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Official Title: Phase 2, Randomized, Parallel-group, Double-blind, Placebo-controlled Study of Sonelokimab in Patients With Active Psoriatic Arthritis

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Statistical Analysis Plan (SAP)

MoonLake

Protocol Title:	Phase 2, Randomized, Parallel-group, Double-blind, Placebo-controlled Study of Sonelokimab in Patients with Active Psoriatic Arthritis
Protocol Number:	M1095-PSA-201
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On behalf of:

MoonLake Immunotherapeutics AG

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LIST OF ABBREVIATIONS

The following abbreviations will be used within this SAP.

Abbreviation	Explanation
ACR	American College of Rheumatology
ACR50	Response rate of participants achieving at least a 50% improvement in the American College of Rheumatology criteria
ACR20	Response rate of participants achieving at least a 20% improvement in the American College of Rheumatology criteria
ACR70	Response rate of participants achieving at least a 70% improvement in the American College of Rheumatology criteria
ADA	Anti-Drug Antibodies
AE	Adverse Event
AESI	Adverse Events of Special Interest
AN	Abscess and inflammatory nodule
ANCOVA	Analysis of Covariance
ATC	Anatomical Therapeutic Chemical
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BLQ	Below the Quantifiable Limit
BMI	Body Mass Index
BP	Blood Pressure
BSA	Body Surface Area
CASPAR	Classification criteria for Psoriatic Arthritis
CI	Confidence Interval
COVID-19	Coronavirus disease 2019
CRF	Case Report Form
CRO	Contract Research Organization
CRP	C-Reactive Protein
CSR	Clinical Study Report
[redacted]	
CV	Coefficient of Variation
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DBP	Diastolic Blood Pressure
DMARD	Disease-Modifying Anti-Rheumatic Drug
DSMB	Data Safety Monitoring Board
DSUR	Development Safety Update Report
ECG	Electrocardiogram

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EOT	End of Treatment
FACIT-F	Functional Assessment of Chronic Illness Therapy-Fatigue
FAS	Full Analysis Set
GLMM	Generalized linear mixed model
GM	Geometric Mean
HAQ-DI	Health Assessment Questionnaire Disability Index
hs-CRP	high sensitivity C-reactive protein
ICH	International Conference on Harmonization
IG	Immunogenicity
IHS4	International Hidradenitis Suppurativa severity score system
IMP	Investigational Medicinal Product
IRT	Interactive Response Technology
ITT	Intention-to-Treat
KM	Kaplan-Meier
LDI	Leeds Dactylitis Index
LEI	Leeds Enthesitis Index
LS	least squares
MAR	Missing at Random
max	Maximum
MCS	Mental Component Summary
MedDRA	Medical Dictionary for Regulatory Activities
min	Minimum
MMRM	Mixed Model for Repeated Measures
mNAPSI	Modified Nail Psoriasis Severity Index
nBLQ	Number of Concentrations Below the Quantifiable Limit
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
NLR	Neutrophil to Lymphocyte Ratio
NRS	Numerical Rating Scale
OR	Odds Ratio
PASI	Psoriasis Area and Severity Index
PCR	Polymerase Chain Reaction
PCS	Physical Component Summary
PDCF	Protocol Deviation Criteria Form
PhGADA	Physician's Global Assessment of Disease Activity

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PK	Pharmacokinetic
PsA	Psoriatic arthritis
PsAID	Psoriatic Arthritis Impact of Disease
PsO	Psoriasis
PT	Preferred Term
PtAAP	Patient's Assessment of Arthritis Pain
PtGADA	Patient's Global Assessment of Disease Activity
Q2W	once every 2 weeks
Q4W	once every 4 weeks
SAE	Serious Adverse Event
SAF	Safety analysis set
SAP	Statistical Analysis Plan
SBP	Systolic Blood Pressure
SC	Subcutaneous
SD	Standard Deviation
SE	Standard Error
SF-36v2	Short-Form-36 Health Survey Questionnaire-Version 2
SJC	Swollen Joint Count
SOA	Schedule of Activities
SOC	System Organ Class
SPARCC	Spondyloarthritis Research Consortium of Canada
TE	Treatment-Emergent
TEAE	Treatment-Emergent Adverse Event
TFLs	Tables, Figures and Listings
TJC	Tender Joint Count
VAS	Visual Analog Scale
WHODDE	World Health Organization Drug Dictionary Enhanced

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1 INTRODUCTION

The purpose of this Statistical Analysis Plan (SAP) is to provide detailed descriptions of the statistical methods, data derivations and data displays for study protocol M1095-PSA-201, Version Final 1.1, "Phase 2, randomized, parallel-group, double-blind, placebo-controlled study of sonelokimab in patients with active psoriatic arthritis (PsA)" dated 12 Jul 2022 for final analysis in support of the Clinical Study Report (CSR), as well as describing the outputs that will used for the sonelokimab Data Safety Monitoring Board (DSMB) and Development Safety Update Report (DSUR). The table of contents and templates for the Tables, Figures and Listings (TFLs) will be produced in a separate document.

Any deviations from this SAP will be described and justified in the CSR.

The preparation of this SAP is based on International Conference on Harmonization (ICH) E9 guidelines.

All data analyses and generation of TFLs will be performed using SAS 9.4® or higher.

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2 STUDY OBJECTIVES

2.1 Primary Objective

The primary objective of this study is to evaluate the efficacy of 3 different dose regimens of sonelokimab (120 mg once every 2 weeks [Q2W], 60 mg Q2W and 60 mg once every 4 weeks [Q4W]) compared with placebo in the treatment of participants with active PsA.

2.2 Secondary Objectives

The secondary objectives of this study are as follows:

- To evaluate the safety and tolerability of 3 different dose regimens of sonelokimab (120 mg Q2W,60 mg Q2W and 60 mg Q4W) compared with placebo in the treatment of participants with active PsA.
- To assess the pharmacokinetics (PK) and immunogenicity (IG) of 3 different dose regimens of sonelokimab (120 mg Q2W, 60 mg Q2W and 60 mg Q4W) in the treatment of participants with active PsA.

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3 STUDY DESIGN

3.1 General Study Design

This is a phase 2, multi-center, randomized, parallel-group, double-blind, placebo-controlled study evaluating the efficacy, safety, PK and IG of sonelokimab in participants with active PsA. This study also has an active reference arm of adalimumab treatment; however, no formal comparison of sonelokimab vs adalimumab is planned.

For US participants, the study includes a screening period of up to 28 days, a 12-week treatment period (Part A) and an 8-week safety follow-up period after the administration of the last dose, which is scheduled to be administered at Week 10. An end of treatment (EOT) visit will be performed at Week 12. A safety follow-up visit will be performed 8 weeks (±7 days) after the administration of the last dose of study treatment. For non-US participants, the study will include screening period of up to 28 days, a treatment period of up to 24 weeks, and a safety follow-up period of 8 weeks after the last dose of study treatment. The treatment period will be divided into 2 parts: Part A (from baseline to Week 12) and Part B (from Week 12 to Week 24). The overall treatment period (Part A+B) will be from baseline to Week 24. The overall treatment period (Part A+B) will be from baseline to Week 24. The final dose of study treatment is scheduled to occur at Week 22. An End of Treatment (EOT) visit will be performed at Week 24. A safety follow-up visit will be performed 8 weeks (±7 days) after the administration of the final dose of study treatment.

On the first day of the Part A (Day 1/Week 0), eligible participants will be randomized 1:1:1:1:1 to one of 5 treatment arms as described in Figure 1.

Randomization will be stratified by sex (Male/Female) and exposure to biologic agents prior to the Screening Visit (Yes/No). The total number of participants with previous use of biologic agents will be capped at 30%.

Dosing in the sonelokimab arms will continue through Week 8. Adalimumab will be given through Week 10. All treatment arms will receive placebo as required to maintain the blinding of the study. The Part A treatment period will end at Week 12 when the primary efficacy analysis will be performed, comparing each of the sonelokimab treatment arms (sonelokimab 120 mg Q2W, sonelokimab 60 mg Q2W, sonelokimab 60 mg Q4W) vs placebo.

At the beginning of Part B (Week 12) TJC68 and SJC66 response will be assessed in all participants. A responder is defined as a participant who achieves at least a 20% reduction in each of the TJC68 and SJC66 assessments at Week 12 compared with baseline. A non-responder is defined as a participant who does not achieve at least a 20% reduction in each of the TJC68 and SJC66 assessments at Week 12 compared with baseline.

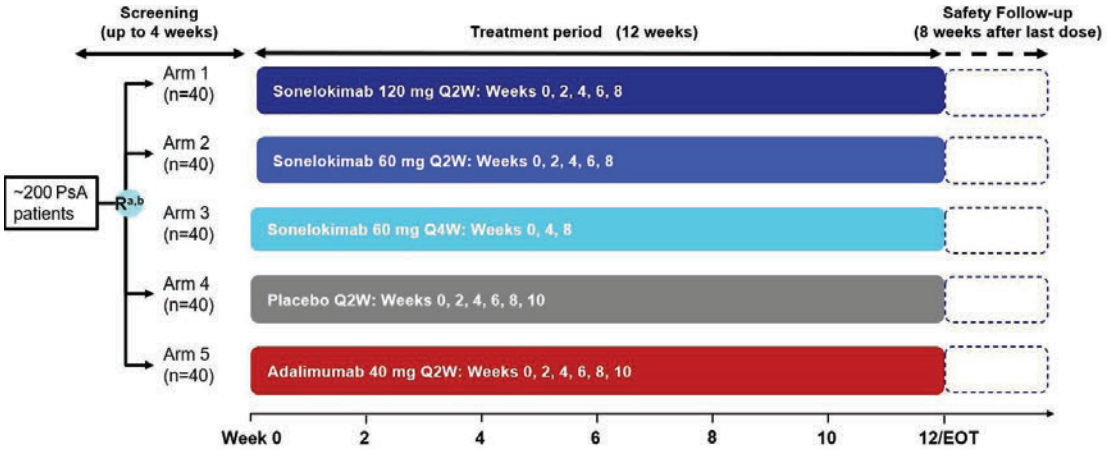
In Part B participants will be allocated to treatment based upon response at Week 12 via the Interactive Response Technology (IRT). Treatment assignments in Part A and the allocation for Part B by responders and non-responders at Week 12 are described in Figure 2 and Table 1.

On an ongoing basis, safety data will be reviewed by an independent DSMB

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The study flow chart is presented in Figure 1 and Figure 2.

Figure 1: Study Flow Chart – Part A



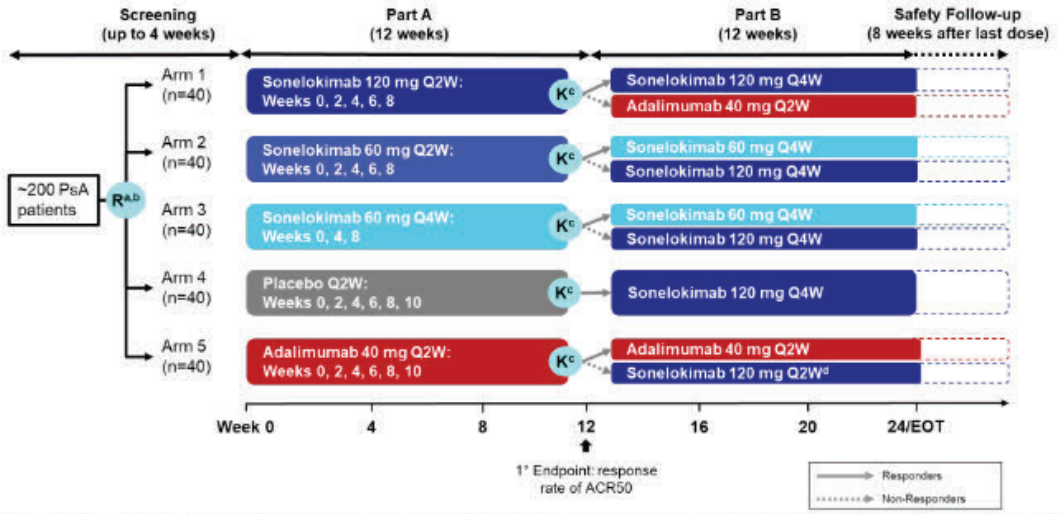
Abbreviations: EOT = End of Treatment; PsA = psoriatic arthritis; Q2W = once every 2 weeks; Q4W = once every 4 weeks; R = randomization; SFU = Safety Follow-Up.

a Randomization stratified by sex (Male/Female) and prior exposure to biologic agents (Yes/No).

b At the beginning of the treatment period at Week 0/Day 1, all eligible participants will be randomized 1:1:1:1:1.

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Figure 2: Study Flow Chart – Part A + B



Abbreviations: ACR50 = response rate of at least 50% improvement in the American College of Rheumatology criteria; EOT = End-of-Treatment; IRT = Interactive Response Technology; K = crossover; PBO = placebo; PsA = psoriatic arthritis; Q2W = once every 2 weeks; Q4W = once every 4 weeks; R = randomization; SC = subcutaneous; SJC = swollen joint count; TJC = tender joint count.

a Randomization stratified by sex (Male/Female) and prior exposure to biologic agents (Yes/No).

b At the beginning of the treatment period at Week 0/Day 1, all eligible participants will be randomized 1:1:1:1:1.

c A responder is defined as a participant who achieves at least a 20% reduction in each of the TJC68 and SJC66 assessments at Week 12 compared with baseline. A non-responder is defined as a participant who does not achieve at least a 20% reduction in each of the TJC68 and SJC66 assessments at Week 12 compared with baseline. Treatment assignments in Part B will be allocated via the IRT based upon response at Week 12 as indicated in the study design diagram.

d In Part B non-responders in Arm 5 will receive sonelokimab 120 mg Q2W with SC injections at Weeks 12, 14, 16, 18, and 20.

3.2 Randomization and Blinding

3.2.1 Randomization – Part A

Randomization will take place on Day 1/Week 0 after confirmation that the participant continues to meet the inclusion/exclusion criteria. Participants will be randomized 1:1:1:1:1 to one of 5 treatment arms, stratified by sex and exposure to biologic agents prior to the screening visit.

The IRT will be responsible for the allocation of unique identification numbers to individual participants.

3.2.2 Treatment allocation – Part B

At the beginning of Part B (Week 12) TJC68 and SJC66 response will be assessed in all participants. A responder is defined as a participant who achieves at least a 20% reduction in each of the TJC68 and SJC66 assessments at Week 12 compared with baseline. A non-responder is defined as a participant who does not achieve at least a 20% reduction in each of the TJC68 and SJC66 assessments at Week 12 compared with baseline.

In Part B participants will be allocated to treatment based upon response at Week 12 via the IRT.

In Part B, the participants and investigators will remain double-blinded to participant treatment. Blinding of participants and investigators will be maintained in the same manner as in Part A.

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3.2.3 Maintenance of Blinding

The blind will be maintained by the use of sonelokimab and matched placebo. The prefilled syringes used for all sonelokimab and placebo doses will be identical in appearance. The adalimumab injector will be different in appearance from syringes used for sonelokimab and placebo. However, the study will be blinded at the carton level. The outer packaging will be labelled in a blinded manner with no indication of the syringe contents (sonelokimab, placebo or adalimumab). Participants will be asked to wear an eye mask for all injections.

The primary analysis of 12-week data will occur at the completion of Part A while the study is still ongoing. All sponsor personnel will remain blinded until Week 12. No unblinded participant-level data will be supplied to the study sites until the final database lock after the conclusion of the study globally.

A DSMB will be setup to review the benefit-risk profile of sonelokimab and to independently safeguard the interests of participants in the studies and to enhance the integrity and credibility of the study. Members of the DSMB will be unblinded to study treatment as will the contract research organization (CRO) unblinded statistician and programmer to support the generation of unblinded outputs for the DSMB review. To maintain the blind, the CRO unblinded statistician and programmer will work in a secure environment not accessible to the CRO study team.

Laboratory personnel performing the bioanalytical PK sample analysis may receive an open randomization list to enable analysis of relevant samples. In addition, a PK analyst and modeling/simulation scientist may receive an open randomization list to enable preparation of modeling/simulation activities. These individuals will not interact with site or CRO personnel.

3.3 Study Treatments and Assessments

For the US participants, the planned study duration for individual participants will be up to 22 weeks, including a screening period of up to 4 weeks, a 12-week treatment period and a 8-week safety follow-up period after the administration of the last dose, which is scheduled to be administered at Week 10.

For the Non-US participants, the planned study duration for individual participants will be up to 34 weeks, including a screening period of up to 4 weeks, a 24-week treatment period, and an 8-week safety follow-up period after the administration of the last dose, which is scheduled to be administered at Week 22.

Randomized treatment assignment in Part A are:

- Arm 1: Sonelokimab 120 mg Q2W,
- Arm 2: Sonelokimab 60 mg Q2W,
- Arm 3: Sonelokimab 60 mg Q4W,
- Arm 4: Placebo,
- Armm 5: Adalimumab 40 mg Q2W.

