DISCLOSURE

REDACTED STATISTICAL ANALYSIS PLAN

CC-220-SLE-001 – ATEP

A PILOT, PHASE 2, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND, STUDY TO EVALUATE EFFICACY, SAFETY, TOLERABILITY, PHARMACOKINETICS, PHARMACODYNAMICS AND PHARMACOGENETICS OF CC-220 IN SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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STATISTICAL ANALYSIS PLAN

A PILOT, PHASE 2, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND, STUDY TO EVALUATE EFFICACY, SAFETY, TOLERABILITY, PHARMACOKINETICS, PHARMACODYNAMICS AND PHARMACOGENETICS OF CC-220 IN SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

STUDY DRUG: **CC-220**

PROTOCOL NUMBER: **CC-220-SLE-001 – ATEP**

DATE FINAL: **31OCT2018**

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SAP TITLE	Statistical Analysis Plan
SAP VERSION, DATE	Version 1.0, 31Oct2018
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SIGNATURE STATEMENT	By my signature, I indicate I have reviewed this SAP and find its contents to be acceptable.
Statistical Therapeutic Area Head Signature PPD Printed Name PPD Date PPD	
Lead Statistician PPD Signature Printed Name PPD Date PPD	
Lead Clinical Research Physician / Clinical Research Physician PPD Signature *{See appended electronic signature page}* Printed Name PPD Date PPD	

Lead Product Safety Physician

Signature *{See appended electronic signature page}* PPD

Printed Name PPD Date PPD

1. LIST OF ABBREVIATIONS

Table 1: Abbreviations and Specialist Terms

Abbreviation	Description
ACR	American College of Rheumatology
ADaM	Analysis Dataset Model
AE	Adverse event
ALT	Alanine aminotransferase/ serum glutamic-pyruvic transaminase (SGPT)
AST	Aspartate aminotransferase/ serum glutamic-oxaloacetic transaminase (SGOT)
ATC	Anatomical Therapeutical Chemical
BMI	Body mass index
CLASI	Cutaneous Lupus Area and Severity Index
CRP	C-reactive protein
ECG	Electrocardiogram
eCRF	Electronic case report form
eGFR	Estimated glomerular filtration rate
ESR	Erythrocyte sedimentation rate
Hgb	Hemoglobin
hs-CRP	High sensitivity C-reactive protein
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IP	Investigational product
LDH	Lactate dehydrogenase
MDRD	Modification of Diet in Renal Disease formula
MedDRA	Medical Dictionary for Regulatory Activities
NSAID	Nonsteroidal anti-inflammatory drug
PGA	Physician's global assessment
PRN	As needed

Abbreviation	Description
PT	Preferred term
QD	Once daily
QOD	Once every other day
RBC	Red blood cells
SAP	Statistical analysis plan
SD	Standard deviation
SE	Standard error
SLE	Systemic lupus erythematosus
SLEDAI	Systemic lupus erythematosus Disease Activity Index
SLICC	Systemic Lupus International Collaborating Clinics
SOC	System organ class
TEAE	Treatment-emergent adverse event
ULN	Upper limit of normal
US	United States
VA	Visual acuity
WBC	White blood cells
WHODD	World Health Organization Drug Dictionary

2. INTRODUCTION

This statistical analysis plan (SAP) describes the analyses and data presentations for Celgene's protocol CC-220-SLE-001 "A Pilot, Phase 2, Randomized, Placebo-Controlled, Double-Blind Study to Evaluate Efficacy, Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Pharmacogenetics of CC-220 in Subjects with Systemic Lupus Erythematosus (SLE)." This SAP pertains to Active Treatment Extension Phase (ATEP) of the study design only. Analyses of Part 1 of the study design are presented in a separate document. This SAP contains definitions of analysis populations, derived variables, and statistical methods for the analysis of efficacy and safety parameters.

This SAP provides a more technical and detailed elaboration of the statistical analyses, as outlined and/or specified in the CC-220-SLE-001 study protocol amendment dated 18Jun2018. The SAP will be finalized and approved prior to the database lock. All statistical analyses detailed in this SAP will be conducted using SAS® Version 9.2 or higher.

3. STUDY OBJECTIVES

3.1. Primary Objective

The primary objective of ATEP

- To evaluate the long-term safety and tolerability of CC-220 in subjects with SLE who completed Part 1 of the core study

3.2. Secondary Objectives

The secondary objective of ATEP

- To evaluate the long-term efficacy of CC-220 in subjects with SLE who completed Part 1 of the core study

CCI [redacted]

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

The Active Treatment Extension Phase (ATEP) is an extension of the core CC-220-SLE-001 study to evaluate the long-term efficacy and safety/tolerability of CC-220 in SLE subjects who completed Part 1 of the core study.

Subjects who complete the Treatment Phase of Part 1 of the core study will be eligible to enter this phase of the study and should be enrolled immediately to avoid dose interruption. In the event the ATEP has not been implemented by a subject's study center at the time they have completed the Treatment Phase, subjects will enter the Observation Phase of the core study and be eligible to enroll in the ATEP upon implementation of the protocol amendment #5. There are no time restrictions on how long subjects can be off CC-220 prior to entering the ATEP as long as they completed treatment in Part 1 of the core study. Subjects who terminate the Treatment Phase of Part 1 early will not be eligible for entry into the ATEP. All subjects who participate in the ATEP will receive the same active treatment they received during their participation in Part 1 with the exception of those on placebo or 0.3 mg QOD or 0.6 mg QD (see below for information on dosing for these subjects).

Subject participation consists of two phases:

- Active Treatment Extension Phase: Up to 2 years
- Observational Follow-up Phase: 28 days

Subjects receiving CC-220 0.3 mg QOD or CC-220 0.3 mg QD during their participation in the core study will be assigned to receive CC-220 0.3 mg QD during the ATEP. Subjects receiving CC-220 0.6 mg/0.3 mg on alternating days during their participation in the core study will remain on the same assigned dose during the ATEP. Subjects receiving CC-220 0.6 mg QD during their participation in the core study were originally permitted to enter the ATEP on the same dose. However, based on data that has become available for Part 1 (Protocol Section 4.2.3), any subject originally enrolled in the ATEP on the 0.6 mg QD dose should be dose reduced to the 0.6 mg/0.3 mg on alternating days dose upon implementation of Protocol Amendment 5.

Subjects receiving placebo during their participation in the core study (Part 1) will receive the CC-220 dose given to those on active drug in their respective cohort. For example, if a subject was taking placebo in Dose Group 3 of Part 1, he or she would receive CC-220 0.6 mg/0.3 mg on alternating days during the ATEP.

Subjects will remain on their assigned treatment for up to 2 years. In the event a subject experiences clinically significant investigational product (IP) related adverse events (AE), a dose interruption for up to 14 days will be permitted (Protocol Section 12.1). If a subject is unable to remain on their assigned dose, he/she may reduce their dose to the next lowest dosing regimen. Dose reductions will occur as follows:

- Subjects on 0.6 mg QD will reduce their dose to 0.6 mg/0.3 mg on alternating days
- Subjects on 0.6 mg/0.3 mg on alternating days will reduce their dose to 0.3 mg QD
- Subjects on 0.3 mg QD will be terminated from the study

A subject will only be permitted to reduce their dose one time during the study (subjects who originally came into the ATEP on 0.6 mg QD and dose reduce to 0.6/0.3 mg QD on alternating days upon implementation of Protocol Amendment 5 will be eligible for one additional dose reduction in the ATEP). The decision to modify IP dosing will be based on the rules provided in Protocol section 8.2.1. The sponsor should be notified of the intent to dose reduce prior to a change in dosing.

