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STATISTICAL ANALYSIS PLAN

Protocol Title:	A Phase 2, randomized, double-blind, placebo-controlled, efficacy and safety study of daxdilimab subcutaneous injection in adult participants with inadequately controlled dermatomyositis or anti-synthetase inflammatory myositis.
Name of Test Drug:	Daxdilimab (AMG 455, HZN-7734)
Protocol Number:	HZNP-DAX-205
Protocol Version (Date):	09 SEP 2024
Analysis Type:	All Planned Analyses
Analysis Plan Version:	3.0
Analysis Plan Author(s):	[redacted]

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LIST OF ABBREVIATIONS

Abbreviation	Definition
ACR/EULAR 2017	American College of Rheumatology/European League Against Rheumatism 2017
ADA	antidrug antibodies
AE	adverse event
AESI	adverse event of special interest
ALT	alanine aminotransferase
ASIM	anti-synthetase inflammatory myositis
AST	aspartate transaminase
ATC	Anatomical Therapeutic Chemical
BMI	body mass index
BP	body pain
CDASI	cutaneous dermatomyositis disease area and severity index
CI	confidence interval
COA	clinical outcome assessment
CSM	core set measures
CTCAE	common terminology for adverse events
DM	dermatomyositis
EGA	extramuscular global assessment
HAQ-DI	health assessment questionnaire-disability index
IFN	interferon
LME	laboratory muscle enzymes
LOCF	last observation carried forward
IP	investigational product
LTE	long-term extension
MedDRA	Medical Dictionary for Regulatory Activities
[redacted]	
MH	mental health
MMT	manual muscle testing
OCS	oral corticosteroid
OLE	open-label extension
[redacted]	
pDC	plasmacytoid dendritic cell

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Abbreviation	Definition
[redacted]	
PhGDA	physician global disease activity
PK	pharmacokinetics
PT	preferred term
PtGDA	patient global disease activity
Q1, Q3	first quartile, third quartile
Q4W	once every 4 weeks
QTc	QT interval corrected for heart rate
QTcB	QT interval corrected for heart rate using Bazett's formula
QTcF	QT interval corrected for heart rate using Fridericia's formula
SAE	serious adverse event
SAP	statistical analysis plan
SC	subcutaneous
SD	standard deviation
SE	standard error
SoA	schedule of assessments
SOC	system organ class
SPP	statistical programming plan
TEAE	treatment-emergent adverse event
TEAESI	treatment-emergent adverse events of special interest
TESAE	treatment-emergent SAE
TIS	total improvement score
ULN	upper limit of normal
VAS	visual analog scale
WHO-DD	World Health Organization Drug dictionary

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SAP REVISION

Effective Date (DD MMM YYYY)	Version	Author	Summary of Changes
1-Feb-2024	1	[redacted]	Original Version
31-Oct-2024	2	[redacted]	[redacted] Efficacy and safety analysis plans are updated to reflect the changes in protocol amendment 2: • Interim and primary analyses are excluded • Statistical hypotheses are excluded • Efficacy estimands and analysis methods are updated • Safety analyses methods are updated • Pharmacokinetics, [redacted] analyses methods are updated
21-August-2025	3	[redacted]	For Manual Muscle Testing missing data handling method and absolute % change calculation method are updated. For CDASI missing data handling method is updated.
5-September-2025	4	[redacted]	1. Removed the following for endpoints TIS20 and TIS40: i. No use of rescue medications before Week 24. ii. No discontinuation of IP before Week 24. 2. Definition for confirmed deterioration is added.

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1 INTRODUCTION

This document describes the statistical analysis for protocol HZNP-DAX-205, a phase 2, randomized, double-blind, placebo-controlled, efficacy and safety study of daxdilimab subcutaneous injection in adult participants with inadequately controlled dermatomyositis or anti-synthetase inflammatory myositis.

Due to recruitment challenges, the sponsor decided to stop enrollment early, thus a Synopsis Clinical Study Report will be developed. This SAP only covers analysis for the Synopsis Clinical Study Report.