Treatment Allocation in Part B Following Response Assessment at Week 12 are:

Table 1: Treatment Allocation in Part A+B

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Treatment Assignment in Part A	Treatment Allocation in Part B (Based Upon Response at Week 12)	
	Responder	Non-responder
Arm 1: Sonelokimab 120 mg Q2W	Sonelokimab 120 mg Q4W	Adalimumab 40 mg Q2W
Arm 2: Sonelokimab 60 mg Q2W	Sonelokimab 60 mg Q4W	Sonelokimab 120 mg Q4W
Arm 3: Sonelokimab 60 mg Q4W	Sonelokimab 60 mg Q4W	Sonelokimab 120 mg Q4W
Arm 4: Placebo	Sonelokimab 120 mg Q4W	Sonelokimab 120 mg Q4W
Arm 5: Adalimumab 40 mg Q2W	Adalimumab 40 mg Q2W	Sonelokimab 120 mg Q2W

3.3.1 Sonelokimab

Sonelokimab drug product is supplied as a fixed-dose, prefilled syringe to be administered via subcutaneous (SC) injection. Syringes and cartons will be supplied in a blinded manner.

Sonelokimab will be administered by a site-approved, study treatment administrator, who is unblinded. Blinded study personnel will not be in attendance while study treatment is being prepared or administered.

In Part A, the 3 sonelokimab treatment arms are as follows:

- Arm 1 (sonelokimab 120 mg Q2W): Sonelokimab 120 mg will be given as SC injection at Weeks 0, 2, 4, 6 and 8. Participants will receive a placebo injection at Week 10 to maintain the blind;
- Arm 2 (sonelokimab 60 mg Q2W): Sonelokimab 60 mg will be given as SC injection at Weeks 0, 2, 4, 6 and 8. Participants will receive a placebo injection at Week 10 to maintain the blind;
- Arm 3 (sonelokimab 60 mg Q4W): Sonelokimab 60 mg will be given as SC injection at Weeks 0, 4 and 8. Participants will receive a placebo injection at Weeks 2, 6 and 10 to maintain the blind.

In Part B, after allocation of responders and non-responders, the sonelokimab treatment arms are as follows:

- Responders from Arm 1, non-responders from Arm 2, non-responders from Arm 3, and participants from Arm 4 will receive sonelokimab 120 mg Q4W until Week 20. Placebo injections will be given at Weeks 14, 18, and 22 to maintain the blind;
- Responders from Arm 2 and responders from Arm 3 will receive sonelokimab 60 mg Q4W until Week 20. Placebo injections will be given at Weeks 14, 18, and 22 to maintain the blind;

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- Non-responders in Arm 5 will receive sonelokimab 120 mg Q2W with SC injections at Weeks 12, 14, 16, 18, and 20. Participants will receive a placebo injection at Week 22 to maintain the blind.

3.3.2 Placebo

Placebo will be identical in appearance and packaging to sonelokimab in a fixed-dose, prefilled syringe to be administered via SC injection.

As with the administration of sonelokimab, placebo will be administered by a site-approved, study treatment administrator, who is unblinded. Blinded study personnel will not be in attendance while study treatment is being prepared or administered.

During Part A, for participants randomized to Arm 4, placebo will be given SC every 2 weeks, with injections at Weeks 0, 2, 4, 6, 8 and 10.

3.3.3 Adalimumab

Adalimumab will be provided in prefilled syringes (40 mg) as sterile solution for SC injection. Adalimumab syringes will be relabelled and repackaged to facilitate maintenance of the study blinding.

Adalimumab will be administered by a site-approved, study treatment administrator, who is unblinded. Blinded study personnel will not be in attendance while study treatment is being prepared or administered.

During Part A, for participants randomized to Arm 5, adalimumab will be given as 40 mg SC every 2 weeks, with injections at Weeks 0, 2, 4, 6, 8 and 10 in accordance with the approved labelling.

In Part B, non-responders from Arm 1 and responders from Arm 5 will receive adalimumab 40 mg Q2W administered by SC injection at Weeks 12, 14, 16, 18, 20, and 22.

A detailed description of procedures and assessments to be conducted during this study is summarized in the Schedule of Activities (SOA) in Table 1 of the protocol.

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4 STUDY ENDPOINTS

4.1 Primary Efficacy Endpoint

The primary efficacy endpoint of this study is response rate of at least 50% improvement in the American College of Rheumatology (ACR50) response criteria at Week 12 compared with baseline.

4.2 Secondary Efficacy Endpoints

The key secondary efficacy endpoints of this study are:

- ACR20 response rate at Week 12 compared with baseline;
- Psoriasis Area and Severity Index (PASI) 90 at Week 12 compared with baseline in the subgroup of participants with psoriasis (PsO) involving at least 3% body surface area (BSA) at baseline.

The other secondary endpoints this study are:

- Response rate compared with baseline at specified timepoints other than Week 12 for the following:
  - ACR20;
  - ACR50
  - PASI90.
- Response rate compared with baseline at specified timepoints for the following
  - ACR70;
  - Minimal disease activity at Week 12, defined as meeting 5 of the 7 following criteria:
    - Tender joint count (TJC) 68 ≤1;
    - Swollen joint count (SJC) 66 ≤1;
    - PASI ≤1 or PsO affecting ≤1% of BSA;
    - Patient's Assessment of Arthritis Pain (PtAAP) ≤15 on a 0 to 100 visual analog scale (VAS);
    - Patient's Global Assessment of Disease Activity (PtGADA) ≤20 on a 0 to 100 VAS;
    - Health Assessment Questionnaire Disability Index (HAQ-DI) ≤0.5;
    - Leeds Enthesitis Index (LEI) ≤1.
  - PASI75 at specified timepoints compared with baseline (in the subgroup of participants with PsO involving at least 3% BSA at baseline);
  - PASI100 at specified timepoints compared with baseline (in the subgroup of participants with PsO involving at least 3% BSA at baseline);

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- Response rate of at least 50% improvement compared with baseline in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI);

[redacted]

- The change from baseline at specified timepoints for the following:
  - TJC68;
  - SJC66;
  - Enthesitis evaluation (LEI and Spondyloarthritis Research Consortium of Canada [SPARCC] enthesitis index);
  - Leeds Dactylitis Index (LDI);
  - Modified Nail Psoriasis Severity Index (mNAPSI);
  - High sensitivity C-reactive protein (hs-CRP);
  - PtGADA;
  - Physician's Global Assessment of Disease Activity (PhGADA);
  - Psoriatic Arthritis Impact of Disease (PsAID)-12;
  - PtAAP;
  - HAQ-DI;
  - Functional Assessment of Chronic Illness Therapy for Fatigue (FACIT-Fatigue);
  - Short-Form-36 Health Survey Questionnaire-Version 2 (SF-36v2) Mental Component Summary (MCS);
  - SF-36v2 Physical Component Summary (PCS);
  - BASDAI;

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4.3 Pharmacokinetic and Immunogenicity Endpoints

The PK and IG endpoints of this study are:

- PK of sonelokimab (trough levels);
- Anti-drug antibodies (ADAs).

[redacted]

4.5 Safety Endpoints

The safety endpoints of this study are:

- Incidence, relatedness, severity and seriousness of adverse events (AEs);
- Withdrawal due to AEs;
- Clinically relevant abnormalities in vital signs (blood pressure [BP] and heart rate) and body weight;
- Standard 12-lead electrocardiogram (ECG) intervals (RR, PR, QRS, QT and QT intervals corrected for heart rate using Bazett's and Fridericia's formulas [QTcB and QTcF, respectively]) including clinically relevant abnormalities in ECG variables;
- Clinically relevant abnormalities in clinical laboratory variables (hematology, biochemistry, and urinalysis).

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5 STUDY ESTIMANDS

5.1 Estimand for the Primary Endpoint

Attribute	Details
Treatments	Sonelokimab at 3 different doses: • sonelokimab 120 mg Q2W or • sonelokimab 60 mg Q2W or • sonelokimab 60 mg Q4W
Target Population	• Adults with a confirmed diagnosis of PsA per the 2006 CASPAR [Taylor W. et al., 2006] with symptoms for ≥6 months prior to the Screening Visit • Analysis Set: Full Analysis Set (FAS)
Endpoint	Percentage of participants achieving ACR50 at Week 12 compared with baseline.
Population-level summary	The primary estimator will be the improvement compared to placebo over the 12-week based on ACR50.
Intercurrent events and strategies to handle those	• Use of prohibited concomitant medication (Section 10.5.1 of protocol): participants will be analyzed as a treatment failure after taking prohibited medication, i.e., non-responder imputation will be performed after the first episode of prohibited medication for all future assessments (composite strategy); • Withdrawal from treatment due to any reason (Section 9.6 of protocol): participants will be considered non-responders to treatment if they discontinue the study prior to the Week 12 (composite strategy); • Study treatment non-adherence (missing doses) or drug administration error: participants will be analyzed in the same way as if the event had occurred or not (treatment policy strategy).

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5.2 Sensitivity Estimand for the Primary Endpoint

The first sensitivity estimand will include data from participants in the target population of the primary estimand plus data collected after the withdrawal of study treatment through Week 12 from participants who discontinue study treatments prior to Week 12 for reasons other than lack of efficacy or response.

Attribute	Details
Treatments	Sonelokimab at 3 different doses: • sonelokimab 120 mg Q2W or • sonelokimab 60 mg Q2W or • sonelokimab 60 mg Q4W
Target Population	• Adults with a confirmed diagnosis of PsA per the 2006 CASPAR [Taylor W. et al., 2006] with symptoms for ≥6 months prior to the Screening Visit • Analysis Set: Full Analysis Set (FAS)
Endpoint	– Percentage of participants achieving ACR50, i.e., at least 50% improvement in the ACR response criteria at Week 12 compared with baseline.
Intercurrent events and strategies to handle those	• Use of prohibited concomitant medication (Section 10.5.1 of protocol): participants will be analyzed as a treatment failure after taking prohibited medication, i.e., non-responder imputation will be performed after the first episode of prohibited medication for all future assessments (composite strategy); • Withdrawal from treatment due to lack of efficacy or adverse event (Section 9.6 of protocol): participants will be considered non-responders to treatment if they discontinue the study prior to the Week 12 (composite strategy); • Withdrawal from treatment due to any reason other than lack of efficacy or adverse event (Section 9.6 of protocol): participants will continue to be followed and use their observed Week 12 Visit (treatment policy strategy). Any missing data for participants who do not have a Week 12 visit will be assumed to be missing at random; • Study treatment non-adherence (missing doses) or drug administration error: participants will be analyzed in the same

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	way as if the event had occurred or not (treatment policy strategy).

The second sensitivity estimand will include data from participants in the target population of the primary estimand targeting the treatment policy estimand such that the difference in response between treatments are analysed regardless of prohibited medication and withdrawal from treatment.

Attribute	Details
Treatments	Sonelokimab at 3 different doses: • sonelokimab 120 mg Q2W or • sonelokimab 60 mg Q2W or • sonelokimab 60 mg Q4W
Target Population	• Adults with a confirmed diagnosis of PsA per the 2006 CASPAR [Taylor W. et al., 2006] with symptoms for ≥6 months prior to the Screening Visit • Analysis Set: Full Analysis Set (FAS)
Endpoint	– Percentage of participants achieving ACR50, i.e., at least 50% improvement in the ACR response criteria at Week 12 compared with baseline.
Intercurrent events and strategies to handle those	• Use of prohibited concomitant medication (Section 10.5.1 of protocol): observed data after taking prohibited medication will used in the analysis (treatment policy strategy); Any missing data for participants who do not have a Week 12 visit will be assumed to be missing at random; • Withdrawal from treatment for any reason (Section 9.6 of protocol): participants will continue to be followed and use their observed Week 12 Visit (treatment policy strategy). Any missing data for participants who do not have a Week 12 visit will be assumed to be missing at random; • Study treatment non-adherence (missing doses) or drug administration error: participants will be analyzed in the same way as if the event had occurred or not (treatment policy strategy).

5.3 Estimand for the Key Secondary Endpoints

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Attribute	Details
Treatments	Sonelokimab at 3 different doses: • sonelokimab 120 mg Q2W or • sonelokimab 60 mg Q2W or • sonelokimab 60 mg Q4W
Target Population	• Adults with a confirmed diagnosis of PsA per the 2006 CASPAR [Taylor W. et al., 2006] with symptoms for ≥6 months prior to the Screening Visit; • Analysis Set: FAS
Endpoint	The key secondary endpoints are as follows: • ACR20 response rate at Week 12 compared with baseline; • PASI90 at Week 12 compared with baseline in the subgroup of participants with PsO involving at least 3% BSA at baseline.
Population-level summary	The primary estimator will be the improvement compared to placebo over the 12-week based on the endpoint of interest.
Intercurrent events and strategies to handle those	• Use of prohibited concomitant medication (Section 10.5.1 of protocol): participants will be analyzed as a treatment failure after taking prohibited medication, i.e., non-responder imputation will be performed after the first episode of prohibited medication for all future assessments (composite strategy); • Withdrawal from treatment due to any reason (Section 9.6 of protocol): participants will be considered non-responders to treatment if they discontinue the study prior to the Week 12 visit due to any reason (composite strategy); • Study treatment non-adherence (missing doses) or drug administration error: participants will be analyzed in the same way as if the event had occurred or not (treatment policy strategy).

5.4 Sensitivity Estimand for the Key Secondary Endpoints

The first sensitivity estimand will include data from participants in the target population of the key secondary estimand plus data collected after the withdrawal of study treatment through Week 12 from

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participants who discontinue study treatments prior to Week 12 for reasons other than lack of efficacy or response.

Attribute	Details
Treatments	Sonelokimab at 3 different doses: • sonelokimab 120 mg Q2W or • sonelokimab 60 mg Q2W or • sonelokimab 60 mg Q4W
Target Population	• Adults with a confirmed diagnosis of PsA per the 2006 CASPAR [Taylor W. et al., 2006] with symptoms for ≥6 months prior to the Screening Visit; • Analysis Set: FAS
Endpoint	The key secondary endpoints are as follows: • ACR20 response rate at Week 12 compared with baseline; • PASI90 at Week 12 compared with baseline in the subgroup of participants with PsO involving at least 3% BSA at baseline.
Intercurrent events and strategies to handle those	• Use of prohibited concomitant medication (Section 10.5.1 of protocol): participants will be analyzed as a treatment failure after taking prohibited medication, i.e., non-responder imputation will be performed after the first episode of prohibited medication for all future assessments (composite strategy); • Withdrawal from treatment due to lack of efficacy or adverse event (Section 9.6 of protocol): participants will be considered non-responders to treatment if they discontinue the study prior to the Week 12 visit (composite strategy); • Withdrawal from treatment due to any reason other than lack of efficacy or adverse event (Section 9.6 of protocol): participants will continue to be followed and use their observed Week 12 Visit (treatment policy strategy). Any missing data for participants who do not have a Week 12 visit will be assumed to be missing at random; • Study treatment non-adherence (missing doses) or drug administration error: participants will be analyzed in the same

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	way as if the event had occurred or not (treatment policy strategy).

The second sensitivity estimand will include data from participants in the target population of the primary estimand targeting the treatment policy estimand such that the difference in response between treatments are analysed regardless of prohibited medication and withdrawal from treatment.

Attribute	**Details**
Treatments	Sonelokimab at 3 different doses: • sonelokimab 120 mg Q2W or • sonelokimab 60 mg Q2W or • sonelokimab 60 mg Q4W
Target Population	• Adults with a confirmed diagnosis of PsA per the 2006 CASPAR [Taylor W. et al., 2006] with symptoms for ≥6 months prior to the Screening Visit • Analysis Set: Full Analysis Set (FAS)
Endpoint	The key secondary endpoints are as follows: – ACR20 response rate at Week 12 compared with baseline; – PASI90 at Week 12 compared with baseline in the subgroup of participants with PsO involving at least 3% BSA at baseline.
Intercurrent events and strategies to handle those	• Use of prohibited concomitant medication (Section 10.5.1 of protocol): observed data after taking prohibited medication will used in the analysis (treatment policy strategy); Any missing data for participants who do not have a Week 12 visit will be assumed to be missing at random; • Withdrawal from treatment for any reason (Section 9.6 of protocol): participants will continue to be followed and use their observed Week 12 Visit (treatment policy strategy). Any missing data for participants who do not have a Week 12 visit will be assumed to be missing at random; • Study treatment non-adherence (missing doses) or drug administration error: participants will be analyzed in the same

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	way as if the event had occurred or not (treatment policy strategy).

5.5 Sample Size and power

The sample size calculation is based on the primary efficacy endpoint (i.e., ACR50 response rate at Week 12 compared with baseline) with the primary comparisons of interest being:

sonelokimab 120 mg Q2W (Arm 1) vs placebo (Arm 4), sonelokimab 60 mg Q2W (Arm 2) vs placebo (Arm 4) and sonelokimab 60 mg Q4W (Arm 3) vs placebo (Arm 4) and determined based on assumed ACR50 response rates as follows:

- 40% with each sonelokimab dose regimen;
- 10% with placebo.