All subjects will be allowed to remain on stable doses of hydroxychloroquine, chloroquine, and/or quinacrine for ≥ 4 weeks prior to their baseline visit and throughout the study. Subjects on antimalarials will be permitted to modify or stop their treatment at any time during the ATEP. Methotrexate (7.5 mg – 25 mg per week), leflunomide (maintenance dosing must not exceed 20 mg daily) or sulfasalazine (dosing not to exceed 3 g daily) will be permitted, although no other additional systemic immunosuppressives will be permitted. In addition, PRN treatment with systemic anti-pruritics and/or systemic analgesics will be permitted. However, subjects must stop using all systemic anti-pruritics 48 hours prior to all study visits and systemic analgesics 12 hours prior to all study visits. Oral NSAIDs may be used PRN, but must be stopped 12 hours prior to all study visits. Use of oral corticosteroids will be permitted only at doses of 10 mg or less per day and must be maintained at a stable dose during study participation. Inhaled corticosteroids for use in a disease other than lupus, eg, asthma, will be allowed. No IV or IM corticosteroids will be permitted during the study. No other topical (with the exception of potency class 6 and 7 topicals only), local or systemic treatments for dermatological manifestations of SLE will be permitted.

Subjects will have regularly scheduled visits to assess IP activity and safety. Required assessments will be completed as depicted in the table of section 16.4.

Upon completion of, or discontinuation from the ATEP, all subjects (including premature discontinuations) will enter a 28 day Observational Follow-up Phase.

4.2. Study Endpoints

Safety and Efficacy endpoints are listed in Sections 4.2.1 through 4.2.3. .

4.2.1. Primary Endpoint

The primary endpoints will assess safety.

The following safety parameters will be evaluated throughout the duration of the study:

- Adverse events
  - Type, frequency, severity and relationship of AEs to IP
  - Number of subjects who discontinue IP due to any AE
- Laboratory evaluations for hematology, serum chemistry, and urinalysis will be collected.
  - Laboratory parameters for hematology will include: red blood cells (RBC), hemoglobin (HgB), hematocrit, white blood cells (WBC) and differential (basophils, eosinophils, lymphocytes, monocytes, neutrophils [percent and absolute]), and platelet count.
  - Laboratory parameters for serum chemistry will include: total protein, albumin, calcium, phosphorus, glucose, uric acid, total bilirubin, alkaline phosphatase, aspartate aminotransferase (AST; serum glutamic-oxaloacetic transaminase [SGOT]), alanine aminotransferase (ALT; serum glutamic pyruvic transaminase [SGPT]), lipase, sodium, potassium, chloride, bicarbonate, blood urea nitrogen, creatinine, lactate dehydrogenase (LDH), and magnesium. Additionally, the central lab will calculate and report the estimated glomerular filtration rate (eGFR) in mL/min using the Modification of Diet in Renal Disease formula (MDRD eGFR).
  - Laboratory parameters for urinalysis dipstick include: microscopic and quantitative protein.
  - Laboratory parameters for micronutrients include: apolipoproteins, total cholesterol, and lipid-soluble vitamins A,D,E,K)
  - Laboratory parameters for inflammation panel include: high sensitivity C-reactive protein (hs-CRP), erythrocyte sedimentation rate (ESR), fibrinogen, and serum amyloid A.
  - Laboratory parameters for assessment of immunoglobulins include: immunoglobulin G (IgG), immunoglobulin M (IgM), and immunoglobulin A (IgA).
  - Laboratory parameters for assessment of blood clotting include: prothrombin time, internationalized normalized ratio, and partial thromboplastin time.
- Laboratory endpoints include:
  - Number and percentage of subjects with marked abnormalities (see Section 16.3)
  - Observed value and change from Baseline over time
  - Shift from Baseline to postbaseline time points and to the worst postbaseline value in terms of normal/abnormal (low or high) in hematology and serum chemistry laboratory parameters

- Vital signs and weight endpoints include:
  - Change from Baseline over time in vital sign parameters (temperature, pulse, weight and seated blood pressure)
  - Shift from Baseline to postbaseline time-points and to worst postbaseline value in terms of normal/abnormal (see Section 11.3) in blood pressure and pulse
- Electrocardiogram (ECG, 12-lead) recordings will be obtained throughout the study and assessed by a central (cardiologist) reader. The cardiologist will interpret all ECGs with relevance to PR interval, QRS duration, heart rate and R-R interval, QT and QTc. The ECG endpoints include:
  - Change from Baseline over time in ECG parameters
  - Shift from Baseline to postbaseline time points and to worst postbaseline value in terms of normal/abnormal in ECG findings
- Physical examination will include skin, nasal cavities, eyes, ears, respiratory, cardiovascular, gastrointestinal, neurological, lymphatic, and musculoskeletal system evaluations. Results of the physical examinations will be recorded only in the source documents, however clinically significant changes in physical examination findings will be captured as AEs.
- Ophthalmological examinations will include visual acuity (VA) and slit lamp exams with fluorescein staining following papillary dilation. Ophthalmological endpoints include:
  - Number and percentage of subjects with clinically significant ophthalmological findings
- Change from Baseline in tetanus toxoid, pneumococcal and influenza titer at Week 1, Week 52, and Week 96.

4.2.2. Secondary Endpoints

The secondary endpoints will assess the efficacy of CC-220.

4.2.2.1. Cutaneous Lupus Area and Severity Index (CLASI)

- The CLASI Activity Score (Protocol Appendix A) ranges from 0 to 70. To generate the activity score erythema is scored on a scale of 0 (absent) to 3 (dark red; purple/violaceous/crusted/hemorrhagic) and scale/hypertrophy are scored on a scale of 0 (absent) to 2 (verrucous/hypertrophic). Both the erythema and scale/hypertrophy scores are assessed in 13 different anatomical locations. In addition, the presence of mucous membrane lesions is scored on a scale of 0 (absent) to 1 (lesion or ulceration), the occurrence of recent hair loss is captured (1=yes; 0=no) and nonscarring alopecia is scored on a scale of 0 (absent) to 3 (focal or patchy in more than one quadrant). To calculate the activity score, all scores for erythema, scale/hypertrophy, mucous membrane lesions and alopecia are added together.

- Change from Baseline and percent change from Baseline in the CLASI Activity score at Week 1, Week 4, Week 12, Week 24, Week 36, Week 48, Week 60, Week 72, Week 84, Week 96, and Week 100.
- The CLASI Damage Score (Protocol Appendix A) ranges from 0 to 56. To generate the damage score, dyspigmentation is scored on a scale of 0 (absent) to 1 (dyspigmentation) and scarring/atrophy/panniculitis are scored on a scale of 0 (absent) to 2 (severely atrophic scarring or panniculitis). Both the dyspigmentation and scarring/atrophy/panniculitis scores are assessed as usually lasting greater than or less than 12 months for the subject. If the dyspigmentation usually lasts greater than 12 months, the dyspigmentation scoring conducted for the 13 anatomical areas is doubled. In addition, scarring of the scalp (judged clinically), is scored on a scale of 0 (absent) to 6 (affects the whole skull). To calculate the damage score, all scores for dyspigmentation, scarring/atrophy/panniculitis, and scarring of the scalp are added together.
- Change from Baseline and percent change from Baseline in the CLASI Damage score at Week 1, Week 4, Week 12, Week 24, Week 36, Week 48, Week 60, Week 72, Week 84, Week 96, and Week 100.