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2 TRIAL OVERVIEW

2.1 Trial Objectives and Endpoints

The objectives and corresponding endpoints are listed below:

Table 1 Objectives and Endpoints

Objectives	Endpoints
Primary Efficacy	
• To evaluate the effect of daxdilimab compared with placebo in reducing disease activity at Week 24.	• TIS at Week 24.
Secondary Efficacy	
• To evaluate the effect of daxdilimab compared with placebo in reducing disease activity at Week 24.	• Proportion of participants with improvement of TIS ≥ 40 and without deterioration at 2 consecutive visits at 24 weeks. • Proportion of participants with improvement of TIS ≥ 20 and without deterioration at 2 consecutive visits at 24 weeks.
• To evaluate the effect of daxdilimab compared with placebo on skin symptoms at Week 24.	• Change in the CDASI activity score from Baseline (Day 1) to Week 24.
• To evaluate the effect of daxdilimab on decreasing the use of corticosteroid at Week 24.	• Proportion of participants on an OCS dose ≥ 10 mg of prednisone or equivalent at Baseline who achieve a clinically meaningful reduction in the OCS dose: either a 25% decrease or an OCS dose of 7.5 mg/day of prednisone or equivalent at Week 24.
Pharmacokinetics and Immunogenicity	
• To characterize the PK and immunogenicity of daxdilimab in participants.	• Serum concentration of daxdilimab over time. • Prevalence at Baseline and incidence and titer of ADA directed against daxdilimab over time.
Safety	
• To evaluate the safety and tolerability of daxdilimab in participants.	• Incidence of TEAEs • Incidence of TESAEs • Incidence of TEAESIs: hypersensitivity reaction, including anaphylaxis, herpes zoster infection, severe (CTCAE Grade 3 or higher) viral infection/reactivation, opportunistic infection, and malignancy (except non-melanoma skin cancer).
Exploratory	
[redacted]	

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[redacted]	

[redacted]PK = pharmacokinetics; TEAEs = treatment-emergent adverse events; TESAEs = treatment-emergent serious adverse events; TEAESIs = treatment-emergent adverse events of special interest; TIS = total improvement score

2.2 Trial Design

This study is a Phase 2, randomized, double-blind, placebo-controlled, proof of concept study to assess the efficacy and safety of daxdilimab in participants aged ≥ 18 to ≤ 75 years with dermatomyositis (DM) or anti-synthetase inflammatory myositis (ASIM).

The study will enroll 2 idiopathic inflammatory myositis participant populations:

- Population 1 or DM: participants with DM with definite or probable myositis according to the American College of Rheumatology/European League Against Rheumatism 2017 (ACR/EULAR 2017) criteria and a DM rash.
- Population 2 or ASIM: participants with ASIM with definite or probable myositis according to ACR/EULAR 2017 criteria and a positive ASIM associated antibody.

Approximately 10 participants will be randomized by population in a 1:1 ratio (2-3 participants per group) to receive investigational product (IP) (daxdilimab 300 mg or placebo) by subcutaneous (SC) injection once every 4 weeks (Q4W):

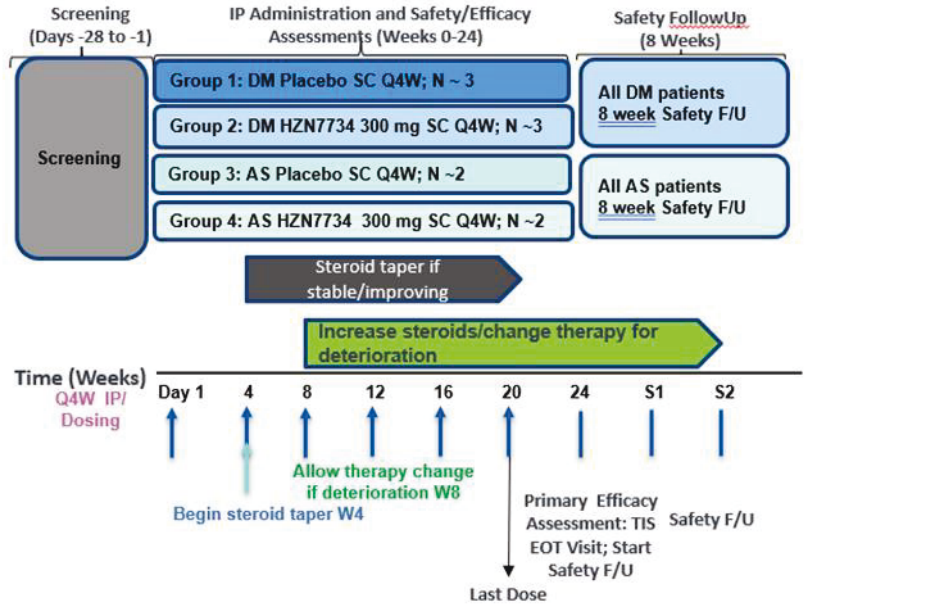
- Group 1: DM placebo
- Group 2: DM daxdilimab 300 mg
- Group 3: ASIM placebo
- Group 4: ASIM daxdilimab 300 mg