The estimated response rates for sample size were based on past IL-17 inhibitors for the treatment of participants with PsA. The Cosentyx FUTURE 2 study showed that ACR50 was achieved in 35% of secukinumab 300 mg and 37% of secukinumab 150 mg, vs 6% in the placebo arm [McInnes I.B. et al., 2015].

A sample size of n = 40 participants in each of the sonelokimab 120 mg Q2W, sonelokimab 60 mg Q2W, sonelokimab 60 mg Q4W and placebo arms (therefore, 160 participants in total) results in a power of more than 80%, while assuming an overall 2-sided alpha of 0.025, a placebo ACR50 response rate of 10% and a difference in ACR50 response rate of 30% between placebo and each sonelokimab dose regimen. An additional 40 participants will be randomized in the adalimumab arm. The adalimumab treatment will be used as an active reference arm, however, no formal comparison of sonelokimab or placebo vs adalimumab is planned.

Eligible participants will be randomized in a 1:1:1:1:1 ratio to sonelokimab 120 mg Q2W (Arm 1), sonelokimab 60 mg Q2W (Arm 2), sonelokimab 60 mg Q4W (Arm 3), placebo (Arm 4) or adalimumab 40 mg Q2W (Arm 5). The total proportion of participants with previous use of biologic agents will be capped at 30%.

Due to the use of the FAS with non-responder imputation, no accounting for dropout is required, therefore a total of approximately 200 participants will be randomized.

All calculations were performed in nQuery® Software version 8.5.1.0.

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6 ANALYSIS POPULATIONS

6.1 Part A

6.1.1 Enrolled Set

The enrolled set is defined as all participants who signed an informed consent.

6.1.2 Safety Analysis Set (SAF)

The safety analysis set (SAF) is defined as all randomized participants who received at least one dose of study treatment. Participants will be analyzed based on the treatment that they actually received, regardless of the treatment they are randomized to.

The SAF will be used for all safety analyses related to the Part A and Part A+B.

6.1.3 Full Analysis Set (FAS)

The FAS is defined as all randomized participants. Participants will be analyzed in accordance with the intention-to-treat (ITT) principle, i.e., based on randomized treatment, irrespective of the treatment they actually received.

The FAS will be used for all efficacy analyses on efficacy endpoints related to the Part A and some Part A+B analyses and will serve as the primary analysis set.

6.1.4 Immunogenicity Analysis Set (IG Analysis Set)

The IG analysis set is defined as all participants who received at least one dose of sonelokimab and who have at least 1 sample obtained for the detection of antibodies to sonelokimab.

In the IG analyses, participants will be analyzed according to the treatment they actually received, regardless of the treatment they are randomized to.

The IG analysis set will be used for all immunogenicity analyses related to the Part A and A+B.

6.1.5 Pharmacokinetic Analysis Set (PK Analysis Set)

The PK analysis set is defined as all participants who received at least one complete dose of sonelokimab and had at least 1 valid blood sample drawn for PK analysis after their first dose of sonelokimab.

In the PK analyses, participants will be analyzed according to the treatment they actually received, regardless of the treatments they are randomized to.

The PK analysis set will be used for all PK analyses related to the Part A and A+B.

6.2 Part B

6.2.1 Safety Analysis Set (SAF-B)

The SAF-B is defined as all randomized participants who received at least one dose of study treatment during Part B. Participants will be analyzed based on the treatment that they actually received, regardless of the treatments they are randomized to.

The SAF-B will be used for all safety analyses related to Part B.

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6.2.2 Full Analysis Set (FAS-B)

The FAS-B is defined as all randomized participants who are assigned treatment for Part B. Participants will be analyzed in according to the intention-to-treat principle, i.e., based on assigned treatment for Part B, irrespective of the treatment they actually received.
The FAS-B will be used for some efficacy analyses on endpoints related to the Part B.

6.3 Protocol Deviations/Violations and Exclusions from Analysis Sets

All protocol deviations will be identified prior to their associated database lock for any intentional or unintentional change or noncompliance with the approved protocol procedures or requirements as mentioned in protocol deviation criteria form (PDCF).

All protocol deviations will be classified as key or non-key and will be reviewed to determine their impact on the primary and key secondary endpoints during a data review meeting.

All exclusions from an analysis population will be documented prior to unblinding, exceptions to this will be protocol deviations based upon unblinded data (e.g PK analysis set) which will documented prior to release of the final outputs.

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7 STATISTICAL CONSIDERATIONS AND ANALYSIS

7.1 Derived Variables

The below table provides the list of derived variables for demographic and baseline characteristics, various duration derivations, drug compliance, baseline derivations and other important derivations applicable for this study.

Variables	Formula
Demographic and Baseline Characteristics	
Body mass index (BMI) (kg/m^2)	weight (kg)/[height (m)^2] Note: 1 lbs = 0.45359237 kg 1 in = 2.54 cm
Duration of PsA (Year)	[(Date of first study drug administration – Date of Initial diagnosis) + 1]/ 365.25 Details for imputing missing or partial start and/or stop dates of PsA are described in Section 7.3.2.
Derivation of Duration	
Study day at any visit	Date of interest – date of first dose of study drug. One day is added if this difference is ≥ 0.
Duration of Exposure (Days) for Part A	Date of Week 12 or EOT visit, whichever occurs first – Date of first randomized study medication intake at baseline + 1.
Duration of Exposure (Days) for Part B	Date of Week 24 or EOT visit, whichever occurs first – Date of first study medication intake for Part B + 1
Duration of Exposure (Days) for Part A+B	Date of Week 24 or EOT visit, whichever occurs first – Date of first sonelokimab intake + 1
Drug Compliance	
Compliance	Compliance (%) = 100 * (number of visits with treatment received/ number of visits with treatment planned) during the participant's participation in the study. Compliance is calculated for Part A, Part B and Part A+B using the number of visits with treatment received during the respective Part and planned number in each Part also.
Baseline Derivations	
Baseline definition	Baseline will be defined as the last non-missing measurement prior to first dose of study medication in Part A For baseline characteristics table, if a subject is randomized and not treated then the latest record will be defined as the baseline.
Baseline definition for ADA	The last sample prior to the first dose of sonelokimab

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Change from baseline	The value at each time point minus the value at baseline
Other Derivations	
Definition for the derived efficacy parameters are given in the respective efficacy analysis sections.	

7.2 Visit Windows

Visit windows will be used for all scheduled assessments. To allow for unscheduled and discontinuation assessments, the data will be summarized using the assessment (whether reported as a scheduled or unscheduled visit) closest to the nominal visit date, calculated from the first day of dosing. The visit result will be missing if no assessment was reported within the specified visit window around the scheduled date. If two assessments are equidistant from a scheduled visit, the earlier of the two will be used.

The visit windows will be calculated by bisecting the scheduled visit assessments. The upper limit of each window will be the mean of the two adjacent planned study days, rounded down to the nearest integer. The lower limit of each window will be the upper limit of the preceding window plus one, except for the first post-treatment visit which will start at 2.

Visit Windows for [redacted] PsAID-12, BASDAI, [redacted] PASI, LDI, Enthesitis evaluation (LEI+SPARCC enthesitis index)

Nominal Week	Nominal Study Day	Visit Window
0	1	All assessments prior to the start of study treatment
4	29	Day 2 – 43
8	57	Day 44 – 71
12	85	Day 72 – 99
16	113	Day 100 – 127
20	141	Day 128 - 155
24	169	Day 156+

Visit Windows for Safety Laboratory Testing (hematology and chemistry) and ESR

Nominal Week	Nominal Study Day	Visit Window
0	1	All assessments prior to the start of study treatment
4	29	Day 2 – 43
8	57	Day 44 – 71
12	85	Day 72 - 99
16	113	Day 100 - 127
20	141	Day 128 - 155

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Visit Windows for Safety Laboratory Testing (hematology and chemistry) and ESR

Nominal Week	Nominal Study Day	Visit Window
24	169	Day 156 - 190
Safety Follow-up*	211	Day 191+

*Subjects who discontinued early, a safety follow-up period of 8 weeks after the last dose of study treatment

Visit Windows for Safety Laboratory Testing (Urinalysis)

Nominal Week	Nominal Study Day	Visit Window
0	1	All assessments prior to the start of study treatment
4	29	Day 2 – 57
12	85	Day 58 - 99
16	113	Day 100 - 141
24	169	Day 142 - 190
Safety Follow-up*	211	Day 191+

*Subjects who discontinued early, a safety follow-up period of 8 weeks after the last dose of study treatment

Visit Windows for PtGADA, PtAAP, HAQ-DI, hs-CRP, PhGADA, TJC68 and SJC66

Nominal Week	Nominal Study Day	Visit Window
0	1	All assessments prior to the start of study treatment
2	15	Day 2 – 22
4	29	Day 23 – 43
8	57	Day 44 – 71
12	85	Day 72 – 92
14	99	Day 93 - 106
16	113	Day 107 - 127
20	141	Day 128 - 155
24	169	Day 156+

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Visit Windows for ADA and PK Sampling

Nominal Week	Nominal Study Day	Visit Window
0	1	All assessments prior to the start of study treatment
2	15	Day 2 – 22
4	29	Day 23 – 43
8	57	Day 44 – 71
12	85	Day 72 – 92
14	99	Day 93 - 106
16	113	Day 107 - 127
20	141	Day 128 - 155
24	169	Day 156 - 190
Safety Follow-up*	211	Day 191+

*Subjects who discontinued early, a safety follow-up period of 8 weeks after the last dose of study treatment

Visit Windows for SF-36v2, FACIT-Fatigue

Nominal Week	Nominal Study Day	Visit Window
0	1	All assessments prior to the start of study treatment
4	29	Day 2 – 57
12	85	Day 58 - 99
16	113	Day 100 - 127
20	141	Day 128+

Visit Windows for ECG

Nominal Week	Nominal Study Day	Visit Window
0	1	All assessments prior to the start of study treatment
12	85	Day 2 – 148
Safety Follow-up*	211	149+

*Subjects who discontinued early, a safety follow-up period of 8 weeks after the last dose of study treatment

Visit Windows for BSA and mNAPSI

DocUUID : 3213b5be-8d63-4760-bea6-7e3ec175e71e

Nominal Week	Nominal Study Day	Visit Window
0	1	All assessments prior to the start of study treatment
12	85	Day 2 – 127
24	169	128+

Visit Windows for Vital Signs

Nominal Week	Nominal Study Day	Visit Window
0	1	All assessments prior to the start of study treatment
2	15	Day 2 – 22
4	29	Day 23 – 36
6	43	Day 37 – 50
8	57	Day 51 – 64
10	71	Day 65 – 78
12	85	Day 79 – 92
14	99	Day 93 - 106
16	113	Day 107 - 120
18	127	Day 121 - 134
20	141	Day 135 - 148
22	155	Day 149 - 162
24	169	Day 163 - 190
Safety Follow-up*	211	Day 191+

*Subjects who discontinued early, a safety follow-up period of 8 weeks after the last dose of study treatment

7.3 Handling of Missing Data and Randomization Stratification Errors

7.3.1 Missing Data Analysis Methods

Missing data in this study may result from participants discontinuing from the study prematurely or missing intermediate visits or selected assessments while remaining on study. Every reasonable effort will be made to obtain the protocol-required data for all study assessments that are scheduled for all participants who have been enrolled.

Dichotomous Efficacy Endpoints

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For all dichotomous endpoints, a non-responder imputation method will be used for the primary analysis. Participants will be considered non-responders if:

- They discontinue the study prior to the Week 12 visit for Part A or prior to the Week 24 visit for Part B and Part A+B (due to any reason). All future visits following the discontinuation will be imputed, or
- Have missing data for the endpoint of interest at baseline or at any intermediate time points. All visits with a missing assessment will be imputed, or
- Take prohibited protocol medication prior to the Week 12 visit for Part A or Week 24 visit for Part B and Part A+B. All future visits following the start date of the prohibited medication will be imputed.

In addition, two sensitivity approaches will be used for the dichotomous primary and key-secondary endpoints for analyses data:

1. The method for handling missing data will be dependent on the reason the data are missing. If a participant has discontinued due to lack of efficacy or an adverse event or starting prohibited medication the data will be imputed as a non-response. If the data are missing for any other reason the data will not be imputed. A multiple imputation for primary and key secondary analysis will be used including all available data up to Week 12 to enable the inclusion of participants with missing data at Week 12.
2. No data will be imputed and the data analysed by visit based on the observed data only.

Continuous Efficacy Endpoints

For continuous efficacy endpoints, missing observations will not be formally imputed. Mixed Model for Repeated Measures (MMRM) analysis will be used with all available data, including participants with partial data (i.e., with missing data) in order to arrive at an estimate of the mean treatment effect. MMRM is based on the assumption of missing at random (MAR), i.e., dropout would behave similarly to other participants in the same treatment group and possibly with similar covariate values, had they not dropped out.

Unless otherwise indicated, in other cases the observed data will be used and no imputation will be performed.

Scoring Derivations

Several instruments will be used in this study to measure some underlying construct. As such, missing data in this type of instruments can occur on the item scores. Missing data will be handled as described by the author of each instrument and detailed in the relevant endpoint section, or, if no information is stated by the author, no imputation will be done and such scores (and any resultant domain/total score) will remain missing.

7.3.2 Handling of Missing or Incomplete Dates

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

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If only Day of AE start date is missing:

If the AE start year and month are the same as that for the first dose date, then:

- If the full (or partial) AE end date is NOT before the first dose date or AE end date is missing, then impute the AE start day as the day of first dose date; otherwise, impute the AE start day as 1.

If the AE start year and month are not same as that for the first dose date, then, impute the AE start day as 1.

Compare the imputed AE start date with treatment-emergent (TE) period to determine whether the AE is pre-treatment AE, treatment-emergent adverse event (TEAE) or post-treatment AE.

If Day and Month of AE start date are missing:

If AE start year = first dose year, then:

- If the full (or partial) AE end date is NOT before the first dose date or AE end date is missing, then impute the AE start Month and Day as the Month and Day of first dose date; otherwise, impute the AE start Month as January and the Day as 1.

If AE start year not same as first dose year, then, impute the AE start MONTH as January and the DAY as 1.

Compare the imputed AE start date with TE period to determine whether the AE is pre-treatment AE, TEAE or post-treatment AE.

If Year of AE start date is missing:

If the year of AE start date is missing or AE start date is completely missing, then query site with no imputation. Also compare the full (or partial) AE end date to the first dose date. If the AE end date is before the first dose date, then the AE should be considered as a pre-treatment AE. Otherwise, the AE will be considered as TEAE.

Imputation rules for missing or partial medication start/stop dates are defined below:

Missing or partial medication start date:

- If only DAY is missing, use the first day of the month.
- If DAY and Month are both missing, use the first day of the year.
- If DAY, Month and Year are all missing, use a date before the first dose date.

Missing or partial medication stop date:

- If only DAY is missing, use the last day of the month.
- If DAY and Month are both missing, use the last day of the year.
- If DAY, Month and year are all missing, then consider the medication is still ‘continuing’ and date will not be imputed.

Imputation rules for missing or partial PsA start dates are defined below:

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Missing or partial PsA start date:

- If only DAY is missing, use the first day of the month.
- If DAY and Month are both missing, use the first day of the year.
- If DAY, Month and Year are all missing, use a date before the first dose date.

7.3.3 Randomization Stratification Errors

Randomization stratification errors can occur if the incorrect Sex or Prior Biologic Use is entered in the IRT system at the time of randomization. The FAS analyses will follow the ITT principle and analyse these participants according to the randomized stratum.

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8 STATISTICAL METHODS

8.1 General Statistical Conventions

All statistical procedures will be completed using SAS version 9.4® or higher.

For continuous variables, descriptive statistics (number of observations, mean, standard deviation (SD), minimum (min), first quartile, median, third quartile and maximum (max) and 95% confidence intervals (CIs) as appropriate) will be presented. Summaries of hs-CRP and PK concentration will include the geometric mean (GM) and coefficient of variation (CV). The count of missing observations will be provided in all descriptive tables.

Categorical variables will be presented as counts and percentages with non-missing values in each category. The number of missing values will be presented as a separate category, if there is at least one missing value. Unless otherwise stated, all statistical testing will be two-sided and will be performed using a significance (alpha) level of 0.05. For all statistical analyses, p-values and 95% CIs will be provided. All sensitivity analyses will be regarded as exploratory and as such no formal adjustment for multiplicity will be made.

Number of decimal places will be presented as follow:

- continuous variables: for min and max, the decimals will be used as captured in the database; arithmetic mean, median and quartiles will be depicted with one more decimal than captured in the database; and SD will be depicted with two more decimals than captured in the database.
- categorical variables: percentages will be rounded to one decimal place and a percentage of 100% will be reported as 100%.
- the p-values will be rounded and displayed to 3 decimal places, values less than 0.001 will be displayed as ‘p<0.001’ and values higher than 0.999 will be displayed as ‘p>0.999’.