4.2.2.2. Swollen and Tender Joint Count

- Using this tool, joint tenderness and swelling will be noted as "present" or "absent," with no quantitation of severity (Protocol Appendix B). In order to maintain consistency throughout the study, the same evaluator should perform the joint assessments for a given subject at a study site at each study visit.
- Change from Baseline and percent change from Baseline in swollen and tender joint count at Week 1, Week 4, Week 12, Week 24, Week 36, Week 48, Week 60, Week 72, Week 84, Week 96, and Week 100.

4.2.2.3. Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) SELENA Modification

- The hybrid SELENA SLEDAI (Protocol Appendix E) measures disease activity through assessment of 24 lupus manifestations using a weighted score of 1 to 8 points. A decrease of 4 or greater points in the Hybrid SELENA SLEDAI is considered clinically meaningful. A manifestation is recorded if it is present over the previous 10 days regardless of severity or whether it has improved or worsened. What differentiates the hybrid SELENA SELEDAI from the SELENA SLEDAI is the definition of proteinuria. The Hybrid SELENA SLEDAI defines proteinuria as > 0.5 gm/24 hours – 'new onset or recent increase of more than 0.5 gm/24 hours' has been removed from the definition.
- Change from Baseline and percent change from Baseline in Hybrid SELENA SLE Disease Activity Index (SLEDAI) at Week 1, Week 4, Week 12, Week 24, Week 36, Week 48, Week 60, Week 72, Week 84, Week 96, and Week 100.
- Proportion of subjects who achieve ≥ 4 point reduction from Baseline in Hybrid SELENA SLEDAI score at Week 1, Week 4, Week 12, Week 24, Week 36, Week 48,

Week 60, Week 72, Week 84, Week 96, and Week 100, in subjects with Baseline Hybrid SELENA SLEDAI score ≥ 4.

4.2.2.4. Pericardial/Pleuritic Numerical Pain Scale

- Each scale (Protocol Appendix G) is scored using numerical values of 1 through 10 with 1 representing 'no pain' and 10 representing 'worst possible pain'. Both pain scales will be self-administered by the subject and gauge the severity of their SLE pain related to pericardial and pleuritic discomfort. Any indication from subjects or study assessments, aside from pain, which indicate clinically significant pericardial or pleuritic manifestations of SLE must be thoroughly investigated. If clinically significant SLE related complications are found, the subject should be discontinued from the study into the Observational Follow-up Period and treated appropriately.
- Change from Baseline and percent change from Baseline in Pericardial/Pleuritic Pain Scale score at Week 1, Week 4, Week 12, Week 24, Week 36, Week 48, Week 60, Week 72, Week 84, Week 96, and Week 100.

4.2.2.5. Physician's Global Assessment (PGA)

- The PGA (Protocol Appendix C) uses a visual analog scale with scores between 0 and 3 to indicate worsening of disease. The scoring is as follows:
    - 0 = none
    - 1 = mild disease
    - 2 = moderate disease
    - 3 = severe disease

  This is a physician administered instrument used to gauge a subject's overall state of health. A 10% increase (0.3 points) is considered a clinically relevant worsening of disease.
- Change from Baseline and percent change from Baseline in the PGA score at Week 1, Week 4, Week 12, Week 24, Week 36, Week 48, Week 60, Week 72, Week 84, Week 96, and Week 100.

4.2.2.6. Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR)

- The SLICC/ACR Damage Index (Protocol Appendix O) measures irreversible impairment since onset of SLE which has to be present for at least 6 months. Damage is defined for 12 separate organ systems: ocular (range 0-2), neuropsychiatric (0-6), renal (0-3), pulmonary (0-5), cardiovascular (0-6), peripheral vascular (0-5), gastrointestinal (0-6), musculoskeletal (0-7), skin (0-3), endocrine (diabetes) (0-1), gonadal (0-1) and malignancies (0-2). The maximum score for this assessment is 47 points.
- Change from Baseline and percent change from Baseline in the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index score at Week 1, Week 4, Week 12, Week 24, Week 36, Week 48, Week 60, Week 72, Week 84, Week 96, and Week 100.

4.2.2.7. British Isles Lupus Assessment Group 2004 (BILAG)

- The BILAG 2004 (Protocol Appendix P) is a composite index that is based on the Classic BILAG index. It is a clinical measure of lupus disease activity. This tool assesses the changing severity of clinical manifestations of SLE using an ordinal scale scoring system that contain 9 systems (constitutional, mucocutaneous, neuropsychiatric, musculoskeletal, cardiorespiratory, gastrointestinal, ophthalmic, renal and hematological). Disease activity is categorized into five levels, Grades A-E.
- The BILAG-2004 global score is calculated by summing up the numerical score equivalents across the organ systems, with the numerical score equivalents given as: A = 12, B = 8, C = 1, D = 0, E = 0.
- Change from Baseline and percent change from Baseline in the British Isles Lupus Assessment Group 2004 global score as well as in each organ system at Week 1, Week 4, Week 12, Week 24, Week 36, Week 48, Week 60, Week 72, Week 84, Week 96, and Week 100.

4.2.2.8. Fatigue Visual Analog Scale (VAS)

- The Fatigue VAS (Protocol Appendix H) will evaluate SLE related fatigue using a 0-100 mm VAS scale. A Fatigue VAS will allow the subject to indicate the degree of SLE related fatigue they experienced over the previous week.
- Change from Baseline and percent change from Baseline in the Fatigue Visual Analog Scale score at Week 1, Week 4, Week 12, Week 24, Week 36, Week 48, Week 60, Week 72, Week 84, and Week 96.