Randomization will take place, at the latest, 28 days after successful screening and it will be stratified by Manual Muscle Testing 8 (MMT8) score (≤ 120 vs > 120) at Baseline (Day 1).

The basic study flow diagram is presented in Figure 1.

Figure 1 Study Flow Diagram

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Note: Participants who have received dosing beyond Week 20 will discontinue treatment and complete the procedures required at the EOT visit 4 weeks after the last dose and then complete the SFU (S1 and S2) visits

ASIM = anti-synthetase inflammatory myositis; DM = dermatomyositis; G = group; IP = investigational product; N = number of participants; Q4W = once every 4 weeks; SC = subcutaneously; SFU = safety

[redacted]

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3 PLANNED ANALYSES

Final Analysis: The final analysis will be conducted after the last participant has completed the study or discontinued early from study.

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4 STATISTICAL METHODS

4.1 General Considerations for Data Analyses

All statistical calculations will be primarily performed using SAS® System Version 9.4 or higher. Analysis results will be presented using descriptive statistics. For categorical variables, the number and percentage of participants in each category will be presented; for continuous variables, the number of participants (n), mean, standard deviation (SD), median, first quartile (Q1), third quartile (Q3), minimum, and maximum will be presented.

For additional details on data presentation, refer to the Statistical Programming Plan (SPP).

Table 2 below provides an overview of the study periods for reporting purposes.

Table 2 Study Periods

Study Period	Description
Stage I	Day 1 to Week 24 efficacy and safety assessments
Stage II	Post Week 24 efficacy and safety assessments + safety follow-up. This is only applicable for participants who entered the Stage II open label extension period.

4.1.1 Definition of Baseline

Unless otherwise specified, baseline is defined as the last non-missing valid observation prior to the first dose of trial intervention. In cases where baseline measurements are taken on the same day as trial intervention and no time is reported, it will be assumed that these measurements are taken prior to trial intervention being administered.

4.1.2 Analysis Windows

Analysis visit windows will be used for all visit-based assessments to map longitudinal observations to scheduled visits and thereby allow for by-visit analyses, since not all assessments are performed on the scheduled day. Unless otherwise specified, all longitudinal efficacy, safety, and biomarker data analyses will be based on the analysis visit windows.

The analysis visit windows will be calculated by bisecting the interval between adjacent scheduled visit days except for the first post-treatment visit and Week 24 visit. The first post-treatment visit will start on Day 2. When mapping to the Week 24 analysis window, this should only occur for assessments on or before the date of the nominal Week 24 dosing. Assessments after this date will be mapped to the following analysis visit windows. All observations will be included in data listings.

No visit windows will be derived for the screening period. For the visits on or after the date of the 1st dose, the actual visit date will be mapped to the derived analysis visit windows based on the study day provided in the following tables, where study day will be defined as below.

- Study Day = Date of assessment – Date of the first dose + 1

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The actual assessment day will be mapped to the windows defined for each scheduled study visit with the following rules:

- If more than one assessment falls within a visit window, the closest non-missing assessment to the scheduled day will be used in the analysis.
- If two non-missing assessment actual dates are equidistant from the scheduled day, the one with later assessment date (time) will be used in the analysis.
- For retest values of laboratory data, the retest value (the last valid observation assessed on the same visit day) will be chosen.

