provided for subject with a drop by >= 15% from Baseline for either PEF or ACT.

10.8.1. Asthma Control Test (ACT)

Subjects with a medical history of asthma will take the ACT at all visits according to Table 1. Subjects with a new (de novo) diagnosis of asthma will take the ACT beginning at the visit the diagnosis was first confirmed and at all subsequent study visits thereafter. Subjects with an ACT score ≤ 19 will be referred to the physician managing their asthma.

The ACT is an assessment to determine if a subject's asthma symptoms are well controlled. The ACT is designed for adults and adolescents 12 years or older and is composed of 5 questions. For each question, the subject will choose the best answer out of 5 possible answers. The test provides a

numerical score ranging from 5 to 25 to assess asthma control; a higher score indicates better asthma control while a score of 19 or less indicates the subject's asthma may not be under control.

Results from ACT test will be summarized by treatment group and visit using descriptive statistics, including observed values and change from baseline values.

Number and frequency of subjects with ACT score ≤ 19 will be summarized by visit and by treatment group.

10.8.2. Respiratory Examination

A respiratory examination will be required to be performed for all subjects at all scheduled visits, according to Table 1. At screening, the investigator should specifically question all subjects about any medical history of asthma and their respiratory health (eg, wheezing, allergies, and infections). After the screening visit, all subjects will be asked non-leading questions about any respiratory changes.

Results will be summarized by treatment group and visit for each question in respiratory examination form per CRF.

10.8.3. Peak Expiratory Flow (PEF)

PEF measurements will be performed for all subjects at Screening, Baseline, Week 8, Week 16, Follow-up Visit, and Early Termination Visit. For subjects reporting a medical history of asthma, PEF measurements will be performed at all visits during the clinical study (ie, PEF testing at Visit 3 and 5 will occur in asthmatic subjects only). For subjects diagnosed with de novo asthma, PEF measurements will be performed at all visits starting with the visit in which the diagnosis was confirmed.

Results from PEF testing [actual PEF rate (L/min) and/or actual PEF rate of the predicated value (%)] will be summarized by treatment group and visit using descriptive statistics, including observed values and change from baseline values.

Number and frequency of subjects with abnormal PEF (actual PEF < 80% of the predictive value) will be summarized by visit, treatment group.

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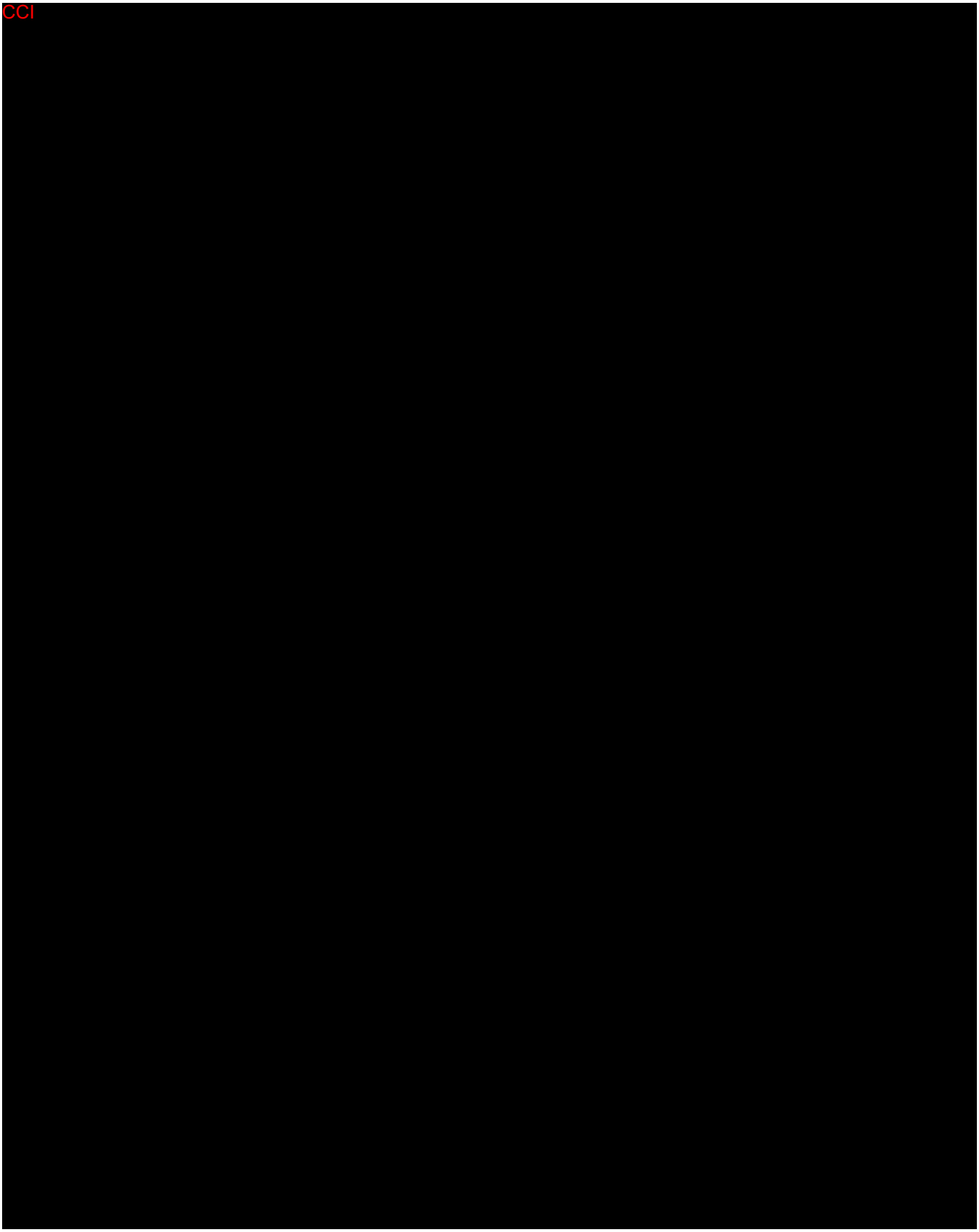