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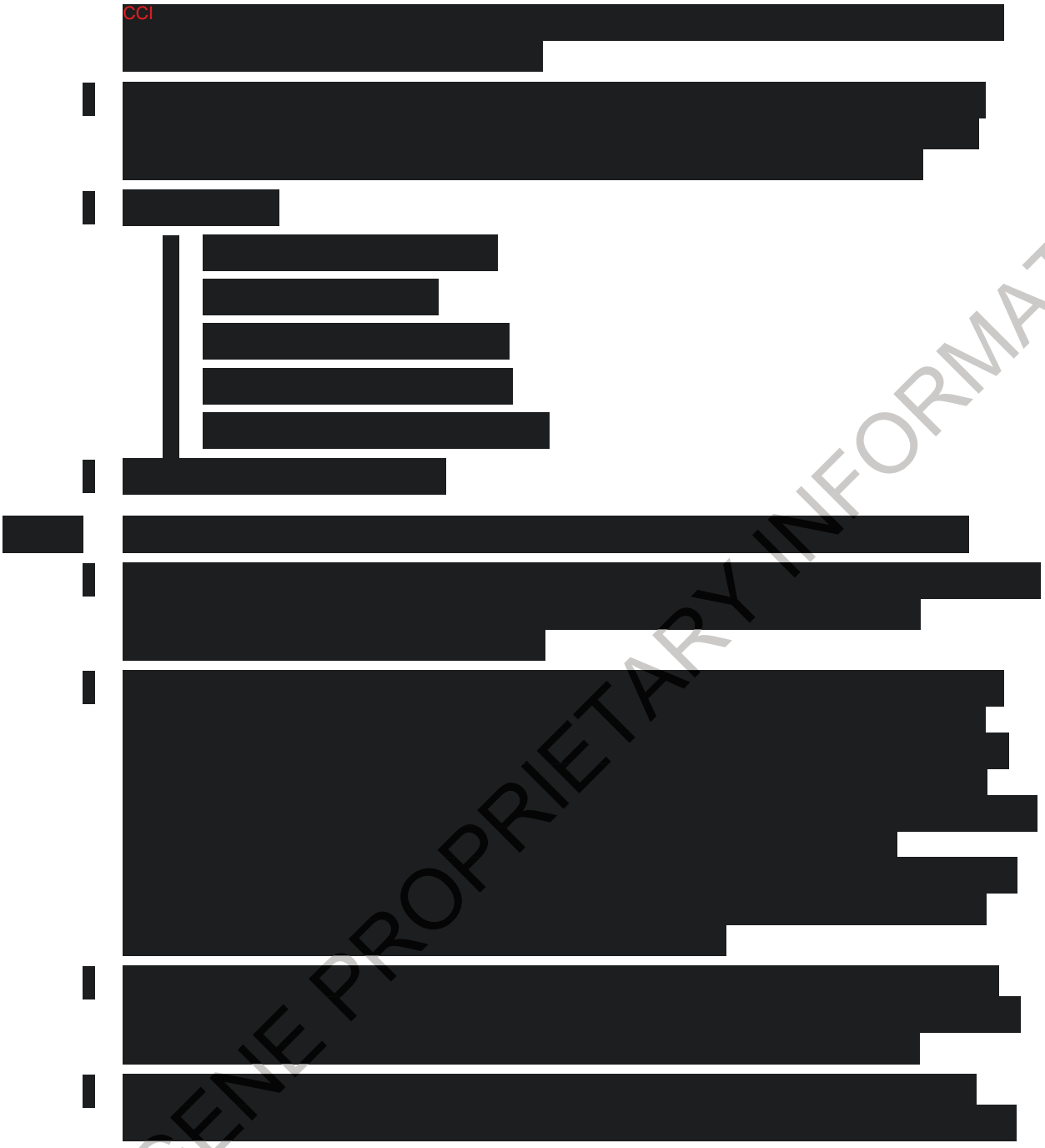

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4.3. Stratification, Randomization, and Blinding

As an extension of core CC-220-SLE-001, Active Treatment Extension Phase will be made up of subjects completing Part 1 and completed the screening and consent process. Subjects will continue their active treatment or be assigned doses as described in section 4.1.

4.4. Sample Size Determination

Subjects who completed Part 1 are eligible to participate in ATEP, no formal sample size or power calculation was performed.

5. GENERAL STATISTICAL CONSIDERATIONS

5.1. Reporting Conventions

Summary statistics for continuous variables include sample size (n), mean, standard deviation (SD), median, minimum, and maximum. All mean and median values will be formatted to one more decimal place than the measured value. Standard deviation values will be formatted to two more decimal places than the measured value. Minimum and maximum values will be presented to the same number of decimal places as the measured value. The frequency summary for categorical variables includes number and percentage. All percentages will be rounded to one decimal place. Number and percentage values will be presented as xx (xx.x). All analysis and summary tables will have the population sample size for each treatment group in the column heading. All laboratory data will be reported using standard international units.

In data derivations requiring the date of the first dose of IP dispensed at a specific visit, in the absence of a definitive record of this date, the study drug dispense date (from the study drug accountability records) associated with that visit, or if this date is also missing, then the visit date, will be used to estimate the date of the first dose of IP in question. In the absence of a definitive record of the date of the last dose of IP for subjects who have completed the study or have discontinued early, the date of the Week 96 visit or the discontinuation visit will be used to estimate the last dose date for subjects who have completed the study or have discontinued early and have the discontinuation visit; for subjects who have discontinued but do not have the discontinuation visit, the last "follow-up" date (ie, the maximum date among the subject's records of study visits, study drug records, AEs [start and end dates], concomitant medications/procedures, laboratory, vital signs, and ECG) will be used to estimate the last dose date.

All tables and listings will be presented by the 0.3 mg QD and 0.3/0.6 mg QD alternating groups, and the tables will additionally present a total group combing the above 2 groups. Subjects originally assigned to 0.3 mg QD and 0.3/0.6 mg QD alternating at the entry into the ATEP will be included in the respective treatment groups, irrespective of the possible dose reduction during the ATEP. Subjects originally assigned to 0.6 mg QD will be included in the 0.3/0.6 mg QD alternating group, regardless of whether or not dose reduction to 0.3/0.6 mg QD alternating per Protocol Amendment 5 has occurred before early discontinuation.

5.2. Baseline Definition

The baseline is defined as the last value measured on or before the day of the first dose of IP during ATEP.

5.3. Time Points

Time points (including the scheduled study weeks per protocol, the end of treatment, and the observational follow-up visit) in all analyses are based on the visits/study weeks as recorded in the database.

Appropriate dates (eg, date of measurement or date of specimen collection) will first be used to ensure only data (including data from scheduled, unscheduled, discontinuation, and observational follow-up visits) measured or collected within the specific analysis period are included, and then the visits/study weeks as recorded in the database will be used to assign one value (possibly missing) to each time point at the subject level according to the following rules:

- If a value is available at a scheduled visit (eg, Week 2/Visit 3), then that value will be used for the study week, regardless of whether a value is available from an unscheduled visit in the corresponding visit window. If the value at a scheduled visit is missing, but an unscheduled visit is available in the corresponding visit window, the value from the nearest earlier unscheduled visit will be used for the study week.
- If the value at a scheduled visit is missing and there is no value available from an unscheduled visit in the corresponding visit window, the value at the study week will be missing.
- A value from the discontinuation visit (for a discontinued subject) will be mapped to the next scheduled visit after the last visit the subject has completed.
- The end of treatment is defined as the last postbaseline visit among all the scheduled and unscheduled visits and, if applicable, the discontinuation visit; the observational follow-up visit is not included in the derivation of the end of treatment value.

5.4. Analysis Populations

5.4.1. ATEP Population

The ATEP Population will include all subjects who are enrolled into ATEP and received at least one dose of IP. All statistical analyses for ATEP data will be based on the ATEP Population. Subjects will be included in the treatment groups as described in Section 5.1.

6. SUBJECT DISPOSITION

The number of subjects screened and the eligibility criteria failed will be summarized. The failed inclusion/exclusion criteria of subjects who were screened and not enrolled will be included in the summary. The above percentages will be based on the number of subjects screened.

The number and percentage of subjects included in each analysis population will be summarized by treatment group. The percentages will be based on the number of subjects enrolled. A listing of subjects excluded from the analysis populations, with the reasons for exclusions, will be provided.

The number and percentage of subjects who entered, completed, and discontinued each study phase (Treatment Phase and Observational Follow-up Phase), and the number and percentage of primary reasons for discontinuation for subjects who early discontinued will be summarized. The percentages will be based on the number of subjects enrolled.

The primary reason for discontinuation is collected in the study disposition electronic case report form (eCRF) and will be summarized with the following categories:

- Death
- Adverse event
- Withdrawal by subject
- Lost to follow-up
- Protocol violation
- Lack of Efficacy
- Other

7. PROTOCOL DEVIATIONS/VIOLATIONS

The protocol deviations will be summarized by treatment group for the ATEP Population. A by-subject listing of subjects with protocol deviations will be provided.

8. DEMOGRAPHICS AND BASELINE CHARACTERISTICS

The demographics and baseline characteristics will be summarized descriptively by treatment group for the ATEP Population. Individual subject listings will be provided to support the summary tables. The demographic data that were collected during part 1 and unchanged (eg, sex, race) will be populated from part 1 and included in the ATEP summary.