4.1.3 Missing Data

In general, missing data will not be imputed unless methods for handling missing data are specified.

4.2 Protocol Deviations

The number and percentage of participants with major protocol deviations by deviation reason (e.g., nonadherence to study drug, violation of select inclusion/exclusion criteria) will be summarized. A by-participant listing will be provided for all protocol deviations.

4.3 Statistical Hypothesis

Not applicable.

4.4 Analysis Sets

4.4.1 Full Analysis Set

The Full Analysis Set includes all randomized participants who receive any dose of IP in the study. Participants will be analyzed according to the treatment randomized. The efficacy analysis will be based on the Full Analysis Set.

4.4.2 Safety Analysis Set

The Safety Analysis Set includes all participants who receive any dose of IP in the study. Participants will be analyzed according to the treatment that they actually received. The safety, ADA, and PD analyses will be based on the Safety Analysis Set.

4.4.3 Pharmacokinetic Analysis Set

The Pharmacokinetic (PK) Analysis Set includes all participants who receive any dose of daxdilimab in the study and have at least one quantifiable serum PK observation post first dose. Participants will be analyzed according to the treatment that they actually received. The PK analysis will be based on the PK Analysis Set.

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4.4.4 Stage II Analysis Set

The stage II analysis set includes all participants who receive at least one dose of daxdilimab during Stage II including Week 24. This is only applicable for participants who entered the Stage II open label extension period.

4.4.5 Any Daxdilimab Analysis Set

The any daxdilimab analysis set includes all participants who receive at least one dose of daxdilimab during the trial.

4.5 Participant Disposition

For each treatment group within the DM and ASIM populations, a summary of participant disposition will be presented using the categories presented below.

- Screened
- Screen failed with reasons
- Randomized
- Randomized but not treated
- Randomized and treated

Stage I:
- Completed treatment for the first 24 weeks (excluding Week 24 dose if applicable)
- Discontinued treatment for the first 24 weeks with reasons (excluding Week 24 dose if applicable)
- Completed the first 24 weeks of study
- Discontinued the first 24 weeks of study with reasons

Overall:
- Completed treatment
- Discontinued treatment with reasons
- Completed study
- Discontinued study with reasons

4.6 Trial Intervention Exposure

The number of doses received, amount of the trial intervention received, durations of the trial intervention exposure, and treatment compliance will be summarized by treatment group and by DM and ASIM populations separately. The summary will be produced using full analysis set for stage I and overall study, using stage II analysis set for stage II if applicable.

- Duration of the trial intervention exposure is defined as follows:
  – Stage I: minimum of (date of last dose before Week 24 + 28 – first dose date +1) and (Week 24 date – first dose date)
  – Stage II: last dose date + 28 – Week 24 date + 1
  Overall study: date of last dose date + 28 – first dose date + 1

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- The amount of trial intervention exposure: if a participant received partial dose at a dosing visit, then the amount of trial intervention at that dosing visit will be estimated based on the actual volume administered.
- Treatment compliance for an individual participant = [Total number of doses received]/[Total number of doses planned per protocol] ×100%.

4.7 Demographics, Baseline Characteristics, and Medical History

The demographics (age, gender, race, ethnicity, height, weight, and body mass index) will be summarized by treatment group and overall, within each of the DM and ASIM populations for the full analysis set.

A summary of baseline disease characteristics, by treatment group and overall within each of the DM and ASIM populations for the full analysis set will include [redacted] PhGDA score, MMT8 bilateral continuous score and binary categories (≤ 120 vs > 120), laboratory muscle enzymes scores including levels of creatine kinase, the transaminases (alanine transaminase (ALT) and aspartate transaminase (AST)), lactate dehydrogenase and aldolase; extramuscular global assessment score, CDASI (activity, damage and total) score, steroid dose, time from initial diagnosis of definite or probable myositis according to ACR/EULAR 2017 criteria to randomization, and other baseline information if needed.