This study has two parts Part A and Part B:

Part A Analysis: For Part A, summaries and analyses will be based on the data collected from the visits Week 0 to Week 12. Unless otherwise stated, the summary statistics and analyses will be presented for the following treatment groups:

- Sonelokimab 120 mg Q2W;
- Sonelokimab 60 mg Q2W;
- Sonelokimab 60 mg Q4W;
- Placebo;
- Adalimumab.
- Total sonelokimab (safety tables only)

Part B: For Part B no statistical testing will be performed. Summary statistics will be based on the data collected from the visits Week 12 to Week 24.

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Unless otherwise stated, the summary statistics will be presented for the following treatment groups:

- Sonelokimab 120 mg Q2W→sonelokimab 120 mg Q4W;
- Sonelokimab 120 mg Q2W→adalimumab 40 mg Q2W;
- Sonelokimab 60 mg Q2W→sonelokimab 60 mg Q4W;
- Sonelokimab 60 mg Q2W→sonelokimab 120 mg Q4W;
- Sonelokimab 60 mg Q4W→sonelokimab 60 mg Q4W;
- Sonelokimab 60 mg Q4W→sonelokimab 120 mg Q4W;
- Placebo→sonelokimab 120 mg Q4W;
- Adalimumab 40 mg Q2W→adalimumab 40 mg Q2W;
- Adalimumab 40 mg Q2W→sonelokimab 120 mg Q2W.
- Total sonelokimab (safety tables only)

Part A+B: For Part A+B no statistical testing will be performed. Summary statistics will be based on the data collected from the visit Week 0 to Week 24. Part A+B tables will only be presented for adverse events.

Unless otherwise stated, the summary statistics will be presented for the following treatment groups:

- Placebo (Part A only)
- Total Sonelokimab 120mg
- Total Sonelokimab 60mg
- Total Adalimumab 40mg Q2W
- Total Sonelokimab

For the total groups they will have different subjects potentially for Part A and Part B and subjects will only have results shown for the Part when they took the relevant treatment.

All participant data, including those derived, will be presented in individual participant data listings. Unless otherwise stated, unscheduled visit results will be included in date/time chronological order, within participant listings only. All listings will be sorted by treatment group, investigational site, participant number, date/time, and visit. The treatment group as well as participant's sex, age and race will be stated on each listing. Unless otherwise stated, safety data listings will be based on SAF and efficacy data listings will be based on FAS.

8.2 Participant Disposition

The number and percentage of participants screened, randomized, randomized and treated, randomized and not treated and the number of participants in each of the analysis sets (including reasons for exclusion) separately for Part A and Part A+B (see section 7) will be summarized by treatment group on the enrolled set.

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The number and percentage of participants will also be summarized for the following participant disposition categories:

- Completed Part A, defined as completing a visit in the Week 12 visit window or a later visit
- Completed study drug for Part A, defined as received the Week 10 dose or a dose at a later visit
- Discontinued study drug in Part A
- Received study drug in Part B, defined as received a dose at Week 12 or a later visit
- Completed study drug treatment for both part A and part B per-protocol;
- Discontinued study drug earlier during Part B (including the primary reason for discontinuation);
- Completed the study at week 24;
- Completed the study including post-treatment follow-up;
- Discontinued from study early (including the reason for discontinuation).

Given data from Part A and Part B will be combined together (including participants not entering Part B), all distinct treatment groups detailed in section 9.1 from Part A and B will be presented.

The time in days to study drug discontinuation due to any reason will be displayed with plot by initial randomized treatment for the FAS during Part A. The time to last visit will be defined as the discontinuation date minus the first dose date plus one.

The plot will be repeated for Part A+B to show the time to discontinuation of sonelokimab. This will only include subjects exposed to sonelokimab in either Part A or B. The time to discontinuation will be defined as the discontinuation date minus the first sonelokimab dose date plus one Subjects who complete the treatment at Week 24 will be censored at the completion day (Week 24).

A listing of participant disposition will be provided for enrolled set.

A listing of analysis set and reasons for exclusion from the analysis set will be provided for enrolled set.

8.3 Protocol Deviations

A summary will be provided for all key protocol deviations by deviation sub-category and treatment group based on the FAS will be presented for Part A and Part A + B separately.

In addition, all protocol deviations will be listed and protocol deviations occurring due to the COVID-19 pandemic will be listed separately for FAS.

8.4 Demographics and Baseline Characteristics

All demographic and baseline characteristics data will be listed and summarized for Part A by treatment group using the FAS. Inferential statistical analysis of demographic or baseline data will not be performed.

8.4.1 Demographics

Continuous variables such as age (years) at screening collected on the case report form (CRF), height (cm), weight (kg) and BMI (kg/m^2) will be summarized using descriptive statistics.

Categorical variables such as age categories (18-64, 65-84, >84), sex, ethnicity and race will be

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summarized using counts and percentages.

Childbearing potential status, contraception methods used and reason for non-child-bearing potential status for female participants will be provided in the listing only.

8.4.2 Baseline and Disease Characteristics

The following variables will be summarized:

- Drug and alcohol history;
- Smoking history;
- PsA medical history;
  - Duration of PsA (Year)
  - Duration of PsA symptoms (Year)
  - Current active psoriasis (yes/no)
  - [redacted]
  - [redacted]
- Geographic region: North America, Western Europe and Eastern Europe;
- Number of prior biologic agents (0;1;2);
- Concomitant methotrexate use (yes/no);
- Concomitant non-biologic disease-modifying anti-rheumatic drug (DMARD) at baseline (yes/no);
- Concomitant corticosteroids at baseline (yes/no);
- Baseline BSA;
- Baseline BSA ≥ 3 (yes/no);
- Baseline TJC68 count;
- Baseline SJC66 count;
- Baseline PASI (in patients with BSA ≥ 3);
- Baseline PtAAP;
- [redacted]
- Baseline PtGADA;
- Baseline PhGADA;
- Baseline HAQ-DI;
- Baseline (PsAID)-12;
- Baseline BASDAI score;
- Baseline hs-CRP;
- Baseline hs-CRP ≥ 6 mg/L (yes/no);
- Baseline hs-CRP > 5 mg/L (yes/no);
- Baseline ESR;
- [redacted]
- Baseline mNAPSI score (in patients with baseline mNAPSI ≥ 0);
- Presence of enthesitis at baseline (yes/no) [based on LEI];
- Baseline LEI score (in patients with baseline LEI ≥ 0);

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- Presence of enthesitis at baseline (yes/no) [based on SPARCC];
- Baseline SPARCC (in patients with baseline SPARCC ≥ 0);
- Presence of dactylitis at baseline (yes/no);
- Baseline LDI (in patients with dactylitis);
- SF-36 PCS score
- Evidence of erosions on hands or feet in patients with a prior x-ray (yes/no);
- Evidence of juxta-articular bone formation on hands or feet in patients with a prior x-ray (yes/no)
- Baseline FACIT-fatigue

Continuous variables will be summarized using descriptive statistics and categorical variables will be summarized using counts and percentages. Percentage calculations will be based on the number of participants in FAS including participants with missing value in each treatment group.

8.4.3 Medical History

Medical history will be summarized by system organ class (SOC) and preferred term (PT) coded using Medical Dictionary for Regulatory Affairs® (MedDRA) Version 25.0 or higher. Counts and percentages will be presented by treatment group using the SAF.

8.4.4 Psoriatic Arthritis Previous Therapies

PsA previous therapies will be summarised by treatment group using the SAF using the following group terms with the individual drug names summarised within the group terms:

- anti-TNF biologics,
- anti-IL-17 biologicals,
- anti-IL23 biologicals
- other biologics coded by World Health Organization Drug Dictionary Enhanced (WHODDE)
- NSAIDs/COX-2 inhibitors
- Other NSAIDs/COX-2 inhibitors coded by WHODDE
- Non-biologic DMARDs
- Other non-biologic DMARDs coded by WHODDE
- Glucocorticoids
- Other glucocorticoids coded by WHODDE
- JAK inhibitors
- High potency opiods
- Systemic retinoids
- Phototherapy
- Inhaled marijuana
- Other treated coded by WHODDE

8.4.5 Inquiries for extra-musculoskeletal PsA manifestation

Inquiries for extra-musculoskeletal PsA manifestation will be listed by using the SAF.

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8.4.6 Previous X-ray images of hands and feet

Previous X-ray images of hands and feet will be listed by using the SAF.

8.4.7 Prior and Concomitant Medications

Prior and concomitant medications will be summarized separately by WHODDE ATC level 2 and preferred name. Counts and percentages will be presented by treatment group using the SAF for Part A and Part A+B and using SAF-B for Part B. Prior medications will be summarized for Part A and concomitant medication will be summarized separately for Part A, Part B and Part A+B.

Prior medications: are defined as those medications with a start date and stop date prior to the first dose of study drug.

Concomitant medications:

- for part A, are defined as those medications with a start date on or after the first dose of study drug of part A but not after the first dose of Part B. A medication which started prior to first dose of part A and continued after first dose will also be considered as concomitant medications for part A.
- for part B, are defined as those medications with a start date on or after the first dose of study drug of part B. A medication which started prior to first dose of part B and continued after first dose of part B will also be considered as concomitant medications for part B.
- for part A+B, are defined as those medications with a start date on or after the first dose of study drug of part A. A medication which started prior to first dose of part A and continued after first dose will also be considered as concomitant medications for part A+B.

Details for imputing missing or partial start and/or stop dates of medication are described in Section 7.3.2.

8.5 Extent of Exposure

Extent of exposure will be listed and summarized using the SAF separately for Part A and Part A+B and SAF-B for Part B.

For Part A+B, only two groups will be presented:

- Sonelokimab 120 mg,
- Sonelokimab 60 mg.

8.5.1 Treatment Duration

The duration (days) (Section 7.1 for derivations) of exposure to study drug will be summarized using descriptive statistics by treatment group. In addition, the number of injections received will be summarized with count and percentages.

8.5.2 Treatment Compliance

Treatment compliance (See Section 7.1 for derivations) will be summarized by treatment group using descriptive statistics. Counts and percentages will be provided using the following categories: <80%; 80% ≤ x < 100%; 100%; 100% < x ≤ 120% and > 120%.

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8.6 Efficacy Analyses

This section addresses the analyses to be conducted on the primary, secondary and exploratory efficacy variables.

8.6.1 Analysis Methods

8.6.1.1 Logistic Regression Model

For the primary analysis, the hypotheses to be tested are that the proportion of participants who achieve ACR50 at Week 12 compared with baseline in the sonelokimab 120 mg Q2W, sonelokimab 60 mg Q2W or sonelokimab 60 mg Q4W arms are different from that of the placebo arm.

The logistic regression will be used to test the pairwise comparisons (placebo and either sonelokimab 120 mg Q2W, sonelokimab 60 mg Q2W, sonelokimab 60 mg Q4W or adalimumab) including fixed effects for treatment and the stratification factors (sex and exposure to biologic agents prior to the screening visit). Baseline score will also be included as a covariate where there is a single score for the endpoint, for example PASI for the analysis of PASI90.

Results will be presented in terms of number and percentage of responders, adjusted response rate, odds ratios (active/placebo), as well as risk difference (active-placebo), 95% CI, and estimated p-value.

The OR is a ratio of two odds, the odds of the event of interest in individuals exposed to active treatment and the odds of the event of interest in individuals exposed to placebo. The OR can be interpreted as:

- An OR=1 indicates that the odds of having the event of interest (e.g. ACR50 responder) is the same in the active and placebo groups,
- An OR>1 indicates that the odds of having the event of interest (e.g. ACR50 responder) is greater in active group than in the placebo group,
- An OR<1 indicates that the odds of having the event of interest (e.g. ACR50 responder) is lower in active group than in the placebo group,

Using the procedure, the null hypothesis to be tested is that the OR is equal to one versus the OR is not equal to one.

In the case of having 0% or 100% response rate in one group, the estimated p-value (from a Fisher's Exact Test) will be presented, but the odds ratio and 95% CI will not be displayed.

The risk difference estimator will also be displayed and is derived from a logistic regression model. The adjusted response rates will be obtained from back transforming the estimates of the odds for each arm from the logistic regression model. The risk difference will be calculated as the difference (active-placebo) of the adjusted response rates. The delta method will be used to estimate the standard error of the risk difference from the logistic regression model (Ge et al. 2011). Appendix M has pseudo code used to create the logistic regression estimator approach.

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8.6.1.2 Mixed Model Repeated Measures

Continuous efficacy endpoints assessed over time will be analyzed using an MMRM model including treatment arm, baseline, visit, sex, prior exposure to biologic agents and treatment by visit interaction as fixed effects and participant as random effect. An unstructured covariance matrix will be used for the MMRM analysis, unless the model does not converge, in which case the covariance matrix (e.g. variance components, autoregressive, compound symmetry, and Toeplitz) will be decided upon model convergence status and the Akaike information criterion.

The MMRM will be used to test for differences in the mean of the endpoint of interest (e.g. change from baseline in TJC68) between groups of interest (e.g. each active treatment group versus placebo).

From the model, the adjusted least squares (LS) means in each group and the difference in LS means for the group comparisons will be estimated together with 95% CIs for the differences and p-values for the pairwise comparisons. Treatment effect estimates will be also extracted by visit.

8.6.1.3 Multiple Imputation

As a sensitivity analysis of the primary and key secondary dichotomous efficacy endpoints (e.g. ACR50 responder), multiple imputation of missing data will be performed and analyzed using logistic regression. Multiple imputation uses a simulation based approach, replacing missing values from multiple draws from conditional distributions given the observed data and covariates. Assuming an arbitrary missing data pattern the missing values for each component will be imputed separately based on a fully conditional specification (FCS) approach, this method uses all variables in the imputation model for any other variable.

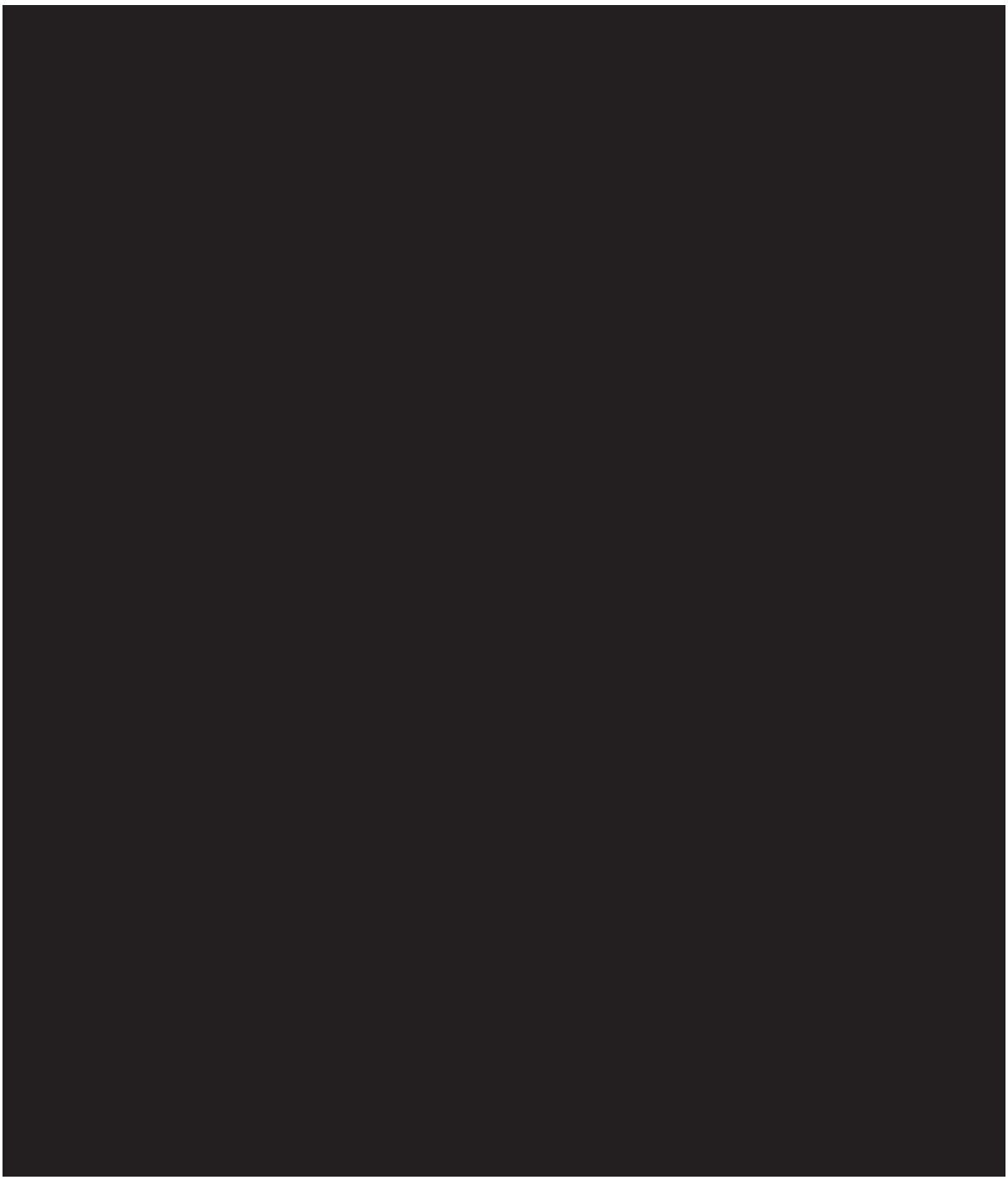
The imputations will be done using the corresponding baseline value, sex and exposure to biologic agents at baseline as covariates. If there are any missing values in those variables they will also be imputed, in the model a single component at a specific visit, will consider all previous visits as covariates. The full conditional specification regression model will be used for continuous variables and the number of imputations will be 100 with 50 burn in imputations and the seed for all imputations will be 4278491. For all visit results a minimum value of 0 will be added to the imputation. If the imputation does not input values within the specified range then the number of maximum iterations by step will be increased accordingly.