8.1. Demographics

Demographic variables include:

- Age (years)
- Age category (< 40, 40 to < 65, ≥ 65 years)
- Sex (male, female)
- Race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Other)
- Ethnicity (Hispanic or Latino, not Hispanic or Latino)
- Weight (kg)
- Weight category (< 70, ≥ 70 to < 85, ≥ 85 to < 100, ≥ 100 kg)
- Height (cm) at Screening
- Body mass index (BMI; kg/m^2)
- BMI category (< 25, ≥ 25 to < 30, ≥ 30 to < 35, ≥ 35 to < 40, ≥ 40 kg/m^2)
- Alcohol use (never, current, former user)
- Tobacco use (never, current, former user)
- Caffeine use (never, current, former user)

8.2. Baseline Characteristics

Baseline characteristics include:

- Duration of SLE (years)
- Baseline CLASI activity score
- Baseline CLASI damage score
- Baseline PGA score
- Baseline non-zero swollen joint counts
- Baseline non-zero tender joint counts

- Baseline Hybrid SELENA SLEDAI score
- Baseline SLICC/ ACR Damage Index
- Baseline of BILAG 2004 global score
- Baseline of Pericardial/Pleuritic Pain Scale
- Baseline of Fatigue VAS score

8.3. Medical History

Only medical events that occurred prior to the first dose in part 1 are included as medical history. Medical events that occurred after the first dose of part 1 and before the first dose of ATEP, are included in the AE results of the part 1 analyses. Medical history will be coded according to the Medical Dictionary for Regulatory Activities (MedDRA; Version 17.0 or higher). A frequency summary of medical history will be presented by treatment group, system organ class (SOC), and preferred term (PT) for the ATEP Population. A data listing including the verbatim and coded terms will be presented.

A frequency summary of SLE medical history will also be presented by treatment group for the ATEP Population.

8.4. Prior and Concomitant Medications

Medications that were initiated prior to the start of study treatment and continued after the start of study treatment in ATEP will be counted as both prior and concomitant medications. The Anatomical Therapeutical Chemical (ATC) coding scheme of the World Health Organization Drug Dictionary (WHODD; Version March 2016 or higher) will be used to group medications into relevant categories. A data listing including the verbatim and coded terms will be presented. Medication use during part 1 or prior to the first dose in ATEP are considered as prior medications for ATEP.

8.4.1. Prior Medications

Prior medications are defined as medications that were started before the start of study treatment in ATEP and either ended before the start of study treatment or continued after study treatment. A frequency summary of prior medications will be provided by treatment group, ATC1 level, and standardized medication name for the ATEP Population.

8.4.2. Concomitant Medications

Concomitant medications are defined as medications that were initiated before the first dose of IP in ATEP and continued during the study treatment, or initiated on/after the date of the first dose of IP and on/before the date of treatment discontinuation. A frequency summary of concomitant medications will be provided by treatment group, ATC1 level and standardized medication name for the ATEP Population.

8.5. Prior and Concomitant Procedures

Procedures will be coded according to MedDRA, Version 19.0 or higher. Medical procedures during part 1 or prior to the first dose in ATEP are considered as prior procedures for ATEP.

8.5.1. Prior Procedures

Prior procedures are defined as procedures or surgeries that occurred before the first dose of IP of ATEP. A frequency summary of prior procedures will be presented by treatment group, SOC, and PT for the ATEP Population.

8.5.2. Concomitant Procedures

Concomitant procedures will be identified similar to the criteria in Section 8.4.2. A frequency summary of concomitant procedures will be provided by treatment group, SOC, and PT for the ATEP Population.

9. STUDY TREATMENTS AND EXTENT OF EXPOSURE

9.1. Treatment Duration

Treatment duration (in weeks) is calculated as (the date of the last dose of IP in ATEP – the date of the first dose of IP in ATEP + 1) / 7 and rounded to one decimal place.

Treatment duration will be summarized by treatment group for the ATEP Population. Frequency summaries of treatment duration will also be presented for the following categories: ≤ 12, >12 – 24, >24 – 36, >36 – 48, >48 – 60, >60 – 72, >72 – 84, > 84 weeks.

A subject data listing of study drug records will be provided.

9.2. Treatment Compliance

As part of the routine recording of the amount of IP taken by each subject, the number of tablets dispensed and returned will be recorded at each visit after Visit 1. These records will be used to calculate cumulative treatment compliance. A subject data listing of drug accountability records will be provided.

The compliance rate (%) for each subject for a period will be computed as 100 times the total number of tablets taken (the total number of tablets dispensed minus the total number of tablets returned) over the duration of treatment divided by the intended total number of tablets that should have been taken.

The intended total number of tablets is calculated as follows. First chronologically order the first dose date, the second dispense date, the third dispense date, etc., up to the last dose date. The first and last dose dates are defined in the same way as those defined for treatment duration calculations (see Section 9.1). The intended number of tablets between any two consecutive dates is calculated as $2 \times n$, where n denotes the number of days between the 2 consecutive dates (ie, the second date minus the first date for all pairs of consecutive dates, and the second date minus the first date plus 1 for the last pair). Then the intended total number of tablets is the sum of all intended numbers of tablets as calculated above from the first dose date through the last dose date. Of note, compliance rate will not be calculated for subjects (if existent) who have only the dispense record at Day 1/Visit 2 and no other drug accountability records.

Treatment compliance will be summarized by treatment group for the ATEP Population. Frequency summaries of compliance rate will also be presented with the following categories: < 75%, ≥ 75% to ≤ 120%, and > 120%.

10. EFFICACY ANALYSIS

All efficacy evaluations will be conducted using the ATEP Population. Missing data will not be imputed, and only observed results will be summarized. For categorical endpoints, only subjects with sufficient data for response determination at the visit of interest will be included in the denominator at that time point. No p-values will be provided.

10.1. Multiplicity

No multiplicity adjustment will be conducted.

10.2. Analysis of Efficacy Endpoints

Summary statistics by visit will be provided for all endpoints.

10.3. Subgroup Analysis

No subgroup analyses will be conducted.

10.4. Assessing Study Center Effect and Treatment-by-Center Interaction

This is not assessed in the ATEP.

11. SAFETY ANALYSIS

The purpose of this section is to define the safety parameters for the study. All summaries of safety data will be performed for the ATEP Population.

For the analyses of TEAEs and marked abnormalities, subject incidence will be provided, unless otherwise specified. Subject incidence (ie, percentage [%] used in a frequency summary) is defined as 100 times the number of subjects with the specific event divided by the number of subjects included in the analysis. Subjects with multiple occurrences of the specific event in the specific analysis period will be counted only once in the numerator.

Summaries of safety parameters over time (eg, summary statistics over time and shifts from Baseline to postbaseline time points in terms of normal/abnormal) will include data collected at scheduled, unscheduled, and discontinuation visits up to 28 days after the last dose of study drug in the study and data collected at observational follow-up visits. Summaries of marked abnormalities and shifts from Baseline to worst postbaseline value will include all data up to 28 days after the last dose of study drug in the study, irrespective of the visits from which these data are collected. The "worst" lab results will be defined using the worst of all post-baseline reference range indicators and grouped into "LOW" or "HIGH" or "Both L and H" or "NORMAL".