Significant medical history findings will be summarized by Medical Dictionary for Regulatory Activities (MedDRA) system organ class (SOC) and preferred term (PT) by treatment group and overall, within each of the DM and ASIM populations for the full analysis set.

4.8 Efficacy Analyses

4.8.1 Primary Efficacy Endpoint and Analysis

Primary efficacy endpoint is TIS at Week 24. TIS is derived from standardized clinical response criteria that are recommended for use as primary endpoint in myositis therapeutic. The criteria use the following 6 CSMs, combining the absolute percentage change in each with varying weights to obtain a TIS on a scale of 0-100. At a minimum, one must enter PhGDA, MMT8 and at least 2 other core set measures for a TIS to be calculated.

- Physician Global Disease Activity (PhGDA) (part of the [redacted] The PhGDA is the physician's judgment of overall disease activity (extramuscular organ systems plus muscle disease activity) based on all clinical laboratory assessments. It uses a 10 cm VAS that ranges from "no evidence of disease activity" to "extreme or maximum disease activity". VAS is used in the calculation of TIS. Range for VAS is 0.0 – 10.0 cm.
- [redacted]

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- [redacted]
- [redacted]
- [redacted]

ranges from “no evidence of disease activity” to “extreme or maximum disease activity”. Range for VAS is 0.0 – 10.0 cm.

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- Laboratory Muscle Enzymes (LME): The levels of creatine kinase, alanine transaminase (ALT), aspartate transaminase (AST), lactate dehydrogenase, and aldolase will be measured to evaluate the effect of daxdilimab in muscle-associated enzymes. The most abnormal enzyme will be used for TIS calculation, which is determined by having the greatest Baseline value divided by its Upper Limit of Normal. Thus, the formula for absolute % of change for muscle enzymes is ((Baseline – Follow-up)/ Upper Limit of Normal)×100.

TIS is the sum of improvement scores of each CSMs.

The TIS calculation uses "Absolute % Change" according to the following formula for all CSMs but MMT8:

Absolute % Change = ((Baseline – Post-baseline)/Upper limit of Range)×100

For MMT8 as the higher score the better, thus the following formula will be applied:

Absolute % Change = ((Post-baseline – Baseline)/Upper limit of Range)×100

For Muscle enzymes, the range was calculated based on a 90% range of enzymes from natural history data, which

- for creatine kinase is 15 times the upper limit of normal (ULN),
- for aldolase is 6 times the ULN,
- and for lactate dehydrogenase, aspartate aminotransferase, and alanine transaminase is 3 times the ULN.

Each CSM will be assigned an improvement score according to the following.

Table 3 Core Set Measures Improvement Scores

Core Set Measure	Level of Improvement Based on Absolute Percentage Change	Improvement Score
Physician Global Disease Activity (PhGDA)	Worsening to 5% improvement >5% to 15% improvement >15% to 25% improvement >25% to 40% improvement >40% improvement	0 7.5 15 17.5 20
Patient Global Disease Activity (PtGDA)	Worsening to 5% improvement >5% to 15% improvement >15% to 25% improvement >25% to 40% improvement >40% improvement	0 2.5 5 7.5 10
Manual Muscle Testing 8 (MMT8) bilateral	Worsening to 2% improvement >2% to 10% improvement >10% to 20% improvement >20% to 30% improvement >30% improvement	0 10 20 27.5 32.5

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Health Assessment Questionnaire-Disability Index (HAQ-DI)	Worsening to 5% improvement >5% to 15% improvement >15% to 25% improvement >25% to 40% improvement >40% improvement	0 5 7.5 7.5 10
Extramuscular Global Assessment (EGA)	Worsening to 5% improvement >5% to 15% improvement >15% to 25% improvement >25% to 40% improvement >40% improvement	0 7.5 12.5 15 20
Laboratory Muscle Enzymes (LME)	Worsening to 5% improvement >5% to 15% improvement >15% to 25% improvement >25% to 40% improvement >40% improvement	0 2.5 5 7.5 7.5

The following criteria will be used to assign TIS improvement to categories of minimal, moderate, and major:

- Minimal: TIS $\geq$ 20
- Moderate: TIS $\geq$ 40
- Major: TIS $\geq$ 60

Note that for each category the displayed degree of improvement represents the highest degree of improvement achieved and implies that lower degrees of improvement were also achieved.