For each completed imputed dataset, the necessary derived variables will be computed using logistic regression as described in section 8.6.1.1 and the results obtained will be combined into one multiple imputation inference using proc MIANALYZE.

The SAS pseudo code for this imputation process is listed below:

[redacted]

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8.6.1.4 Multiplicity

The following multiplicity adjustments will be used to control the overall type I error rate at 0.05 for the primary endpoint and key secondary endpoints. All sensitivity analyses will be regarded as exploratory and no formal adjustment for multiplicity will be made.

Primary Endpoints

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To adjust for multiple testing and to control the family-wise error rate, the Bonferroni-Holm method will be applied first to sonelokimab 120 mg Q2W (Arm 1) and sonelokimab 60 mg Q2W(Arm 2), followed by a step-down procedure to test for sonelokimab 60 mg Q4W (Arm 3).

The Bonferroni-Holm procedure will work as follows:

1) Let $p_{SLK120mg,Q2W}$ and $p_{SLK60mg,Q2W}$ be the p-value resulting from the comparison between sonelokimab 120 mg,Q2W vs placebo and sonelokimab 60 mg,Q2W vs placebo groups respectively.
2) If the smallest p-value obtained in step 1 is greater than or equal to alpha/2 = 0.025, the procedure is stopped and no p-values are significant.
3) If the smallest p-value is declared significant (i.e p-value less than alpha/2 = 0.025), then compare the largest p-value with alpha = 0.05. If the p-value is less than 0.05, then declared as significant. Otherwise not significant.
4) If both $p_{SLK120mgQ2W}$ and $p_{SLK60mgQ2W}$ are significant then the testing procedure will continue with the key secondary endpoints. The Bonferroni-Holm procedure used for the primary endpoint will be applied to each key secondary endpoint sequentially.
5) If the procedure passes all the key secondary endpoints for both doses (Arm 1 and Arm 2), then sonelokimab 60 mg Q4W (Arm 3) will be compared to alpha = 0.05 first for the primary endpoint and then sequentially through the key secondary endpoints.

8.6.1.5 Treatment-by-Center Interaction Analysis (Multi-Center Study)

Unless otherwise specified, data from all investigational centers/sites will be pooled for analyses.

8.6.2 Analysis of Primary Efficacy Endpoint

The primary analysis will be performed using the FAS.

All sensitivity analyses will be performed using FAS population. Summaries for Part B will be performed using the FAS-B population.

8.6.2.1 American College of Rheumatology 50 Clinical Response

The ACR50 will be assessed at Week 2, Week 4, Week 8, Week 12, Week 14, Week 16, Week 20 and Week 24 however the primary endpoint is the proportion of ACR50 responders at Week 12.

ACR50 response criteria is defined as:

- ACR50 Responder: *participant who had improvement in the ACR response criteria ≥ 50%;*
- ACR50 Non-responder: *Otherwise.*

ACR50 response is:

• At least a 50% improvement in TJC68;

• At least a 50% improvement in SJC66;

• At least a 50% improvement in at least 3 of the following 5 variables:

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- PtAAP;
- PtGADA;
- PhGADA;
- HAQ-DI;
- hs-CRP.

A Non-responder imputation method will be used for all missing data for the primary estimand as detailed in section 7.3.2.

The null hypotheses to be tested are that the proportion of ACR50 responders at Week 12 are no different for the following comparisons:

- sonelokimab 120 mg Q2W versus placebo
- sonelokimab 60 mg Q2W versus placebo
- sonelokimab 60 mg Q4W versus placebo

[redacted]

To test these hypotheses, a pairwise stratified logistic regression will be used as detailed in Section 8.6.1.1. This analysis will also be conducted for Weeks 2, 4 and 8.

The data for Part B will be presented by FAS-Part B and will be split by Part A and Part B treatment.. Non-responder imputation and As-Observed summaries will be presented. No statistical analysis will be presented. These results will also be presented in a line plot.

The following sensitivity analysis of the Part A data will be presented:

- the first sensitivity estimand will be analysed using logistic regression, with the same covariates as for the primary analysis. Missing data will be imputed as described in section 5.2 with multiple imputation applied as described in 8.6.1.3such that subjects who had prohibited medication or discontinued due to efficacy or adverse events are set as non-responders, all other missing data is imputed with multiple imputation methods.
- the second sensitivity estimand will be analysed using logistic regression, with the same covariates as for the primary analysis with multiple imputation applied as described in 8.6.1.3
- An observed analysis using logistic regression model but with no imputation of missing data.

Line plots for ACR50 response rate by week will also be provided, with week on the x axis and ACR50 response rate on the y axis. Graphs for Part A and Part B (FAS) will be presented.

The responders by visit and treatment group will be summarized descriptively for Part A and Part B

The change from baseline for each component of the ACR endpoint will be analyzed using the method described in 8.6.1.2, Descriptive summaries by treatment group and visit will also be displayed for Part A and Part B.

For Part A and B there will also be a NRI/LOCF analysis. Subjects who completed the study at Week 12 due to country-specific protocol requirements (US participants) or subjects who switched arm at Week 12 will have their Part B scheduled visits be imputed with LOCF from their Week 12 visits. All

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other missing data is imputed as a non-response. A summary of the number of responders by Part A treatment arm for all scheduled visits will be displayed.

8.6.2.2 TJC68

The total number of tender joints from the 2 temporomandibular, 2 sternoclavicular, 2 acromioclavicular joints, 2 shoulders, 2 elbows, 2 wrists, 10 metacarpophalangeal, 10 proximal interphalangeal, 8 distal interphalangeal joints of the hands, the 2 hips, 2 knees, 2 ankles, 2 mid-tarsal, 10 metatarsophalangeal, and 10 proximal interphalangeal joints of the feet.

8.6.2.3 SJC66:

The total number of swollen joints from the same joints as assessed for tenderness, excluding the hip joints.

8.6.2.4 Health Assessment Questionnaire (HAQ-DI)

The health assessment questionnaire (HAQ-DI) is a twenty-item PRO instrument which assesses current physical function/disability. It covers 8 categories (dressing and grooming, hygiene, arising, reach, eating, grip, walking and common daily activities). There are 4 response options ranging from 0 (no difficulty) to 3 (unable to do) (See Appendix A).

To calculate the HAQ-DI, the highest sub-category score determines the value for each category, unless aids or devices are used. There must be at least 6 out of 8 categories answered or else the score cannot be calculated. Each category scored is averaged into an overall HAQ-DI score ranging from 0 to 3.

The aids used for adjustment by category are: dressing – devices used for dressing; rising – built up or special chars; eating – built up or special utensils; walking – canes, walkers or crutches; hygiene – raised toilet seats, bathtub seats, bathtub bars, long handles appliances in bathroom; reach – long-handled appliances for reaching; and grip – jar openers.

If an aid is required for any category, or another person is required to help for any category then that category score increases a score of 0 or 1 to a 2. Scores already at 2 and 3 are not modified. Aids and devices considered recorded in the 'other' category will not be considered in the analysis.

Scores of 0 to 1 represent mild to moderate disability, 1 to 2 represent moderate to severe disability and 2 to 3 indicate severe to very severe disability.

8.6.2.5 Patients Assessment of Arthritis pain

The patients' assessment of arthritis pain (PtAAP) is a self-administered pain visual analogue score (VAS). It is performed using a horizontal 100mm VAS, ranging from 0 (no pain) to 100 (severe pain) after the question: "Please indicate with a vertical mark (|) through the horizontal line the most pain you had from your psoriatic arthritis today. (See Appendix B)

8.6.2.6 Patients Global Assessment of Disease Activity

The patients global assessment of disease activity (PtGADA) is self-administered and performed using a horizontal 100mm VAS ranging from 0 (very well) to 100 (very poor) after the question "Considering

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all the ways PsA affects you, please indicate with a vertical mark (|) through the horizontal line how well you are doing today." (See Appendix C)

8.6.2.7 Physician's Global Assessment of Disease Activity

The physician's global assessment of disease activity (PhGADA) is assessed by the investigator or a qualified designee on a VAS ranging from 0 (very well) to 100 (very poor). (See Appendix D)

8.6.2.8 Hs-CRP

Hs-CRP values are assessed at Baseline, Week 2, Week 4, Week 8, Week 12, Week 14, Week 16, Week 20 and Week 24.

Hs-CRP values which are recorded as <LLQ (i.e <0.10 mg/L) will be set to be half the value of the LLQ for these values (i.e 0.05 mg/L) for analysis purpose.

To test hs-CRP, the data will be log transformed prior to using a MMRM including as detailed in section 8.6.1.2. The results will be back-transformed to be presented in terms of adjusted least-squares (LS) geometric means, and ratios in LS geometric means together with 95% CIs and p-values.

If the data suggest that either endpoint is normally distribution rather than log-normally distributed then the analysis will be performed on the change from baseline without log-transformation.

The CRP assessments as well as the corresponding ratio to baseline will also be summarized descriptively by treatment group and visit for Part A and Part B.

The hs-CRP analysis will also be repeated, only including subjects with a baseline hs-CRP >ULN (5mg/L).

8.6.2.9 ACR Components

For all the continuous components which make up the ACR as well as MMRM analysis, they will summarized by visit, treatment arm and Part.

For Part A and B there will also be a Last Observation Carried Forward (LOCF) summary of the ACR components to present the absolute, change from baseline and percent change from baseline by the randomized treatment arm. All missing data will be imputed using LOCF and subjects who completed the study at Week 12 due to country-specific protocol requirements (US participants) or subjects who switched arm at Week 12 will have their Part B scheduled visits be imputed with LOCF from their Week 12 visits.

8.6.3 Analysis of Key Secondary Efficacy Endpoints

For the key secondary endpoints, summaries and analyses will be performed using the FAS.

In addition, for the key secondary dichotomous endpoints, a sensitivity analysis will be performed using the FAS. Summaries of part B will be performed using the FAS-B population.

8.6.3.1 American College of Rheumatology 20 Clinical Response

A key secondary endpoint is the proportion of ACR20 responders at Week 12 compared with baseline.

ACR20 response criteria is defined as:

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- ACR20 Responder: *participant who had improvement in the ACR response criteria ≥ 20%;*
- ACR20 Non-responder: *Otherwise.*

ACR20 response is:

- • At least a 20% improvement in TJC68;
- • At least a 20% improvement in SJC66;

At least a 20% improvement in at least 3 of the following 5 variables:

- PtAAP;
- PtGADA;
- PhGADA;
- HAQ-DI;
- hs-CRP.

ACR20 will be analysed using the same methods as used for ACR50.

8.6.3.2 Psoriasis Area and Severity Index 90

A key secondary endpoint is change from baseline in PASI90 at Week 12 in the subgroup of participants with psoriasis [PsO] involving at least 3% body surface area [BSA] at baseline. This is expected to be between 50% and 67% of the FAS.

The PASI is a validated tool to dynamically assess PsA severity.

The PASI score is an established measure of clinical efficacy for PsO medications, which provides a numeric scoring for the participant's overall PsO disease state, ranging from 0 to 72. It is a linear combination of percent of surface area of skin that is affected and the severity of erythema, infiltration and desquamation over 4 body regions (Head, Trunk, Upper extremities, Lower extremities).

These correspond to 10%, 30%, 20% and 40% of the total body area respectively.

The area of psoriatic involvement of these 4 areas (Ah, At, Au, and Al) is given a numerical value:

• 0 = No involvement;

• 1 = <10%;

• 2 = 10% to <30%;

• 3 = 30% to <50%;

• 4 = 50% to <70%;

• 5 = 70% to <90%;

• 6 = 90% to 100% involvement.

The signs of severity, erythema (E), infiltration (I), and desquamation (D) of lesions are assessed using a numeric scale 0 to 4 where 0 is a complete lack of cutaneous involvement and 4 is the

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severest possible involvement; scores are made independently for each of the areas, h, t, u and l and represent a composite score for each area.

An illustration of judging erythema follows:

• 0 = No erythema;

• 1 = Slight erythema;

• 2 = Moderate erythema;

• 3 = Striking erythema;

• 4 = Exceptionally striking erythema.

The PASI score is calculated according to the following formula:

PASI = 0.1(Eh+Ih+Dh)Ah + 0.3(Et+It+Dt)At + 0.2(Eu+Iu+Du)Au + 0.4(El+Il+Dl)Al

PASI90 is defined as an improvement of 90% of more in the PASI from baseline score.

The PASI90 will be assessed at Baseline, Week 4, Week 8, Week 12, Week 16, Week 20 and Week 24, but the key secondary endpoint is the assessment at Week 12.

The null hypotheses to be tested are that the proportion of PASI90 responders at Week 12 are not different for the following comparisons:

- sonelokimab 120 mg Q2W versus placebo
- sonelokimab 60 mg Q2W versus placebo
- sonelokimab 60 mg Q4W versus placebo

[redacted]

To test these hypothesis, a logistic regression will be used as detailed in section 8.6.1.1. This analysis will also be conducted for Week 2, 4 and 8.

The same sensitivity as for the primary endpoint will be presented and the same graphs and descriptive statistics will also be displayed for Part A and Part B.

8.6.4 Analysis of Other Secondary Efficacy Endpoints

For the other secondary endpoints, no confirmatory statistical testing will be performed, but statistical analyses may be used for exploratory proposes.

FAS will be used for all other secondary endpoints analysis. Summaries of part B will be performed using the FAS-B population.

8.6.4.1 American College of Rheumatology Clinical Response (ACR20/50)

Other secondary endpoints are:

- Proportions of ACR20 responders over time.
- Proportions of ACR50 responders over time.

ACR20 and ACR50 response criteria are defined in section 8.6.3.1 and in section 8.6.2.1 respectively.

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A Non-responder imputation method will be used for all missing data as detailed in section 7.3.1

The ACR20/50 will be assessed at Week 2, Week 4, Week 8, Week 12, Week 14, Week 16, Week 20 and Week 24. Only Part A will be included in logistic regression analysis.

The exploratory null hypothesis to be tested are that the proportion of ACR20/50 responders at each time point in Part A are not different for the comparisons of interest for Part A. For exploratory purposes, the comparisons of interest will be:

- sonelokimab 120 mg Q2W versus placebo
- sonelokimab 60 mg Q2W versus placebo
- sonelokimab 60 mg Q4W versus placebo

[redacted]

ACR20/50 responders will be also summarized for all weeks for Part A, Part B and will be displayed by treatment group and visit as described in section 8.1.

8.6.4.2 American College of Rheumatology 70 Clinical Response (ACR70)

Other secondary endpoint include the proportion of ACR70 responders over time.

ACR70 response criteria is defined as:

- ACR70 Responder: *participant who had improvement in the ACR response criteria ≥ 70%;*
- ACR70 Non-responder: *Otherwise.*

ACR70 response is:

• At least a 70% improvement in TJC68;

• At least a 70% improvement in SJC66;

• At least a 70% improvement in at least 3 of the following 5 variables:

  - PtAAP;
  - PtGADA;
  - PhGADA;
  - HAQ-DI;
  - hs-CRP.

The exploratory null hypotheses to be tested are that the proportion of ACR70 responders at each time point are not different for the comparisons of interest for Part A, a logistic regression will be performed as described in section 8.6.1.1. For exploratory purposes the comparison of interest will be:

- sonelokimab 120 mg Q2W versus placebo
- sonelokimab 60 mg Q2W versus placebo
- sonelokimab 60 mg Q4W versus placebo

[redacted]

ACR70 responders will also be summarized descriptively by treatment group and visit for Part A and Part B.

8.6.4.3 Psoriasis Area and Severity Index (PASI75/90/100)

Other secondary endpoints include the proportion of PASI75/90/100 responders over time.

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PASI is derived as detailed in section 8.6.3.2. PASI75/90/100 are defined as an improvement in PASI score of 75%, 90% and 100% respectively.

The exploratory null hypotheses to be tested are that the proportion of PASI75/90/100 responders at each time point are not different for the comparisons of interest for Part A, a logistic regression will be performed as described in section 8.6.1.1. For exploratory purposes the comparison of interest will be:

- sonelokimab 120 mg Q2W versus placebo
- sonelokimab 60 mg Q2W versus placebo
- sonelokimab 60 mg Q4W versus placebo

[redacted]

PASI75/90/100 responders will also be summarized descriptively by treatment group and visit for Part A and Part B.

8.6.4.4 Minimal Disease Activity

Other secondary endpoints include the proportion of patients with minimal disease activity at Week 12.