In summaries of continuous variables with summary statistics by time point, values for Baseline, time point, and change from Baseline will be summarized at each time point for subjects who have both values at Baseline and at the time point. Similarly, in frequency summaries of shifts from Baseline, only subjects who have both values at Baseline and at the time point will be included in the summaries of shifts to the scheduled study days per protocol and only subjects who have a Baseline value and at least one postbaseline value will be included in the summaries of shifts to the end of period and to the worst postbaseline value.

11.1. Adverse Events

Adverse events will be analyzed in terms of treatment-emergent adverse events (TEAE) which are defined as any AEs that begin or worsen on or after the start of study drug in ATEP through 28 days after the last dose of study drug or study treatment discontinuation date, whichever is later. All AEs will be coded using MedDRA Version 17.0 or higher. A subject data listing of all AEs, including the verbatim and coded terms, will be presented.

Unless otherwise specified, AEs will be summarized by SOC and PT, with SOCs presented in the standard international order and PTs within each SOC in descending order of subject incidence (and then alphabetically if needed).

An overall summary of the following AE categories will be provided:

- Any TEAE
- Any drug-related TEAE
- Any severe TEAE
- Any serious TEAE

- Any serious drug-related TEAE
- Any TEAE leading to drug interruption
- Any TEAE leading to drug withdrawal
- Any TEAE leading to death

Specific TEAEs under each of the above categories will be summarized.

A drug-related TEAE is defined as a TEAE which is considered to be of suspected relationship to study drug. Adverse events with missing relationship to study drug will be assessed as drug-related.

11.1.1. All Treatment-emergent Adverse Events

All TEAEs will be summarized by SOC and PT as well as by PT only (in descending order of subject incidence).

All TEAEs will be summarized by age category (< 40, ≥ 40 years) and sex (Male, Female).

All TEAEs occurring after the date of the last dose of IP and up to 28 days after the last dose of IP will also be summarized by SOC and PT for subjects who enter the observational follow-up phase during the ATEP.

11.1.2. Drug-related Treatment-emergent Adverse Events

Drug-related TEAEs will be summarized.

11.1.3. Treatment-emergent Adverse Events by Maximum Severity

All TEAEs will be summarized by maximum severity (mild, moderate, severe, and, if needed, missing). If a subject reports multiple occurrences of a specific event within a specific analysis period, the subject will be counted only once by the maximum severity. If the severity is missing for one or more of the occurrences, the maximum severity of the remaining occurrences will be used. If the severity is missing for all of the occurrences, the subject will be counted only once in the "missing" category of severity.

11.1.4. Serious Treatment-emergent Adverse Events

Serious TEAEs will be summarized by SOC and PT as well as by PT only (in descending order of subject incidence).

Serious drug-related TEAEs will be summarized.

A subject data listing of all serious AEs (both TEAEs and non-TEAEs) will be provided.

11.1.5. Treatment-emergent Adverse Events Leading to Drug Interruption and Leading to Drug Withdrawal

Treatment-emergent AEs leading to drug interruption will be summarized.

Treatment-emergent AEs leading to drug withdrawal will also be summarized. A subject data listing of TEAEs leading to drug withdrawal will be provided.

11.1.6. Treatment-emergent Adverse Events Leading to Deaths

Treatment-emergent AEs leading to death will be summarized. A subject data listing of all deaths will be provided.

CCI

11.2. Clinical Laboratory Evaluations

Summary statistics of observed values and changes from Baseline in hematology and serum chemistry laboratory parameters will be provided over time. Frequency summaries (shift tables) of shifts from Baseline to postbaseline time points and to the worst postbaseline value in terms of normal/abnormal will be provided for hematology and serum chemistry. The urinalysis results will be provided only in a listing.

Laboratory marked abnormalities (see Table 6 in Section16.3) will be summarized; subject incidence for each abnormality will be calculated based on subjects with a baseline value and at least one postbaseline value for criteria requiring baseline or subjects with at least one postbaseline value for criteria not requiring baseline. A subject data listing of laboratory marked abnormalities will be provided.

A subject data listing of all laboratory data will be provided.

11.3. Vital Sign Measurements

Summary statistics of observed values and changes from Baseline in vital signs will be provided over time. Frequency summaries (shift tables) of shifts from Baseline to postbaseline time points and to the worst postbaseline value in terms of normal/abnormal will be provided for pulse and blood pressure. The normal ranges are defined as: 60 to 100 beats/minute for pulse, 90 to 140 mm Hg for systolic blood pressure, and 60 to 90 mm Hg for diastolic blood pressure.

A subject data listing of all vital signs and weight data will be provided.

11.4. Electrocardiograms

Summary statistics of observed values and changes from Baseline in ECG findings will be provided over time. For each parameter, triplicate ECG readings will be averaged and this average used as the result in summary statistics. The overall ECG interpretation will be summarized by presenting the number and percentage of subjects with 'Normal' and 'Abnormal' by treatment. The shift from Baseline to worst during the treatment in the overall ECG interpretation will be displayed for each treatment.

11.5. Ophthalmological Examination

The overall interpretation will be summarized by presenting the number and percentage of subjects with 'Normal', 'Abnormal, not clinically significant', and 'Abnormal, clinically significant' by treatment. The shift from Baseline to Week 24, Week 48, Week 72, and Week 96 in the overall interpretation will be displayed for each treatment.

11.6. Physical Examination

No summary of physical examination findings will be provided. Clinically significant changes in physical examination findings will be captured as AEs.

11.7. Tetanus Toxoid, Pneumococcal and Influenza Titers

Summary statistics of observed values and change from Baseline will be provided over time.

CCI [redacted]

13. PHARMACOKINETIC [redacted] ANALYSIS

The ATEP does not collect Pharmacokinetic [redacted] data.

14. CHANGES TO THE STATISTICAL ANALYSES SECTION OF THE PROTOCOL

No changes to the statistical analyses section of the protocol are made in this SAP.

15. REFERENCES

■ CCI [redacted]

16. APPENDICES

16.1. Handling of Dates

Dates will be stored as numeric variables in the SAS analysis files and reported in DDMMMYYYY format (ie, the Date9. datetime format in SAS). Dates in the clinical database are classified into the categories of procedure dates, log dates, milestone dates, outcome dates, and special dates.

- **Procedure Dates** are the dates on which given protocol-specified procedure are performed. They include the dates of laboratory testing, physical examinations, tumor scans, etc. They should be present whenever data for a protocol-specified procedure are present and should only be missing when a procedure is marked as NOT DONE in the database. Procedure dates will not be imputed.
- **Log Dates** are dates recorded in CRF data logs. Specifically, they are the start and end dates for AEs and concomitant medications/procedures. They should not be missing unless an event or medication is marked as *ongoing* in the database. Otherwise, incomplete log dates will be imputed according to the rules in Appendix 16.2 (eg, for duration or cycle assignment, etc.). However, in listings, log dates will be shown as recorded without imputation.
- **Milestone Dates** are dates of protocol milestones such as randomization, study drug start date, study drug termination date, study closure date, etc. They should not be missing if the milestone occurs for a subject. They will not be imputed.
- **Special Dates** cannot be classified in any of the above categories and they include the date of birth. They may be subject to variable-specific censoring and imputation rules.

Dates recorded in comment fields will not be imputed or reported in any specific format.

16.1.1. Calculations Using Dates

Calculations using dates (eg, subject's age or relative day after the first dose of study drug) will adhere to the following conventions:

16.1.1.1. Study Day

Study days after the start day of study drug (first dose date) will be calculated as follows:

- **For dates of interest on or after the first dose date:** The study days will be calculated as the difference between the date of interest and the first dose date of study medication plus 1 day.