4.8.1.1 Primary Efficacy Analysis

Within each of the DM and ASIM populations, the primary efficacy endpoint of TIS at Week 24 will be summarized descriptively based on the observed data using the Full Analysis Set.

Longitudinal presentations of results over time up to Week 24 based on the same analysis will be created.

4.8.2 Secondary Efficacy Endpoints and Analyses

CDASI is an outcome measure used to assess the severity of cutaneous DM and detect improvement in disease activity. The scale rates disease involvement in 15 different body areas using 3 activity (erythema, scale, erosion/ulceration) and 2 damage (poikiloderma, calcinosis) measures. Additional factors contributing to the total score include the activity and/or damage due to Gottron's papules on the hands, recent hair loss, and periungual changes thus are also captured. The activity score is a sum of scores of 3 activity categories (erythema, scale, erosion/ulceration) and the following if present: Gottron's, periungual, alopecia and ranges from 0 to 100; similarly, the damage score is a sum of scores of 2 damage categories (poikiloderma, calcinosis) and Gottron's if present and ranges from 0 to 32. Higher scores indicate greater disease severity. Total CDASI score is a sum of activity score and damage score. A CDASI activity score increase of 8 points reflects both a

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clinically significant change and a notable worsening in quality of life. If less than 50% of items are missing, the missing individual items are imputed using LOCF approach before calculation of total score (activity, damage). The total activity or damage score will not be calculated and will be treated as missing if 50% or more of items are missing.

For the endpoints of

- Proportion of participants with improvement of TIS ≥ 40 and without deterioration at 2 consecutive visits at 24 weeks.
- Proportion of participants with improvement of TIS ≥ 20 and without deterioration at 2 consecutive visits at 24 weeks.

Confirmed deterioration is defined as follows:

- On 2 consecutive visits: PhGDA worsening ≥ 2 cm and MMT8 worsening ≥ 20%

  or

- On 2 consecutive visits: EGA worsening ≥ 2 cm on the [redacted] VAS

  or

- On 2 consecutive visits: any 3 of 5 CSM (excluding enzymes) worsening by ≥ 30%

For all criteria worsening will be determined by comparing to baseline value.

4.8.2.1 Secondary Efficacy Analyses

Within each of the DM and ASIM populations, the binary secondary endpoints will be summarized descriptively based on the observed Stage I data using the Full Analysis Set. Clinically meaningful oral corticosteroid (OCS) reduction summary will be based on participants in the Full Analysis Set with OCS dose ≥ 10 mg prednisone or equivalent at Baseline.

Within each of the DM and ASIM populations, the change from Baseline to Week 24 in



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4.8.3.1 Exploratory Efficacy Analyses

All exploratory endpoints will be summarized descriptively using the observed data from the Full Analysis set during Stage I for each of the DM and ASIM populations.

4.9 Safety Analyses

Unless otherwise specified, analyses will be conducted for each of the DM and ASIM populations separately and combined participants from daxdilimab and placebo across two populations.

4.9.1 Adverse Events

In general, if an adverse event (AE) occurs on or after the first dose of trial intervention, the AE will be considered as a treatment-emergent adverse event (TEAE). Otherwise, the AE will be considered as a non-TEAE.

The TEAEs will be summarized for study periods which are defined in the table below.

Table 4 TEAEs for Different Study Periods

Study Period	Inclusion of TEAEs for Summary
Stage I (safety analysis set)	Include AEs with an onset on or after the first dose of trial intervention in Stage I up to the time prior to the first dose of daxdilimab in Stage II (Week 24) for participants who were dosed in Stage II, and AEs with an onset on or after the first dose of trial intervention in Stage I for participants who were not dosed in Stage II.
Stage II (stage II analysis set)	Include AEs with an onset on or after the first dose of daxdilimab in Stage II (Week 24) for participants who entered and dosed in Stage II.