Criteria for assessing minimal disease activity, listed below, covering all of the domains of the disease have been developed to determine whether the participant has reached minimal disease activity based on key outcome measures in PsA. Minimal disease activity is defined as meeting 5 of the 7 following criteria:

1. TJC68 ≤1;

2. SJC66 ≤1;

3. PASI ≤1 or PsO affecting ≤1% of BSA;

4. PtAAP ≤15 on a 0 to 100 VAS;

5. PtGADA ≤20 on a 0 to 100 VAS;

6. HAQ-DI ≤0.5.

7. Leeds Enthesitis Index (LEI) ≤1

The null hypotheses to be tested are that the proportion of responders at Week 12 are no different for the following comparisons:

- sonelokimab 120 mg Q2W versus placebo
- sonelokimab 60 mg Q2W versus placebo
- sonelokimab 60 mg Q4W versus placebo

[redacted]

To test the hypotheses, a logistic regression will be used as detailed in section 8.6.1.1. Descriptive summaries by treatment group and visit will also be displayed for Part A and Part B. An LOCF/NRI analysis by visit similar to in section 8.6.2.1 will also be displayed for all scheduled visits in Part A and B.

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[redacted]

8.6.4.6 Leeds Enthesitis Index (LEI) and Spondyloarthritis Research Consortium of Canada Enthesitis Index (SPARCC)

The LEI is a validated enthesitis index which uses 6 sites for evaluation of enthesitis (lateral epicondyle humerus [R/L], Achilles tendon insertion [R/L] and medial condyle femur [R/L] giving an overall score range of 0 to 6 (see Appendix E).

The proportion of subjects with enthesitis resolution, defined as LEI = 0 will be tested using pairwise stratified logistic regression as detailed in section 8.6.1.1 in the subgroup of subjects with LEI>0 at baseline. .

The change from baseline in LEI will be analyzed using the method described in 8.6.1.2, including only subjects with LEI > 0 at baseline. Descriptive summaries by treatment group and visit will also be displayed for Part A and Part B.

The SPARCC Index uses 18 sites, greater trochanter (R/L), quadriceps tendon insertion into the patella (R/L), patellar ligament insertion into the patella or tibial tuberosity (R/L), achilles tendon insertion (R/L), plantar fascia insertion (R/L), medial epicondyle (R/L) and supraspinatus insertion into greater tuberosity of humerus (R/L). The maximum score is 16.

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The change from baseline in SPARCC will be analyzed using the method described in 8.6.1.2, including subjects with SPARCC > 0 at baseline. Descriptive summaries by treatment group and visit will also be displayed for Part A and Part B. For Part A and B there will also be an LOCF summary of the LEI and SPARCC to present the absolute, change from baseline and percent change from baseline by the randomized treatment arm.

8.6.4.7 Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

The BASDAI will be assessed at Week 4, Week 8, Week 12, Week 16, Week 20 and Week 24 however the secondary endpoint is the proportion of BASDAI responders at Week 12.

BASDAI response criteria is defined as:

- BASDAI Responder: *participant who had improvement in the BASDAI response criteria ≥ 50%;*
- BSDAI Non-responder: *Otherwise.*

The BASDAI is a validated composite index consisting of 6 participant numerical rating scales (NRS) to measure severity of the following:

• Fatigue;

• Axial involvement;

• Peripheral articular involvement;

• Localized tenderness/enthesopathy;

• Severity of morning stiffness;

• Time of morning stiffness.

Each NRS has a range of 0 to 10 where 0 represents “none” and 10 represents “very severe.” For

Question 6, 0 represents no stiffness and 10 represents 2 or more hours of stiffness.

The composite BASDAI score is calculated as the average of questions 5 and 6 (Severity and time of morning stiffness), then as the mean of first 4 questions and the average of questions 5 and 6.

$$BASDAI = \frac{Q1 + Q2 + Q3 + Q4 + \frac{(Q5 + Q6)}{2}}{5}$$

A response rate of BASDAI is calculated as subjects with at least a 50% improvement in BASDAI.

A Non-responder imputation method will be used for all missing data as detailed in Section 8.3.1.

The null hypotheses to be tested are that the proportion of BASDAI50 responders at Week 12 are no different for the following comparisons:

- sonelokimab 120 mg Q2W versus placebo

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- sonelokimab 60 mg Q2W versus placebo
- sonelokimab 60 mg Q4W versus placebo

[redacted]

To test these hypotheses, a pairwise stratified logistic regression will be used as detailed in Section 8.6.1.1. Descriptive summaries by treatment group and visit will also be displayed for Part A and Part B

The change from baseline in BASDAI will be analyzed using the method described in 8.6.1.2. Descriptive summaries by treatment group and visit will also be displayed for Part A and Part B.

8.6.4.8 Psoriatic Assessment Impact of Disease-12

The psoriatic assessment impact of disease-12 (PsAID-12) is self-administered by the participant and is a questionnaire including 12 health domains related to PsA. Each domain is evaluated on a score of 0 (None) to 10 (Extreme). The 12 domains are: pain, fatigue, skin problems, work and/or leisure activities, functional capacity, discomfort, sleep disturbance, coping, anxiety, embarrassment and/or shame, social participation, and depression (See Appendix F).

The PsAID-12 final value is calculated by summing each weighted domain which is calculated by multiplying the score (range of 0 to 10) by the weighted value as given in the table below and then dividing the total by 20:

Domain NRS Value	Multiplication
Pain	3
Fatigue	2
Skin	2
Work and/or leisure activities	2
Function	2
Discomfort	2
Sleep	2
Coping	1
Anxiety	1
Embarrassment	1
Social Life	1
Depression	1

A PsAID-12 ≤ 3 responder is a subject who has a final value of 3 of below.

A Non-responder imputation method will be used for all missing data as detailed in Section 8.3.1.

The exploratory null hypotheses to be tested are that the proportion of PsAID-12 ≤ 3 at Weeks 4, 8 and 12 are no different for the following comparisons:

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- sonelokimab 120 mg Q2W versus placebo
- sonelokimab 60 mg Q2W versus placebo
- sonelokimab 60 mg Q4W versus placebo

[redacted]

To test these hypotheses, a pairwise stratified logistic regression will be used as detailed in Section 8.6.1.1. Descriptive summaries by treatment group and visit will also be displayed for Part A, Part B and Part A+B.

The change from baseline in PsAID-12 will be analyzed using the method described in 8.6.1.2. Descriptive summaries by treatment group and visit will also be displayed for Part A and Part B. For Part A and B there will also be an LOCF summary of the PsAID-12 to present the absolute, change from baseline and percent change from baseline by the randomized treatment arm.

8.6.4.9 Leeds Dactylitis Index

The Leeds Dactylitic index (LDI) is assessed by an individual suitably qualified and experienced in the administration of the instrument. It measures the ratio of the circumference of the affected digit to the circumference of the digit on the opposite hand or foot, using a minimum difference of 10% to define a dactylitic digit. The ratio of circumference is multiplied by a tenderness score, using a modification of LDA which is a binary score (1 for tender, 0 for non-tender) (See Appendix G). If both sides are considered involved, or the circumference of the contralateral digit cannot be obtained, the number will be compared to data provided in the standard reference table for hands and feet.

The dactylitis count is the number of fingers and toes with dactylitis, ranging from 0 to 20.

The final total LDI score is calculated as:

$$[\{(A/B) - 1\} \times 100] \times C$$

where

A = Total circumference involved digit

B = Contralateral Digit

C = Tenderness Score

Descriptive summaries by treatment group and visit will also be displayed for Part A and Part B, including subjects with presence of dactylitis at baseline (LDI >0). In the final total LDI score calculation, only digits with >=10% difference from contralateral score will be included.

[redacted]

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[redacted]

8.6.4.11 Modified Nail Psoriasis Severity Index

The nNAPSI is a tool to assess nail involvement in participants with PsA with an index score ranging to 0 to 130 for all fingernails.

Three features or groups of features (pitting, onycholysis and oil-drop dyschromia and crumbling) or each fingernail will be graded on a score of 0 to 3.

The number of pits for each finger nail is scores as 0 = 0, 1-10 = 1, 11- 49 = 2 and >50 = 3.

The score percent of nail with crumbling present it scored as no crumbling = 0, 1-25% = 1, 26 – 50% = 2 and >50% = 3.

The score percent of nail with onycholysis and/or oil drop dyschromia is: none = 0, 10% = 1, 11-30% = 2, >30% = 3.

Four features (leukonychia, splinter hemorrhages, hyperkeratosis, and red spots in the lunula) will be graded as either present (1) or absent (0) in each fingernail.

The total score is calculated by summing the score for each feature and each fingernail.

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The change from baseline in mNAPSI will be analyzed using the method described in 8.6.1.2 for subjects with nail psoriasis at baseline (mNAPSI > 0). Descriptive summaries by treatment group and visit will also be displayed for Part A and Part B. For Part A and B there will also be an LOCF summary of the mNAPSI to present the absolute, change from baseline and percent change from baseline by the randomized treatment arm.

8.6.4.12 Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue)

Other secondary endpoints include:

- Change from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) score

FACIT-Fatigue is a 13-item self-assessment of fatigue and the effect on daily activities and function over the previous 7 days (See Appendix H). The 13 items use a 5-point Likert-type scale (0 = "Not at all", 1 = "A little", 2 = "Somewhat", 3 = "Quite a bit", 4 = "Very much"). The FACIT-Fatigue assessment score range between 0-52 with 0 corresponding to the highest level of fatigue and 52 corresponding to the lowest level of fatigue. The scores for the 11 items where a higher score indicates more fatigue are reversed (4-score) before being summed together with the other 2 items to give the total. If any items are missed, then the total score is adjusted by multiplying by 13 and dividing by the number of items answered.

The FACIT-Fatigue will be self-administered by the participant at Baseline, Week 4, Week 12, Week 16 and Week 20.

The exploratory null hypotheses to be tested are that the mean change from baseline over time are not different for the comparisons of interest. To test these hypotheses, a MMRM will be used including the Part A visits as detailed in section 8.6.1.2

Descriptive summaries by treatment group and visit will also be displayed for Part A and Part B.

8.6.4.13 Short Form-36 Health Survey Version 2

Other secondary endpoints include:

- Short-Form-36 Health Survey Questionnaire-Version 2 (SF-36v2) Mental Component Summary (MCS);
- SF-36v2 Physical Component Summary (PCS);

The SF36v2 is a 36-item generic HRQoL instrument that uses a recall period of 4 weeks.

Each item on the survey is answered by subjects on scales of 1 to 2, 1 to 3, 1 to 5 or 1 to 6. Some of the answers are recoded that that across all questions, a higher score indicates a better health state.

Questions 2, 3A-3J, 4A-4D, 5A-5C, 9B, 9C, 9F, 9G, 9I, 10, 11A and 11C are scored as recorded. The other questions are transformed as shown in the table below:

Question	Original Code and re-code response

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1 Original	1	2	3	4	5	
1 Recoded	5	4.4	3.4	2	1	
6, 11B, 11D Original	1	2	3	4	5	
6, 11B, 11D Recoded	5	4	3	2	1	
7 Original	1	2	3	4	5	6
7 Recoded	6	5.4	4.2	3.1	2.2	1
8 (if 7 is answered) original	1	1	2	3	4	5
Original Response to 7	1	2-6	1-6	1-6	1-6	1-6
Recoded Response	6	5	4	3	2	1
8 (if 7 is not answered) original	1	2	3	4	5	
8 Recoded	6	4.75	3.5	2.25	1	
9A, 9D, 9E, 9H Original	1	2	3	4	5	
9A, 9D, 9E, 9H Recoded	5	4	3	2	1	

The raw score of each of the 8 scales is calculated by summing the re-coded scores for its relevant questions. If <50% of questions within a scale are answered then the raw score is not calculated. If more than 50% of questions are answered but <100% then take the recoded values and sum them. Then the average score is calculated for the non-missing scores and the average scored is used for the value of the missing questions.

Physical Functioning: 3A to 3J

Role limitations due to physical health (RP): 4A to 4D

Bodily pain: 7, 8

General Health: 1, 11A to 11D

Vitality: 9A, 9E, 9G, 9I

Social Functioning: 6, 10

Role limitation due to emotional problems (RE): 5A to 5C

Mental health: 9B, 9C, 9D, 9F, 9H.

Once the raw score is calculated, then it is converted to a normalized score (on a scale of 0 to 100) using the following transformation:

(raw score – lowest possible raw score) / possible raw score range x 100.

The normalized scale score is then standardized using the following formula:

(Normalized score – A) / B.

The lowest possible raw score, possible raw score range, A and B for each scale are shown in the table below:

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Scale	Lowest Possible Raw Score	Possible Raw Score Range	A	B
Physical Functioning	10	20	83.29094	23.75883
Limitation due to Physical health (RP)	4	16	82.50964	25.52028
Bodily Pain	2	10	71.32527	23.66224
General health	5	20	70.84570	20.97821
Vitality	4	16	58.31411	20.01923
Social Functioning	2	8	84.30250	22.91921
Limitation due to emotional problems (RE)	3	12	87.39733	21.43778
Mental health	5	20	74.98685	17.75604

The physical and mental component raw scores are then calculated based on multiplying each standardized scale score by a constant, and then adding the 8 scales together. The constants to use for the two component scores are shown below:

Score	Physical health component	Mental health Component
Physical Functioning	0.42402	-0.22999
Limitation due to Physical health (RP)	0.35119	-0.12329
Bodily Pain	0.31754	-0.09731
General health	0.24954	-0.01571
Vitality	0.02877	0.23534
Social Functioning	-0.00753	0.26876
Limitation due to emotional problems (RE)	-0.19206	0.43407
Mental health	-0.22069	0.48581

The physical and mental component norm based scores is calculated by multiplying the component raw scores by 100 and adding 50.

The change from baseline in the mental component summary (MCS) and physical component summary (PCS) will be analyzed using the method described in 8.6.1.2. Descriptive summaries by treatment group and visit will also be displayed for Part A and Part B.

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8.6.4.15 ACR and PASI Composite Endpoints

4 composite endpoints will be created combining ACR and PASI endpoints:

- ACR50 and PASI90
- ACR50 and PASI100
- ACR70 and PASI90
- ACR70 and PASI100.

A subject is considered a responder for the composite endpoints at a particular timepoint if they are a responder for both of the relevant endpoints at that same timepoint. If either is missing or non-responder then the subject will be considered a non-responder.

To test these hypotheses, a pairwise stratified logistic regression will be used as detailed in Section 8.6.1.1. Descriptive summaries by treatment group and visit will also be displayed for Part A and Part B combined for NRI/LOCF.

8.7 Pharmacokinetic and Immunological Analyses

For PK and IG Analyses, no confirmatory statistical testing will be performed, but statistical tests may be used for exploratory proposes only. IG and PK analysis sets will be used.

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8.7.1 Immunological Analyses

Antibodies to sonelokimab will be evaluated in serum samples collected for Arms 1, 2, & 3 (120 mg Q2W, 60 mg Q2W and 60 mg Q4W sonelokimab) at Baseline, Week 2, Week 4, Week 8, Week 12, Week 14, Week 16, Week 20, Week 24 and the safety follow-up visit. At dosing visits, the samples will be collected prior to dose administration.

Up to three separate ADA types may be assessed: ADAs that bind to sonelokimab ('ADA'); ADA to a modified version of sonelokimab ('mADA') and ADA that neutralise the activity of sonelokimab ('NAb ADA'). Results for mADA will only be available for ADA baseline positive participants. NAb ADA results will only be available for the ADA positive samples.

Summary tables for each ADA type will be prepared to record where applicable the number and percentage of participants who are:

- ADA positive at baseline;
- ADA positive at any visit post-baseline;
- ADA positive at baseline and any visit post-baseline;
- ADA positive post-baseline but not at baseline;
- Treatment-emergent ADA defined as either:
    - ADA positive post-baseline but not at baseline, or
    - Treatment boosted: > 4-fold increase in ADA titers at any post-baseline timepoint compared to baseline, if ADA positive at baseline. [10^(post-baseline log10 titer – baseline log10 titer) > 4]
- persistent positive (positive at more than one post-baseline visit where the first and last ADA-positive visits are separated by a period of 12 weeks or longer; or positive at last post-baseline assessment and not at baseline; or positive at a visit with less than 12 weeks before an ADA-negative last visit);
- transient positive (positive at only 1 post-baseline visit and not at baseline; or positive at two or more visits where the first and last ADA-positive visits are separated by a period less than 16 weeks and the last visit is negative).

The log10 titer values for the ADA and mADA (not NAb ADA) will be summarised by visit and treatment arm.

Additional analyses may be performed at the sponsor's discretion but they are beyond the scope of this SAP and will be specified in a separate document, if needed.

8.7.2 Pharmacokinetic Analyses

Blood samples will be collected for the measurement of trough serum sonelokimab levels at Baseline, Week 2, Week 4, Week 8, Week 12, Week 14, Week 16, Week 20 and Week 24. At dosing visits the samples will be collected prior to dose administration.