  STUDY DAY= (TARGET DATE – DSTART) + 1;
  where DSTART = the first dose date.

- **For dates of interest prior to the first dose date:** The study days will be calculated as the difference between the date of interest and the first dose date of study medication only.

  STUDY DAY= TARGET DATE – DSTART;
  where DSTART = the first dose date.

- Study Day 1 is the first day of treatment of study drug. Negative study days are reflective of observations obtained during the baseline/screening period.
- Partial dates for the first study drug are not imputed in general. All effort should be made to avoid incomplete study drug start dates. Some analyses may exclude subjects without study drug start date. The SAP may be amended on a case-by-case basis, including guideline and suggestion such as imputing Day 1 by consent date of treated patient.

16.1.1.2. Age

Age (expressed in years) is calculated as the difference between the date of birth and the informed consent date plus 1 day. Age will be transformed to years by dividing the difference by 365.25 days, then truncating.

AGE at part 1 = Integer portion of (DATE of CONSENT at part 1 – DATE of BIRTH + 1) /365.25

AGE at ATEP = Integer portion of (DATE of CONSENT at ATEP– DATE of BIRTH + 1) /365.25

- Preference is for using calculated age from clinical database. When not available, calculated age from CRF or IVRS may be used
- Partial birth date: impute missing day as 15th of the month; impute missing month as July; set missing age for missing year
- Intervals that are presented in weeks will be transformed from days to weeks by using (without truncation) the following conversion formula:
  WEEKS = DAYS /7
- Intervals that are presented in months will be transformed from days to months by using (without truncation) the following conversion formula:
  MONTHS = DAYS /30.4167

16.1.1.3. Duration of Systemic Lupus Erythema

Duration of SLE (expressed in years) is calculated as the difference between the date of diagnosis of SLE and the informed consent date plus 1 day divided by 365.25 days, then rounded to 1 decimal.

Duration of SLE = (DATE of CONSENT – DATE of SLE DIAGNOSIS + 1) /365.25

Partially missing SLE diagnosis dates will be imputed as specified in Section 16.2.3.

16.2. Date Imputation Guideline

16.2.1. Adverse Events

Partially missing AE start dates will be imputed in the analysis dataset model (ADaM) dataset for AEs, but partially missing AE end dates will not be imputed in the same dataset. If the AE end date is complete with no missing year, month, or day, and the partially missing start date imputed by the rules below is after the AE end date, then the start date will be imputed by the AE end date.

The principle of the imputation rules is to treat the AE as treatment-emergent, ie, occurring on or after the date of the first dose of IP, if possible.

Let an AE start date be represented as "$D_{Event}/M_{Event}/Y_{Event}$", and the date of the first dose of IP in ATEP as "$D_{IP}/M_{IP}/Y_{IP}$". The imputation rules for partially missing AE start dates are stated in Table 2.

Table 2: Imputation Rules for Partially Missing Adverse Event Start Date

Scenario	Condition	Imputation Rule
A. Partially missing date includes year only (both month and day are missing)		
1	$Y_{Event} < Y_{IP}$	$31/12/Y_{Event}$
2	Otherwise, ie, $Y_{IP} \leq Y_{Event}$	Max (date of first dose of IP, $01/01/Y_{Event}$)
B. Partially missing date includes both year and month (only day is missing)		
1	$Y_{Event} < Y_{IP}$, or ($Y_{Event} = Y_{IP}$ and $M_{Event} < M_{IP}$)	Last date of M_{Event}/Y_{Event}
2	Otherwise, ie, $Y_{IP} < Y_{Event}$, or ($Y_{IP} = Y_{Event}$ and $M_{IP} \leq M_{Event}$)	Max (date of first dose of IP, $01/M_{Event}/Y_{Event}$)

16.2.2. Prior/Concomitant Medications/Procedures

Partially missing start/stop dates for prior/concomitant medications and partially missing start dates for prior/concomitant procedures will be imputed in the ADaM dataset. For prior/concomitant medications, if the stop date is complete with no missing year, month, or day, and the partially missing start date imputed by the rule below is after the stop date, then the start date will be imputed by the stop date.

Partially missing prior/concomitant medication/procedure start dates will be imputed by the earliest possible date given the non-missing field(s) of the date.

Partially missing prior/concomitant medication stop dates will be imputed by the latest possible date given the non-missing field(s) of the date.

Let a prior/concomitant medication/procedure start/stop date be represented as "$D_{Event}/M_{Event}/Y_{Event}$". The imputation rules for partially missing prior/concomitant medication start dates are stated in Table 3. The imputation rules for partially missing prior/concomitant medication stop dates are stated in Table 4.

Table 3: Imputation Rules for Partially Missing Prior/Concomitant Medication/Procedure Start Dates

Scenario	Condition	Imputation Rule
1	Partially missing date includes year only (both month and day are missing)	$01/01/Y_{Event}$
2	Partially missing date includes both year and month (only day is missing)	$01/M_{Event}/Y_{Event}$

Table 4: Imputation Rules for Partially Missing Prior/Concomitant Medication Stop Dates

Scenario	Condition	Imputation Rule
1	Partially missing date includes year only (both month and day are missing)	$31/12/Y_{Event}$
2	Partially missing date includes both year and month (only day is missing)	Last date of M_{Event}/Y_{Event}

16.2.3. Medical History

Partially missing medical history start dates will be imputed in the ADaM dataset for medical history (for the purposes of calculating duration of SLE). The 16th of the month will be used to impute a partially missing start date that has only the day missing, and July 1st will be used to impute a partially missing start date that has both the month and day missing.

Let a medical history start date be represented as "$D_{Event}/M_{Event}/Y_{Event}$". The imputation rules for partially missing medical history start dates are stated in Table 5 .

Table 5: Imputation Rules for Partially Missing Medical History Start Dates

Scenario	Condition	Imputation Rule
1	Partially missing date includes year only (both month and day are missing)	$01/07/Y_{Event}$
2	Partially missing date includes both year and month (only day is missing)	$16/M_{Event}/Y_{Event}$

16.3. Marked Abnormalities Criteria

The laboratory marked abnormality criteria is presented in Table 6.

Table 6: Laboratory Marked Abnormality Criteria

Category / Analyte	SI Units	Criteria
Chemistry		
Alanine Aminotransferase (SGPT)	U/L	> 3 xULN
Albumin	Kg/m^3	< 25
Alkaline Phosphatase	U/L	> 400
Aspartate Aminotransferase (SGOT)	U/L	> 3 x ULN

Category / Analyte	SI Units	Criteria
Total Bilirubin	µmol/L	> 1.8 x ULN
Blood Urea Nitrogen	mmol/L	> 15
Calcium	mmol/L	< 1.8 > 3.0
Creatinine	µmol/L	> 1.7 x ULN
Glucose	mmol/L	< 2.8 > 13.9
Hemoglobin A1C	%	> 9
Lactate Dehydrogenase	U/L	> 3 x ULN
Magnesium	mmol/L	> 1.2
Phosphate	mmol/L	< 0.64 > 1.60
Potassium	mmol/L	< 3.0 > 5.5
Sodium	mmol/L	< 130 > 150
Triglycerides	mmol/L	> 3.4
Urate	umol/L	Male: > 590; Female: > 480
Alanine Aminotransferase (SGPT) Aspartate Aminotransferase (SGOT) Total Bilirubin	U/L U/L µmol/L	(ALT > 3xULN or AST > 3xULN) and Total Bilirubin > 1.5x ULN
Hematology		
Hemoglobin	g/L	Male: < 105, Female: < 85 Male: > 185, Female: > 170
Leukocytes	10^9/L	< 1.5
Lymphocytes	10^9/L	< 0.8
Neutrophils	10^9/L	< 1.0
Platelets	10^9/L	< 75 > 600