AEs will be coded using the most recent version of MedDRA and will be summarized for each treatment group. All TEAEs will be summarized overall and by MedDRA system organ class (SOC) and preferred term (PT), by severity and by relationship to IP. The number and percentage of participants reporting TESAEs and TEAESIs will also be summarized. Specific AEs will be counted once for each participant for calculating rates, but all events will be presented in participant listings. In addition, if the same AE occurs multiple times within a particular participant, the highest severity and level of causality will be reported.

An overall summary table will present the number and percentage of participants with at least one event in any of the following categories:

- TEAE
- TESAE
- TEAE resulting in death
- Grade 3 or higher TEAE using CTCAE v5.0
- TEAE leading to discontinuation of trial intervention
- Serious and/or grade 3 or higher TEAE

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- Trial intervention related TEAE
- Trial intervention related TESAE

The following AE summaries will also be provided by SOC and PT:

- TEAE
- TESAE
- TEAE resulting in death
- Grade 3 or higher TEAE using CTCAE v5.0
- TEAE leading to discontinuation of trial intervention
- Trial intervention related TEAE
- Trial intervention related TESAE

An AESI is an AE (serious or nonserious) of scientific and medical concern specific to the Sponsor's product or program, for which ongoing monitoring and rapid communication by the Investigator to the Sponsor may be appropriate. Such events may require further investigation in order to characterize and understand them. AESIs for this protocol include:

- Hypersensitivity reaction, including anaphylaxis
- Herpes zoster infection
- Severe viral infection/reactivation (CTCAE Grade 3 or higher)
- Opportunistic infection
- Malignancy (except non-melanoma skin cancer)

Treatment-emergent AESIs will be summarized by SOC and PT.

TESAEs will be summarized by serious adverse event (SAE) criteria as well. In addition, a summary of TEAEs sorted by frequency will be presented by PT. Listings will be provided for all TEAEs and non-treatment-emergent AEs.

4.9.2 Clinical Laboratory Evaluations

Clinical laboratory evaluations will be summarized for each treatment group. The descriptive summary of clinical laboratory data will be generated for Stage I data based on the safety analysis set, and for the Stage II data based on Stage II analysis set, except for the descriptive summary of the observed values and changes from baseline, which will be provided using the safety analysis set for the overall study.

The following summary will be provided for hematology and chemistry.

- Observed values and changes from the baseline by visit
- Worst toxicity grade
- At least 2-grade shift from baseline to worst toxicity
- Shift from the baseline relative to the normal range

In addition, the number and percentage of participants with the following liver-related abnormalities will be summarized if meet the following criteria at any post-baseline visit.

- AST or ALT: (a) ≥ 3 × ULN; (b) ≥ 5 × ULN; (c) ≥ 8 × ULN

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- Total bilirubin: ≥ 2 × ULN
- ALT or AST ≥ 3 x ULN and total Bilirubin ≥ 2 × ULN
- ALT or AST ≥ 3 × ULN for more than 4 weeks

The following summary will be provided for urinalysis.

- Observed values and changes from the baseline
- Shift from the baseline relative to the normal range

4.9.3 Vital Signs

The observed values, along with the changes from baseline, will be summarized for systolic blood pressure, diastolic blood pressure, body temperature, heart rate, and respiratory rate using the safety analysis set based on the overall study. In addition, a summary of participants with clinically significant vital signs values (meeting any of the following criteria) will also be provided. The summary of vital signs will be generated by visit using the safety analysis set for Stage I and Stage II analysis set for Stage II.

- Systolic blood pressure: < 90 mmHg, > 160 mmHg
- Diastolic blood pressure: < 60 mmHg, > 100 mmHg
- Heart rate: < 50 beats/min, > 100 beats/min
- Respiratory rate: < 12 breaths/min, > 23 breaths/min
- Temperature: < 36°C, >38°C

4.9.4 Prior and Concomitant Medications

Medications collected at screening and during the trial will be coded using the current version of the World Health Organization Drug dictionary (WHO-DD). Number (%) of participants who received prior medications and concomitant medications will be summarized by WHO-DD Anatomical Therapeutic Chemical (ATC) category and PT. At each level of summarization, a participant is counted once if the participant reported one or more medications at that level. The summary of prior and concomitant medications during Stage I will be based on full analysis set and safety analysis set, respectively. The concomitant medications during Stage II will be summarized based on the Stage II analysis set. The prior and concomitant medications are defined as below.