All PK parameters will be listed by subject.

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13. Interim Analyses

No interim analysis will be performed.

14. Changes from Analysis Planned in Protocol

14.1. Concomitant Medications and Therapies

In protocol Section 9.6 (Prior and Concomitant Therapies), concomitant medications/therapies are defined as any therapies taken during the study (ie, from the screening visit to the end of study).

However, for the analysis purpose, the medications are classified as taken prior or concomitantly with the study drug administration. Concomitant medications/therapies are defined as medications/ therapies which start or stop on or after the 1st injection of study drug. The purpose of this analysis is to provide information separately on:

- the medication taken in addition to the study drug;
- the medication taken prior to the study drug administration.

This analysis could be used to identify any medication that could potentially interact with the study drug.

14.2. Analysis of Secondary Endpoints

In protocol Section 16.5.1 (Secondary Efficacy Endpoints), for binary efficacy endpoints, one sensitivity analysis is to have CMH analysis conducted based on observed data, with data post rescue medication set to treatment failure. This sensitivity analysis is removed in current SAP, since the rest analyses provide sufficient assessment.

For continuous secondary efficacy endpoints, analysis using ANCOVA on OC will not be performed as the current analyses provide sufficient assessment on these endpoints.

MI analyses will be performed using MAR assumption instead of MNAR assumption. This is to align with the overall Arcadia program of the study drug; also, the MNAR models require to have sufficient amount of non-missing data in reference group in each of the stratums, and the issue of MNAR models failing to impute the missing data with MNAR assumption due to lack of sufficient non-missing data in the reference group was observed during the dry-run. Thus, it is determined that MI with MAR assumption will be employed in the final run.

14.3. Estimands Section

Description of estimands for main primary endpoints were listed in section 3.1

14.4. Analysis of Vaccine Secondary Endpoints

Additional vaccine secondary endpoints will be provided, computing the Geometric Mean Concentration/Titers ratios from Week 16 to Baseline

15. Programming Considerations

15.1. General Considerations

- One SAS program can create several outputs.
- One output file can contain several outputs.
- Output files will be delivered in Word format (.rtf) and portable document format (.pdf).
- Numbering of TFLs will follow International Conference on Harmonization (ICH) E3 guidance.

15.2. Table, Listing, and Figure Format

15.2.1. General

- All TFLs will be produced in landscape format, unless otherwise specified.
- All TFLs will be produced using the Courier New font, size 8.
- The data displays for all TFLs will have a minimum blank 1-inch margin on all 4 sides.
- Headers and footers for figures will be in Courier New font, size 8.
- Legends will be used for all figures with more than 1 variable, group, or item displayed.
- TFLs will be in black and white (no color), unless otherwise specified
- Specialized text styles, such as bolding, italics, borders, shading, and superscripted and subscripted text, will not be used in the TFLs, unless otherwise specified.
- Only standard keyboard characters will be used in the TFLs. Special characters, such as non-printable control characters, printer-specific, or font-specific characters, will not be used. Hexadecimal-derived characters will be used, where possible, if they are appropriate to help display math symbols (e.g., µ). Certain subscripts and superscripts (e.g., cm^2, C_{max}) will be employed on a case-by-case basis.
- Mixed case will be used for all titles, footnotes, column headers, and programmer-supplied formats, as appropriate.