16.4. Schedule of Events

		Year 1															Year 2												Observational Follow-Up[i]
Visit(s) ±1 Day – for all visits[h]	0 Screening	1[a] Baseline for ATEP	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Week(s)	-6	0	1	2	4	8	12	16	20	24	28	32	36	40	44	48	52	56	60	64	68	72	76	80	84	88	92	96	100
Study Entry																													
Informed Consent	X	X[b]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Inclusion/Exclusion Criteria	X	X[b]	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Safety Assessments																													
Ophthalmology Exams	-	X	-	-	-	-	-	-	-	X	-	-	-	-	-	X	-	-	-	-	-	X	-	-	-	-	-	X	-
Complete Physical Exam[c]	X	X	-	-	-	-	-	-	-	X	-	-	-	-	-	X	-	-	-	-	-	X	-	-	-	-	-	X	-
Targeted Physical Exam[c]	-	-	X	X	X	X	X	X	X	-	X	X	X	X	X	-	X	X	X	X	X	-	X	X	X	X	X	-	X
Vital Signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Hepatitis B and C	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hematology, Chemistry and Urinalysis[d]	X	X	X	-	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Amylase and Lipase	-	X[b]	-	-	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	X
eGFR, protein creatinine ratio	X	X[b]	-	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
IgA, IgM and IgG	X	X	-	-	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	X
Inflammation Panel	-	X	-	-	X	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	X
Serum β-HCG Pregnancy Test[e]	X	X	-	-	X	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	X
Urine Pregnancy Test[e]	-	X[b]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-	X

		Year 1															Year 2												Observational Follow-Up[i]
Visit(s) ±1 Day – for all visits[h]	0 Screening	1[a] Baseline for ATEP	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Week(s)	-6	0	1	2	4	8	12	16	20	24	28	32	36	40	44	48	52	56	60	64	68	72	76	80	84	88	92	96	100
Tetanus toxoid, pneumococcal and influenza titers[j]	-	X	X	-	-	-	-	-	-	-	-	-	-	-	-	-	X	-	-	-	-	-	-	-	-	-	-	X	-
Apolipoproteins, total cholesterol and lipid-soluble vitamins A, D, E and K	-	X	-	-	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-
PT, INR and PTT	-	X	-	-	X	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-
Lupus Autoantibody/Complement Panel	X	X	-	-	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-
Lupus Anti-Phospholipid Profile	-	X	-	-	-	-	-	-	-	X	-	-	-	-	-	X	-	-	-	-	-	X	-	-	-	-	-	X	-
12-Lead ECG	X	X	X	-	X	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	X
Adverse Events	X	X[b]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Prior/Concomitant Meds and Procedures	X	X[b]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Testosterone, FSH and LH[f]	-	X	-	-	-	-	-	-	-	X	-	-	-	-	-	X	-	-	-	-	-	X	-	-	-	-	-	X	-
Celgene Pregnancy Prevention Counseling Program (CPPCP)[g]	X	X[b]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Efficacy Assessments																													
BILAG 2004	X	X[b]	X	-	X	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	X
CLASI Activity	X	X	X	-	X	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	X

		Year 1															Year 2												Observational Follow-Up[i]
Visit(s) ±1 Day – for all visits[h]	0 Screening	1[a] Baseline for ATEP	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Week(s)	-6	0	1	2	4	8	12	16	20	24	28	32	36	40	44	48	52	56	60	64	68	72	76	80	84	88	92	96	100
CLASI Damage	-	X	X	-	X	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	X
Hybrid SELENA SLEDAI	X	X	X	-	X	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	X
Swollen and Tender Joint Count	-	X	X	-	X	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	X
PGA	-	X	X	-	X	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	X
Pericardial/Pleuritic Pain Scale	X	X	X	-	X	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	X
SLICC/ACR SLE Damage Index	-	X	X	-	X	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	X
CCI [redacted]																													
Fatigue VAS	-	X[b]	X	-	X	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-	-	X	-
Investigational IP																													
Dispense IP	-	X[b]	-	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-
IP Compliance	-	-	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-

HCG = beta human chorionic gonadotropin; ECG = electrocardiogram; IgG = immunoglobulin G; IgM = immunoglobulin M; IgA = immunoglobulin A; IP = investigational
product; PK = pharmacokinetics; VAS = visual analog scale; PPRMP= Pregnancy Prevention Risk Management Plans; PT=prothrombin time; INR=internationalized normalized
ratio; PTT=partial thromboplastin time; HBsAg=Hepatitis B surface antigen; CLASI=Cutaneous Lupus Area and Severity Index; PGA=physician global assessment; SLEDAI=
Systemic Lupus Erythematosus Disease Activity Index; CCI [redacted]; FSH=follicle-stimulating hormone; LH=luteinizing hormone; IRB=institutional review board.

[a] **FCBP are required to have 2 negative pregnancy tests (sensitivity of at least 25 mIU/mL) prior to starting IP. The first pregnancy test must be performed within 10 to
14 days prior to the start of IP and the second test must be performed within 24 hours of starting IP.** The subject may not receive IP until the Investigator has verified that
the results of these pregnancy tests are negative. FCBP with regular cycles must have pregnancy testing weekly for the first 28 days of study participation and then every 28
days while on study, at study discontinuation and at Day 113 and Day 169 following IP discontinuation (if urine pregnancy test is positive on Day 113, a serum pregnancy test
must be conducted to confirm result). If menstrual cycles are irregular or do not occur, the pregnancy testing must occur weekly for the first 28 days and then every 14 days
while on study, at treatment discontinuation and at 14 and 28 days following treatment discontinuation.

[b] All male and FCBP subjects must be counseled about pregnancy precautions and risks of fetal exposure as described in the Pregnancy Prevention Plan. All subjects must also be counseled against sharing investigational product and donating blood during and within 28 days of discontinuing investigational product.

[c] Collection of these analytes must occur **at the same time of day (± 1 hour)** at the Baseline (Visit 2) and Day 85 (End of Treatment or Early Termination Visit) **for males only**.
For example, if collected at the Baseline Visit at 9 AM, the Final Treatment/Early Termination Visit sample must be collected between 8 and 10 AM.

[d] On Day 1 and Day 29 PK blood samples will be collected at pre-dose (Time=0 hours), 1, 2, 3, 4, between 6 and 8 hours and 24 hours (±5 hours) after administration of IP.

[e] Subjects who discontinue treatment early should enter into the Observational Follow-up Phase. Subjects who elect to enter the ATEP (at sites which have IRB approval for the
ATEP) will not enter the Observational Follow-Up Phase and directly enter the ATEP. Those subjects who conclude their treatment at a site which does not have IRB approval
for the ATEP must enter the Observational Follow-Up Phase. Subjects who would like to enter ATEP, but whose site does not have IRB approval may enter the Observational
Follow-Up Phase and then enter the ATEP once the site's IRB approves the amendment containing the ATEP.

[f] If a subject is planning to receive a primary booster dose of pneumococcal vaccine at any time during the study, a prevaccination blood sample should be obtained to measure the prevaccination titer.