Serum concentrations of sonelokimab will be summarized by visit including number of observations, number of concentrations below the quantifiable limit (nBLQ), mean, SD, GM, CV, median, min and max. All concentration values reported as no results (not collected or ND) will be treated as missing. For the calculation of concentration summaries, all concentrations below the quantifiable limit (BLQ) will be set to the BLQ value/2.

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The PK measurements for sonelokimab will be listed by-participant, by visit and by treatment group. Individual values of concentrations and PK parameters will be presented with 3 significant digits.

Two plots of the PK concentrations will be presented for Part A:

1. A plot of the individual PK concentration profiles with study week on the x-axis and concentration on the y-axis, with log10 spacing on the y-axis. One page will be used for each Sonelokimab arm, with the individual concentration profiles overlaid for each dose.
2. A single plot of the geometric mean concentration profiles for each Sonelokimab arm with study week on the x-axis and concentration on the y-axis, with log10 spacing on the y-axis.

Additional analyses may be performed at the sponsor's discretion, but they are beyond the scope of this SAP and will be specified in a separate document, if needed.

[redacted]

8.9 Safety Analyses

For all the safety endpoints, no formal statistical testing will be performed. Safety summaries will be presented by treatment group separately for the Part A (SAF), Part B (SAF-Part B), and Part A+B (SAF).

For Part A, 6 groups will be considered:

- Sonelokimab 120 mg (Q2W),
- Sonelokimab 60 mg (Q2W),
- Sonelokimab 60 mg (Q4W),
- Placebo,
- Adalimumab 40 mg (Q2W),
- Total sonelokimab.

For Part B and follow-up period, 10 groups will be considered:

- Sonelokimab 120 mg Q2W→sonelokimab 120 mg Q4W;
- Sonelokimab 120 mg Q2W→adalimumab 40 mg Q2W;
- Sonelokimab 60 mg Q2W→sonelokimab 60 mg Q4W;
- Sonelokimab 60 mg Q2W→sonelokimab 120 mg Q4W;
- Sonelokimab 60 mg Q4W→sonelokimab 60 mg Q4W;
- Sonelokimab 60 mg Q4W→sonelokimab 120 mg Q4W;
- Placebo→sonelokimab 120 mg Q4W;

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- Adalimumab 40 mg Q2W→adalimumab 40 mg Q2W;
- Adalimumab 40 mg Q2W→sonelokimab 120 mg Q2W.
- Total sonelokimab

For Part A+B, 5 groups will be considered:

- Placebo (Part A only)
- Total Sonelokimab 120mg
- Total Sonelokimab 60mg
- Total Sonelokimab
- Total Adalimumab 40mg Q2W

The placebo group will include all subjects who were randomized to placebo in Part A and will only include Part A summary visits.

The total Sonelokimab 120mg group will include all subjects who were randomized to Sonelokimab 120mg Q2W in Part A and subjects who had Sonelokimab 120mg Q2W or Q4W in Part B. Subjects will only be included for summary visits during the Part they were assigned 120mg Q2W.

The total Sonelokimab 60mg group will include all subjects who were randomized to Sonelokimab 60mg Q2W or Q4W in Part A and subjects who had Sonelokimab 60mg during part B (Sonelokimab 60mg Q2W responders and Soenlokimab 60mg Q4W responders). Subjects will only be included for summary visits during the Part they were assigned Sonelokimab 60mg.

The total Adalimumab 40mg Q2W group will include all subjects who were randomized to Adalimumab 40mg Q2W during Part A and subjects who had Adalimumab 40mg Q2W during part B (Adalimumab 40mg Q2W responders and Sonelokimab 120mg Q2W non-responders).

The total Sonelokimab arm will include subjects who received sonelokimab at any time in the study. Subjects will only be included for summary visits during the Part they were assigned Sonelokimab.

8.9.1 Adverse Events

All AEs will be classified by Primary SOC and PT according to MedDRA Version 25.0 or higher and will be graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0.

AEs will be summarized by SOC and PT using counts and percentage (i.e., number and percentage of participants with an AE). AEs will be sorted by decreasing frequency within each SOC and PT as per the overall column.

Where a participant has the same AE, based on PT reported multiple times, the participant will only be counted once at that PT level. Where a participant has multiple AEs within the same SOC, the participant will only be counted once at that SOC level.

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If a participant experiences the same AE more than once with different severity grades, then the event with the highest severity will be tabulated by maximum severity. In addition, AEs with a missing severity will be presented in the summary table under the category of 'Missing' and will not be imputed.

TEAEs are defined as any AE occurring or worsening on or after the first dose of study treatment.

TEAEs will be assigned to Part A, Part B and Part A+B using the event start date and time and will be defined as:

- Part A: events started on or after the first dose of study medication for Part A but not after Part B or events present prior to the first dose of study medication for Part A but increased in severity on or after dosing on Part A but not after Part B
- Part B: events started on or after the first dose of study medication for Part B or events present prior to the first dose of study medication for Part B but increased in severity on or after dosing on Part B

For Part A+B treatment emergent AEs relating to the Part when the subject was on the corresponding treatment are considered as TEAE.

Adverse events with an onset on Day 1 which are based upon pre-dose lab tests will be considered as not treatment emergent. These are defined as:

- Adverse events which begin on study day 1 with SOC = "Investigations" or PT in ("Hypercholesterolaemia" "Hyperlipidaemia" "Dyslipidaemia", "Type V hyperlipidaemia").
- The latest lab test taken on Day 1 has a time which is before the treatment start time.

Treatment-related AEs are those events with relationship to study drug 'Related' as recorded on the CRF. If the relationship to study drug is missing, the AE will be considered as treatment related.

[redacted]

Separate summary tables by treatment will be presented with the total number of events and number and percentage of participants with:

- All TEAEs
- Grade 3/4/5 TEAEs
- TEAEs by maximum intensity
- Related TEAEs
- TEAE leading to treatment discontinuation

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- TEAE leading to study discontinuation
- Serious adverse events (SAEs)
- Related SAEs
- Fatal AEs
- AESI.

AEs by DSUR safety topics (Hypersensitivity reactions SMQ; Opportunistic Infections SMQ; Gastrointestinal nonspecific inflammation and dysfunctional conditions SMQ).Where a participant has the same AE, based on PT reported multiple times, the participant will only be counted once at that PT level. Where a participant has multiple AEs within the same SMQ, the participant will only be counted once at that SMQ level. AEs by DSUR safety topics will only be presented for DSUR analysis.

An overall summary presenting the categories above will also be prepared by treatment group for Part A, Part B, and Part A+B. In addition, the total number of participant treatment years and exposure adjusted incidence rates [EAIR] will be provided as described in Appendix J.

8.9.2 Clinical Laboratory Evaluations

All central laboratory (hematology, biochemistry, urinalysis) parameters will be collected as described in Appendix I.

Observed and change from baseline values for clinical laboratory parameters will be summarized using descriptive statistics by treatment group and visit separately for Part A and Part B. Shift from baseline to each scheduled assessment and the worst post treatment value according to normal ranges criteria will be presented. Shift from baseline to each scheduled assessment and the worst post treatment value according to CTCAEv5.0 criteria will also be presented. CTCAEv5.0 criteria are described in Appendix L. Participants meeting any grade 3 criteria will also be listed.

In addition, the number and percentage of participants meeting the criteria for normal ranges in laboratory parameters will be summarized by treatment group separately for Part A and Part B.

Laboratory results together with the normal ranges will be listed, flagging values that are below or above the normal range. Serum/urine pregnancy tests assessments will be listed only.

Boxplots of the observed and change from baseline values for all clinical laboratory parameters will be presented by treatment group and visit for Part A and Part B. Reference lines for the normal ranges, that consistent across all participants being presented, will be displayed.

For participants with an AE of grade 3 or higher the hematology and chemistry lab parameters for that participant will be presented in a panel plot with a panel for each lab parameter. The x-axis will be the study week and the y-axis will be the absolute lab value.

8.9.3 Vital Signs

Vital sign parameters collected are weight (kg), systolic and diastolic blood pressure (SBP and DBP) (mmHg), heart rate (beats/min), respiratory rate (breaths/min) and temperature (°C).

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Observed values and the corresponding change from baseline values will be summarized using descriptive statistics by treatment group and visit separately for Part A and Part B.

In addition, the number and percentage of participants meeting criteria for potentially clinically significant abnormalities in vital signs (SBP, DBP and heart rate) and body weight will be summarized by treatment group separately for Part A and Part B. The following table presents the Criteria for clinically relevant abnormalities.

Table: Criteria for Clinically Relevant Abnormalities in Vital Sign Parameters

Parameter	Criteria
SBP (mmHg)	Value ≤90 or decrease ≥20 mmHg from baseline Value ≥180 or increase ≥20 mmHg from baseline
DBP (mmHg)	Value ≤50 or decrease ≥15 mmHg Value ≥105 or increase ≥15 mmHg
Heart Rate (beats/min)	Value ≤50 bpm or decrease from baseline ≥20 bpm Value ≥120 bpm or increase from baseline≥20 bpm
Weight (kg)	≥7% decrease from baseline ≥7% increase from baseline

8.9.4 Physical Examinations

The following parameters and body systems will be examined and any abnormalities described general appearance, skin (presence of rash), HEENT (head, ears, eyes, nose, throat), lungs (auscultation), heart (auscultation for presence of murmurs, gallops, rubs), lower extremity exam, abdomen (palpation and auscultation), neurologic (mental status, station, gait, reflexes, motor and sensory function, coordination) and lymph nodes.

All physical examination findings will be listed only.

8.9.5 Electrocardiograms

The standard 12-lead ECG parameters collected are: intervals (RR, PR, QRS, QT and QT intervals corrected for heart rate using Bazett's and Fridericia's formulas [QTcB and QTcF, respectively]).

Observed values and the corresponding change from baseline values will be summarized using descriptive statistics at each scheduled assessment by treatment group separately for Part A and Part B.

The overall ECG interpretation will be summarized by presenting the number and percentage of participants with 'Normal' and 'Abnormal' by visit and treatment group for Part A and Part B. Shift tables from baseline (Normal/Abnormal) to each visit and to the worst post-baseline ECG interpretation will be summarized.

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ECG data will be listed by participants at each visit and time point collected with indicated clinically significant results.

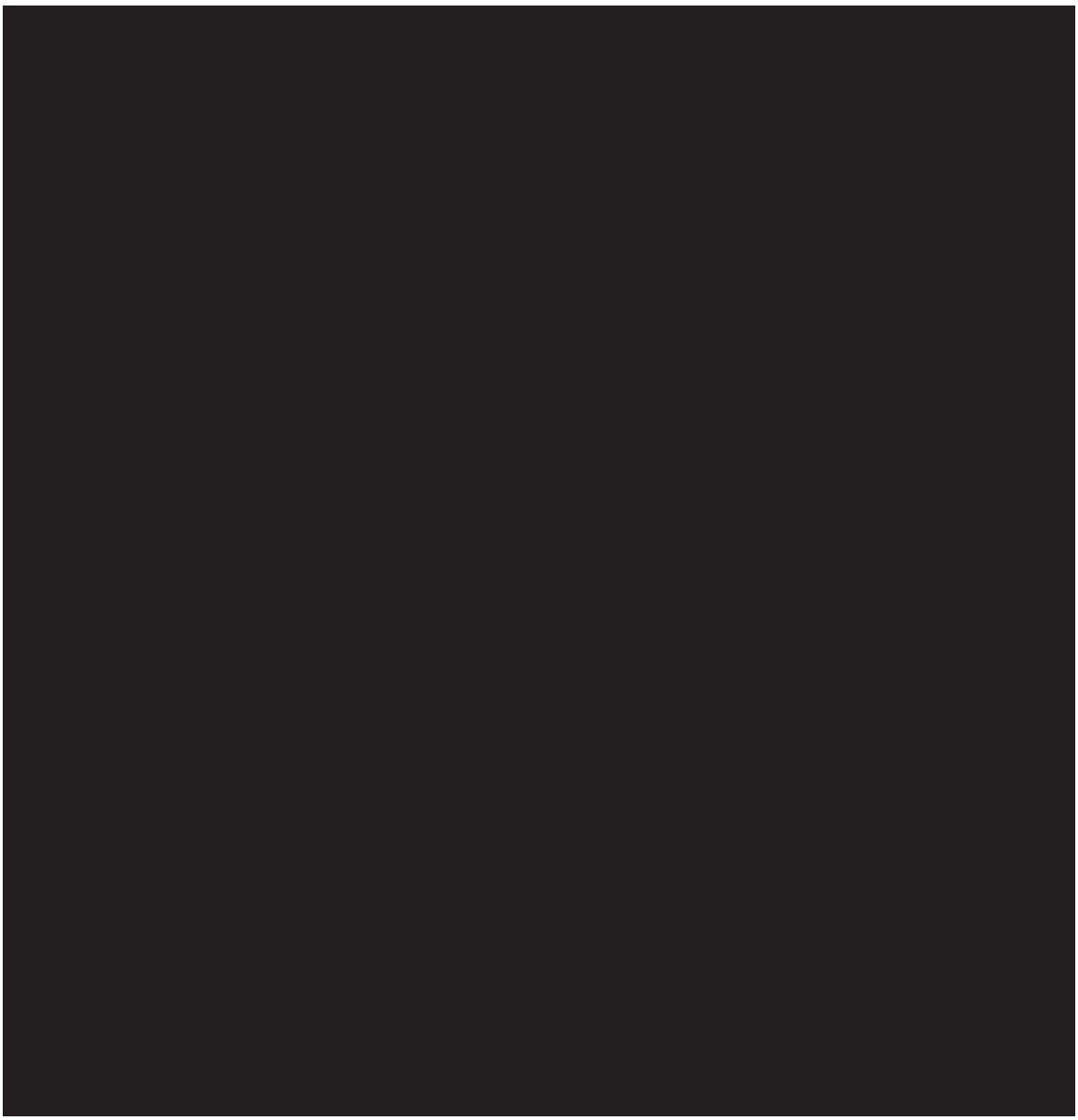
In addition, the number and percentage of participants meeting the criteria for potentially clinically significant abnormalities in ECG parameters will be summarized by treatment group separately for Part A and Part B. The following table presents the criteria for clinically relevant abnormalities.

Table: Criteria for Clinically Relevant Abnormalities in ECG Parameters

Parameter	Criteria
PR Interval	>200 ms >200 ms and increase from baseline ≥25% > 220 ms >220 ms and increase from baseline ≥25% > 240 ms > 240 ms and increase from baseline ≥25%
QRS Interval	>110 ms >110 msec and increase from baseline ≥25% >120 ms >120 ms and increase from baseline ≥25%
QT Interval	>500 ms
QTcB and QTcF	**Absolute Values** >450 to ≤480 msec >480 to ≤500 msec >500 msec **Change from baseline:** Change from baseline >30 to ≤60 msec Change from baseline >60 msec

[redacted]

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8.10 Subgroup Analysis

Subgroup analyses for the primary endpoint and key secondary endpoints may be considered for the following baseline variables:

- Sex (male, female);
- Weight (< 100kg, ≥ 100kg);
- Prior exposure to biologic agents (yes/no);
- Concomitant DMARD use (yes/no)

These subgroup analyses will be carried out using the participants from FAS for Part A only.

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Categorical variables will be analysed using a logistic regression model as per Section 8.6.1.1 but with the addition of the subgroup and subgroup by treatment interaction as covariates.

A forest plot will be used to display the results of the subgroup analyses.

If an individual subgroup for a variable includes fewer than 5% of the total planned study size, the subgroup analyses for that variable may be omitted.

Additional subgroup analyses may be performed at the sponsor's discretion. These additional analyses are beyond the scope of this SAP and will be specified in a separate document, if needed.

Subgroup analysis will be done pairwise to match with the main analysis. A logistic regression model including fixed effects for treatment and stratification factors sex and exposure to biologic agents prior to the screening visit is used for the odds ratio and 95% CI. The adjusted risk difference and 95% confidence interval will be found in the same way as for the main analysis, calculated for each combination of treatments within each subgroup category.

8.11 Interim Analysis

Not applicable.

8.12 Primary Analysis Timing

The primary analysis and unblinding of the data will be performed when all data up to and including Week 12 has been collected and database lock declared.

The study will be continued regardless of the results of the primary analysis.

8.13 Data Safety Monitoring Board

As required, a select number of safety outputs will be generated for the review of the DSMB. For full details of the scope of the DSMB, please see the DSMB charter. In addition a summary of the observed ACR50 responders will be presented for FAS.

8.14 Development Safety Update Report

As required, the below DSUR summaries will be generated (until unblinding only a blinded column will be presented):

- Number of participants randomized;
- Number of participants exposed by age and sex;
- Number of participants exposed by race;
- Number of SAEs within the DSUR reporting period;
- Number of SAEs;
- Listing of SAEs.

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9 CHANGES TO PLANNED ANALYSIS FROM STUDY PROTOCOL

An additional sensitivity analysis targeting treatment policy where response is analyzed regardless of intercurrent events will also be performed on the primary endpoint.

The sensitivity estimand will also include subjects who discontinued due to adverse events.