15.2.2. Headers

- All output should have the following header at the top left of each page:

  Galderma Protocol RD.06.SPR.118380
  Draft/Final Run
- All output should have Page n of N at the top or bottom right corner of each page. TFLs are internally paginated in relation to the total length (i.e., the page number should appear sequentially as page n of N, where N is the total number of pages in the table).

- The date output was generated should appear along with the program name as a footer on each page.

15.2.3. Display Titles

- Each output are identified by the designation and a numeral. (i.e., Table 14.1.1). The title is centered. The analysis set is identified on the line immediately following the title. The title and table designation are single-spaced. A solid line spanning the margins will separate the display titles from the column headers. There will be 1 blank line between the last title and the solid line.

Table x.y.z
First Line of Title
Second Line of Title if Needed
(XX Analysis Set)

15.2.4. Column Headers

- Column headings are displayed immediately below the solid line described above in initial upper-case characters.

- Analysis set sizes will be presented for each treatment group in the column heading as (N=xx) (or in the row headings, if applicable). This is distinct from the 'n' used for the descriptive statistics representing the number of subjects in the analysis set.

- The order of treatments in the tables and listings will be Placebo first in the case of placebo controlled studies and Active comparators first in the case of active comparator trials, followed by a total column (if applicable).

15.2.5. Body of the Data Display

15.2.5.1. General Conventions

Data in columns of a table or listing are formatted as follows:

- Alphanumeric values are left-justified;

- Whole numbers (e.g., counts) are right-justified;

- Numbers containing fractional portions are decimal aligned.

15.2.5.2. Table Conventions

- Units will be included where available.

- If the categories of a parameter are ordered, then all categories between the maximum and minimum category are presented in the table, even if n=0 for all treatment groups in a given category that is between the minimum and maximum level for that parameter.

- If the categories are not ordered (e.g., Medical History, Reasons for Discontinuation from the Study, etc.), then only those categories for which there is at least 1 subject represented in 1 or more groups are included.

- Unless otherwise specified, the estimated mean, median, Q1 and Q3 for a set of values are printed out to 1 more significant digit than the original values, and standard deviations are printed out to 2 more significant digits than the original values. The minimum and maximum should report the same significant digits as the original values.

- P-values are output in the format: “0.xxx”, where xxx is the value rounded to 3 decimal places. Every p-value less than 0.001 will be presented as <0.001. If the p-value is returned as >0.999, then present as >0.999.

- Percentage values are printed to one decimal place, in parentheses with no spaces, one space after the count (e.g., 7 (12.8%), 13 (5.4%)). Unless otherwise noted, for all percentages, the number of subjects in the analysis set for the treatment group will be the denominator. Percentages after zero counts should not be displayed and percentages equating to 100% are presented as 100%, without decimal places.

- Where a category with a subheading (such as system organ class) has to be split over more than one page, output the subheading followed by “(cont)” at the top of each subsequent page. The overall summary statistics for the subheading should only be output on the first relevant page.

15.2.5.3. Listing Conventions

- Listings will be sorted for presentation in order of treatment groups as above, subject number, visit/collection day, and visit/collection time.

- Missing data are represented on subject listings as either a hyphen (“-”) with a corresponding footnote (“- = unknown or not evaluated”), or as “N/A”, with the footnote “N/A = not applicable”, whichever is appropriate.

- Dates are printed in SAS DATE9.format (“DDMMMYYYY”: 01JUL2000). Missing portions of dates are represented on subject listings as dashes (--JUL2000). Dates that are missing because they are not applicable for the subject are output as “N/A”, unless otherwise specified.

- All observed time values are to be presented using a 24-hour clock HH:MM or HH:MM:SS format (e.g., 11:26:45, or 11:26). Time will only be reported if it was measured as part of the study.

- Units will be included where available.

15.2.6. Footnotes

- A solid line spanning the margins will separate the body of the data display from the footnotes.

- All footnotes will be left justified with single-line spacing immediately below the solid line underneath the data display.

- Footnotes should always begin with “Note:” if an informational footnote, or 1, 2, 3, etc. if a reference footnote. Each new footnote should start on a new line, where possible.

- Subject specific footnotes are avoided, where possible.

- Footnotes will be used sparingly and add value to the table, figure, or listing. If more than six lines of footnotes are planned, then a cover page is strongly recommended to be used to display footnotes, and only those essential to comprehension of the data will be repeated on each page.

- The last line of the footnote section will be a standard source line that indicates the name of the program used to produce the data display, date the program was run (eg., 'Program : myprogram.sas Table Generation: DDMMMYYY HH:MM').

16. Quality Control

SAS programs are developed to produce output such as analysis data sets, summary tables, data listings, figures or statistical analyses.

PPD End-to-End Process of the Production of Analysis Datasets (ADs) and Tables, Figures and Listings (TFLs) SOP (3922) and the SAS Programming and Validation Plan describe the quality control procedures that are performed for all SAS programs and output. Quality control is defined here as the operational techniques and activities undertaken to verify that the SAS programs produce the output by checking for their logic, efficiency and commenting and by review of the produced output.

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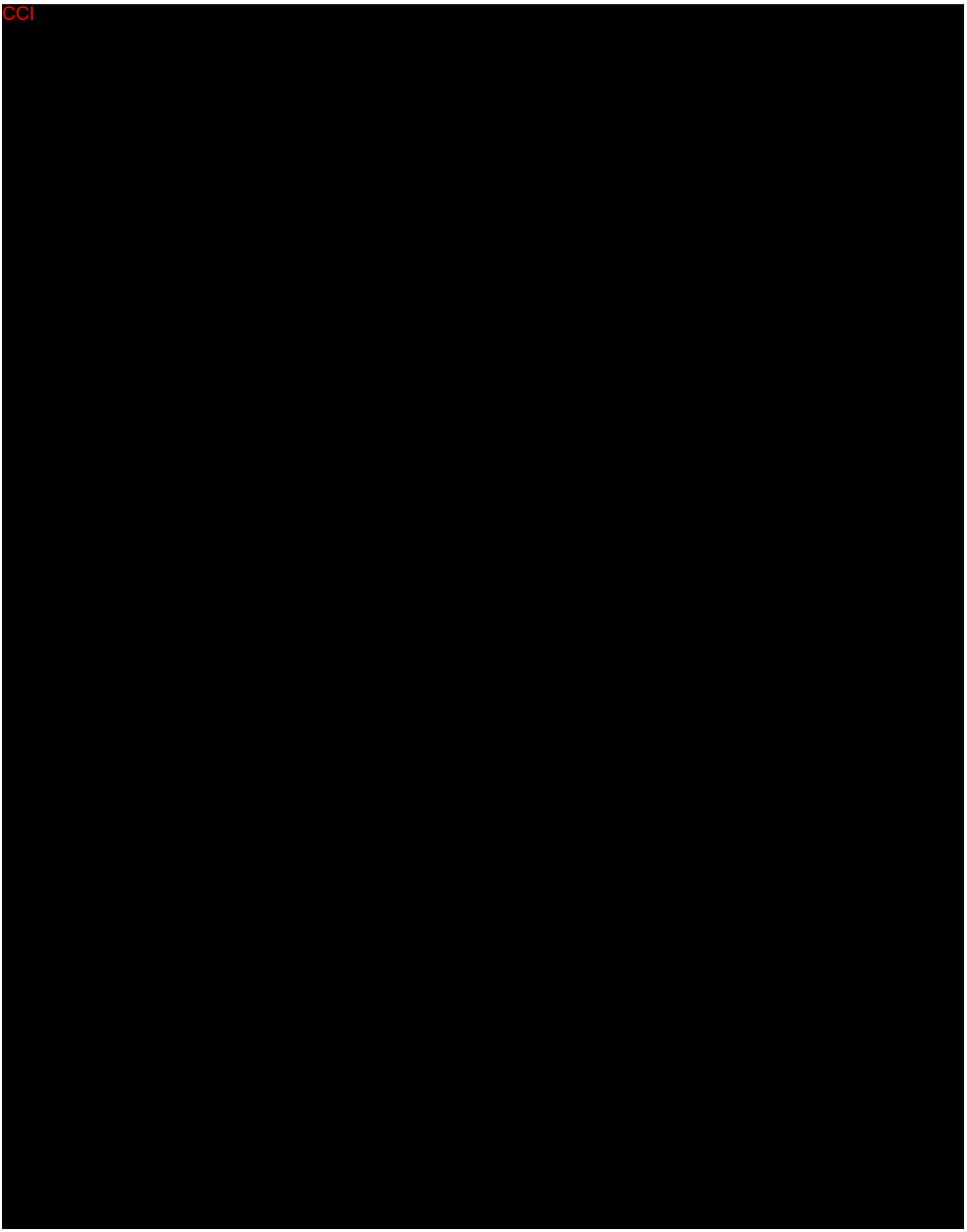

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