Logistic regression estimator approach for population-level difference of proportions will be used instead of logistic regression with multiple covariates.

[redacted]

Composite endpoints for ACR+PASI are added.

LOCF/NRI analysis is added for responder parameters and LOCF for continuous.

BASDAI derivation is re-calculated according to SAP.

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10 REFERENCES

1. ICH Topic E3: Structure and Content of Clinical Study Reports (CPMP/ICH/137/95- adopted December 1995).
2. ICH Topic E9: Statistical Principles for Clinical Trials (CPMP/ICH/363/96 – adopted March 1998).
3. Taylor W, Gladman D, Helliwell P, et al. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum 2006;54(8):2665-73.
4. Ge, Durham, Meyer, Xie, Thomas. Covariate-adjusted Difference in Proportions From Clinical Trials Using Logistic Regression and Weighted Risk Differences, DIG, 2011 45:481

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11 APPENDICES

Appendix A: **HAQ-DI**

HEALTH ASSESSMENT QUESTIONNAIRE

Name_____ **Date**_____

In this section we are interested in learning how your illness affects your ability to function in daily life. Pleas

feel free to add any comments on the back of this page.

Please check the response which best describes your usual abilities OVER THE PAST WEEK:

	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	UNABLE To Do
DRESSING & GROOMING				
Are you able to:				
- Dress yourself, including tying shoelaces and doing buttons?	_____	_____	_____	_____
- Shampoo your hair?	_____	_____	_____	_____
ARISING				
Are you able to:				
- Stand up from a straight chair?	_____	_____	_____	_____
- Get in and out of bed?	_____	_____	_____	_____
EATING				
Are you able to:				
- Cut your meat?	_____	_____	_____	_____
- Lift a full cup or glass to your mouth?	_____	_____	_____	_____
- Open a new milk carton?	_____	_____	_____	_____
WALKING				
Are you able to:				
- Walk outdoors on flat ground?	_____	_____	_____	_____
- Climb up five steps?	_____	_____	_____	_____

Please check any AIDS OR DEVICES that you usually use for any of these activities:

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_____ Cane
_____ Devices used for dressing (button hook, zipper pull, long-handled shoe horn, etc.)
_____ Walker
_____ Built up or special utensils
_____ Crutches
_____ Special or built up chair
_____ Wheelchair
_____ Other (Specify:_____)

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

_____ Dressing and Grooming
_____ Eating
_____ Arising
_____ Walking

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Please check the response which best describes your usual abilities OVER THE PAST WEEK:

	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	UNABLE To Do
HYGIENE				
Are you able to:				
- Wash and dry your body?	_____	_____	_____	_____
- Take a tub bath?	_____	_____	_____	_____
- Get on and off the toilet?	_____	_____	_____	_____
REACH				
Are you able to:				
- Reach and get down a 5 pound object (such as a bag of sugar) from just above your head?	_____	_____	_____	_____
- Bend down to pick up clothing from the floor?	_____	_____	_____	_____
GRIP				
Are you able to:				
- Open car doors?	_____	_____	_____	_____
- Open jars which have been previously opened?	_____	_____	_____	_____
- Turn faucets on and off?	_____	_____	_____	_____
ACTIVITIES				
Are you able to:				
- Run errands and shop?	_____	_____	_____	_____
- Get in and out of a car?	_____	_____	_____	_____
- Do chores such as vacuuming or yardwork?	_____	_____	_____	_____

Please check any AIDS OR DEVICES that you usually use for any of these activities:

_____ Raised toilet seat
_____ Bathtub seat
_____ Jar opener (for jars previously opened)
_____ Bathtub bar
_____ Long-handled appliances for reach
_____ Long-handled appliances in bathroom
_____ Other (Specify: _____)

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Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

_____ Hygiene _____ Gripping and opening things

_____ Reach _____ Errands and chores

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Appendix B: **Patients Assessment of Arthritis Pain (PtAAP)**

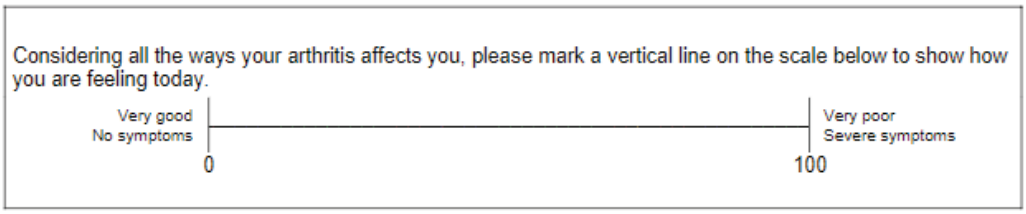
How much pain have you had because of your arthritis TODAY:

PLACE A VERTICAL (I) MARK ON THE LINE TO INDICATE THE SEVERITY OF THE PAIN.

NO PAIN		MOST SEVERE PAIN
0	_____	100

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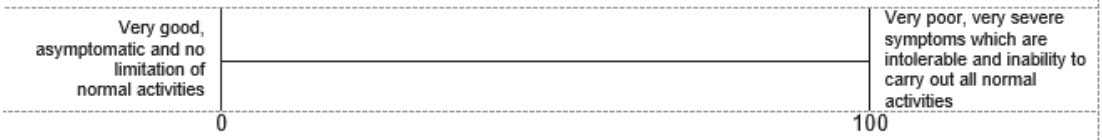
Appendix C: **Patients Global; Assessment of Disease Activity (PtAAP)**



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Appendix D: **Physician's Global; Assessment of Disease Activity (PtAAP)**

Please indicate your assessment of the patient's overall disease activity by marking a vertical line through the line below.



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Appendix E: **Leeds Enthesitis Index (LEI)**

LEEDS ENTHESITIS INDEX (LEI)		
1.	Date of LEI [Date of assessment]	**[Date of assessment]** **[Date of assessment] (DD/MM/YYYY)** ☐ Done Date of LEI __/__/____ ☐ Not Done
2.	Lateral epicondyle - Left [Lateral epicondyle - Left]	**[Lateral epicondyle - Left]** ☐ Present ☐ Absent ☐ Not Done ☐ Not Applicable
3.	Medial femoral condyle - Left [Medial femoral condyle - Left]	**[Medial femoral condyle - Left]** ☐ Present ☐ Absent ☐ Not Done ☐ Not Applicable
4.	Achilles tendon insertion - Left [Achilles tendon insertion - Left]	**[Achilles tendon insertion - Left]** ☐ Present ☐ Absent ☐ Not Done ☐ Not Applicable
5.	Lateral epicondyle - Right [Lateral epicondyle - Right]	**[Lateral epicondyle - Right]** ☐ Present ☐ Absent ☐ Not Done ☐ Not Applicable
6.	Medial femoral condyle - Right [Medial femoral condyle - Right]	**[Medial femoral condyle - Right]** ☐ Present ☐ Absent ☐ Not Done ☐ Not Applicable
7.	Achilles tendon insertion - Right	**[Achilles tendon insertion - Right]** ☐ Present ☐ Absent ☐ Not Done ☐ Not Applicable
8.	**LEI score:** _____	**LEI score:** _____

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Appendix F: **Psoriatic Assessment Impact of Disease-12**

We want you to indicate how much your psoriatic arthritis impacts your health. Please tell us how you have been feeling this last week.

Pain

Circle the number that best describes the pain you felt due to your psoriatic arthritis during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

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Result x3 ☐

Fatigue

Circle the number that best describes the overall level of fatigue due to your psoriatic arthritis you have experienced during the last week:

No fatigue	0	1	2	3	4	5	6	7	8	9	10	Totally exhausted

Result x2 ☐

Skin problems

Circle the number that best describes the skin problems including itching you felt due to your psoriatic arthritis du[redacted] week:

Result x2 ☐

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None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Work and/or leisure activities

Circle the number that best describes the difficulties you had to participate fully in work and/or leisure activities due to your psoriatic arthritis during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Result x2 ☐

Functional capacity

Circle the number that best describes the difficulty you had in doing daily physical activities due to your psoriatic [illegible]ng the last week:

No difficulty	0	1	2	3	4	5	6	7	8	9	10	Extreme difficulty

Result x2 ☐

Discomfort

Circle the number that best describes the feeling of discomfort and annoyance with everyday tasks due to your psoriatic arthritis during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Result x2 ☐

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Sleep disturbance

Circle the number that best describes the sleep difficulties (i.e., resting at night) you felt due to your psoriatic arthr[illegible]e last week:

No difficulty	0	1	2	3	4	5	6	7	8	9	10	Extreme difficulty

Result x2 ☐

Coping

Considering your psoriatic arthritis overall, how well did you cope (manage, deal, make do) with your psoriatic a[illegible] the last week?

Very well	0	1	2	3	4	5	6	7	8	9	10	Very poorly

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Result x1 ☐

Anxiety, fear and uncertainty

Circle the number that best describes the level of anxiety, fear and uncertainty (for example about the future, treatments, fear of loneliness) due to your psoriatic arthritis you have experienced during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Result x1 ☐

Embarrassment and/or shame

Considering your psoriatic arthritis overall, circle the number that best describes the level of embarrassment and/or shame due to your appearance experienced during the last week:

Result x1 ☐

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None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Social participation

Circle the number that best describes the difficulties you had to participate fully in social activities (including relationships with family and/or people very close to you) due to your psoriatic arthritis during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Result x1 ☐

Depression

Circle the number that best describes the level of depression due to your psoriatic arthritis you have experienced during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Result x1 ☐

THANK YOU FOR ANSWERING THIS QUESTIONNAIRE

Final PsAID out of 20

Add up the ☐ and divide by 20:

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Appendix G**: Leeds Diactylitis Score**



Finger / Toe	Circumference Involved Digit (A)	Contralateral Digit (or Tables) (B)	Tenderness Score (C)	Final Score: [{(A/B)-1}x100]xC
TOTAL	0	0	0	0

Standard reference: Table - hands

Digit	Men	Women
Thumb	70	58
Index	63	54
Middle	63	54
Ring	59	50
Little	52	44

Table – feet

Digit	Men	Women
Great toe	82	72
Second	52	46
Middle	50	44
Fourth	50	44
Little	52	45

Tenderness score: response to squeeze
0 no tenderness
1 tender
2 tender and wince
3 tender and withdraw

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Appendix H: **FACIT-Fatigue Scale**

Below is a list of statements that other people with your illness have said are important. **Please select one number per line to indicate your response as it applies to the past 7 days.**

		Not at all	A little bit	Some-what	Quite a bit	Very much
HI7	I feel fatigued	0	1	2	3	4
HI12	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble starting things because I am tired	0	1	2	3	4

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An4	I have trouble finishing things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4
An7	I am able to do my usual activities	0	1	2	3	4
An8	I need to sleep during the day	0	1	2	3	4
An12	I am too tired to eat	0	1	2	3	4
An14	I need help doing my usual activities	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
An16	I have to limit my social activity because I am tired	0	1	2	3	4

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Appendix J: **Clinical Laboratory Tests**

Laboratory Testing Profile	Tests Included
Laboratory tests required prior to first study treatment dose only	QuantiFERON TB-gold test (or equivalent IGRA), HIV testing, hepatitis B serology (HBV PCR if required) including hepatitis B surface antigen and antibody and hepatitis B core antibody, hepatitis C serology, HCV antibodies, confirmatory HCV PCR, SARS-CoV-2 PCR, RF, CCP antibodies, FSH, serum pregnancy
Blood Chemistry	Sodium, potassium, chloride, bicarbonate, total protein, blood urea nitrogen, serum creatinine, albumin, alkaline phosphatase, AST, ALT, total bilirubin, direct bilirubin, indirect bilirubin, calcium, GGT, creatine kinase, hs-CRP
Hematology	Hemoglobin, hematocrit, WBC with differentials (monocytes, eosinophils, basophils, neutrophils, lymphocytes) as an absolute value, RBC count, platelet count, ESR
Urinalysis	Local urine testing Routine urinalysis will be performed locally with urine dipstick test (semi-quantitative "dipstick" evaluation of specific gravity, pH, glucose, protein, bilirubin, ketones, leukocytes, blood). If the dipstick urine test indicates any abnormal findings, the urine sample will be sent to the central laboratory for further assessments, as appropriate (reflex testing). Central lab urine testing (reflex testing) Urine chemistry (albumin:creatinine and protein:creatinine ratios) to be performed if dipstick indicates protein; Microscopy and/or culture to be performed if clinically indicated or if urinalysis results positive (blood, protein or leukocyte esterase/WBC)

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Urinalysis	Note: Urine hCG pregnancy testing for WOCBP; may be repeated more frequently than indicated if required by local practice, if a menstrual cycle is missed, or if potential pregnancy is suspected
Fasting Lipid Panel and Glucose to be performed at Day 1/Week 0 and EOT	Fasting: glucose, total cholesterol, low density lipoprotein, high density lipoprotein, triglycerides,

Abbreviations: ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CCP = cyclic citrullinated peptide; EOT: End of Treatment; ESR: erythrocyte sedimentation rate; FSH: Follicle stimulating hormone; GGT: gamma-glutamyl transferase, HBV: hepatitis B virus; HCV: hepatitis C virus; HIV: Human immunodeficiency virus; hs-CRP: high-sensitivity C-reactive protein, IGRA = interferon-gamma release assay; PCR: Polymerase chain reaction; RBC: red blood cells; RF = rheumatoid factor; TB = tuberculosis; SARSCoV2: Severe Acute Respiratory Syndrome Coronavirus 2; WBC: white blood cells; WOCBP = women of childbearing potential

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Appendix K: **Exposure adjusted incidence rate**

It will be assumed that for each of n participants in a clinical trial the time tj (j=1,...,n) to the first occurrence of a certain event is observed, or if the event was not experienced, the (censored) time to the end of the observation period for each treatment group. The sequence of first occurrences of an event will be modeled to follow approximately a Poisson process with constant intensity θ. The rate parameter θ will be estimated as λ=D/T, where $T = \sum_{j=1}^{n} t_j$ and D is the number of participants with at least one event. The end of the observation period for subjects randomized in Part A to sonelokimab is the last visit date in Part B or study discontinuation date. The end of the observation period for subjects randomized to placebo or Adalimumab will be the first dose of Part B study medication or study discontinuation if discontinued during Part A. The start of the observation period of sonelokimab for subjects who were randomized to placebo or Adalimumab in Part A will be the first dose of Part B study medication.

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Appendix L: **CTCAE v5.0 laboratory grades**

Lab parameter	Units		Grade 1	Grade 2	Grade 3	Grade 4
sodium	mmol/L	low	130 - < LLN	125-129	120-124	<120
		high	>ULN - 150	>150 - 155	> 155-160	> 160
potassium	mmol/L	low	3.0 - < LLN	3.0 - < LLN	2.5 - < 3.0	< 2.5
		High	> ULN – 5.5	> 5.5 – 6.0	> 6.0 – 7.0	> 7.0
Alanine aminotransferase	U/L	High	>ULN – 3* ULN if baseline normal; >1.5 – 3*ULN if baseline abnormal	> 3 – 5*ULN	> 5 – 20*ULN	> 20*ULN
Alkaline phosphatase	U/L	High	>ULN – 2.5* ULN if baseline normal; >2.0 – 2.5*ULN if baseline abnormal	> 2.5 – 5*ULN	> 5 – 20*ULN	> 20*ULN
Aspartate aminotransferase	U/L	High	>ULN – 3* ULN if baseline normal; >1.5 – 3*ULN if baseline abnormal	> 3 – 5*ULN	> 5 – 20*ULN	> 20*ULN
Total bilirubin	umol/L	High	>ULN – 1.5* ULN	> 1.5 – 3*ULN	> 3 – 10*ULN	> 10*ULN
Serum creatinine	umol/L	High	> ULN – 1.5* ULN	> 1.5 – 3.0*ULN	> 3.0 – 6.0 ULN	> 6.0*ULN
Creatine kinase	U/L	High	> ULN – 2.5* ULN	> 2.5 – 5.0*ULN	> 5.0 – 10.0 ULN	> 10.0*ULN
Albumin	g/L	low	30 - < LLN	20 - <30	< 20	
Calcium	mmol/L	Low	2.0 - < LLN	1.75 - < 2.0	1.5 - < 1.75	< 1.5
		High	>ULN – 2.9	>2.9 – 3.1	>3.1 – 3.4	>3.4
GGT		High	>ULN – 2.5*ULN if baseline normal; >2.0 – 2.5*ULN if baseline abnormal	>2.5 – 5.0*ULN	>5.0-20.0*ULN	>20.0*ULN
Hemoglobin	g/L	low	100 - <LLN	80 - < 100	< 80	
		High	Increase >0-20	Increase >20-40	Increase >40	
Neutrophils	10^9/L	Low	1.5 - < LLN	1.0 - <1.5	0.5 - <1.0	<0.5
Lymphocytes	10^9/L	Low	0.8 - <LLN	0.5 - <0.8	0.2 - <0.5	<0.2
		High	-	>4-20	>20	-
Platelets	10^9/L	Low	75 - <LLN	50 - <75	25 - <50	<25

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