- Prior medications are defined as medications with a stop date occurring before the first trial intervention administration date.
- Concomitant medications during Stage I are defined as follows:
  - Medications with a start date before Week 24 trial intervention administration and stop date on or after the first trial intervention administration date for the participants entering Stage II.
  - Medications with stop date on or after the first trial intervention administration date for participants not entering Stage II.
- Concomitant medications for Stage II are defined as medications with a stop date on or after Week 24 daxdilimab administration date.

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Use of disease-related medications at baseline, defined as all disease-related medications (such as methotrexate, mycophenolate mofetil, azathioprine, ciclosporin, plaquenil and corticosteroid) with an intake at the date of first dose of trial intervention (i.e, start date on or before the date of first dose and end date on or after date of first dose or ongoing) will be summarized for the full analysis set. The number and percentage of participants who received rescue medications will be summarized using full analysis set for Stage I and using Stage II analysis set for Stage II by WHO-DD ATC category and PT. Rescue medications are:

- Any new permitted background therapy for DM or ASIM, or
- An increase in dose above on Day 1 baseline of any permitted therapy given to participants: methotrexate, mycophenolate mofetil, azathioprine, ciclosporin, plaquenil and corticosteroid.

The detailed rescue medications will be identified and finalized by medical monitor before database lock of each planned analysis. The missing start/stop date will be imputed as appropriate, and the details of the imputation will be included in the SPP.

4.9.5 Electrocardiogram Results

The observed values, along with the changes from baseline, will be summarized for ventricular heart rate, PR interval, QRS duration, QT interval, and the corrected QT interval (QTc) using the safety analysis set. The number (%) of participants meeting the following criteria will be summarized:

- QTc > 450 msec
- QTc > 480 msec
- QTc > 500 msec
- QTc increases from baseline > 30 msec
- QTc increases from baseline > 60 msec

Corrected QT (QTc) intervals will be derived using Fridericia's correction (QTcF) and Bazett's correction (QTcB). In addition, the overall clinical evaluation of electrocardiogram results (normal, abnormal, not clinically significant abnormal, clinically significant abnormal) will also be summarized. The summary will be produced by visit using the safety analysis set for the overall study.

4.9.6 Other Safety Measures

4.9.6.1 Overdose

The incidence of TEAEs associated with overdose will be summarized by MedDRA SOC and PT, if applicable.

4.9.6.2 Physical Examination and Weight

The observed values and the changes from baseline in the weight and body mass index (BMI) using safety analysis set will be summarized. Physical examination results will be presented in a listing. Any abnormal measurements, including those that worsen from baseline, considered clinically meaningful in the medical and scientific judgement of the

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investigator (i.e., not related to progression of underlying disease, or more severe than expected for the participant's condition) will be considered as an AE.

4.9.6.3 Local injection tolerability

The incidence of TEAEs associated with local injection tolerability will be summarized by MedDRA SOC and PT, if applicable.

4.10 Pharmacokinetic Analyses

The PK analysis will be based on the PK Analysis Set. For each of the DM and ASIM populations, descriptive statistics of the serum daxdilimab concentration will be tabulated by visit and by treatment group. Mean serum concentration-time profiles of daxdilimab by treatment group will be plotted. Individual serum concentration-time data will be listed.

Additional PK analyses may be conducted as appropriate and reported separately from the clinical study report.

4.11 Immunogenicity Analyses

The ADA status will be summarized by the categories defined in Table 5. If data allow the ADA titer for the ADA positive participants will be summarized.

The ADA summary will be produced for the overall study using any daxdilimab analysis set. The baseline positive is defined as any positive ADA prior to the first administration of daxdilimab. Analyses will be conducted for each of the DM and ASIM populations separately.

Table 5 Definition of anti-drug antibodies (ADA) Status

ADA Status	Definition
Prevalence (Positive during the study)	ADA positive observed at least once during the study (baseline included)
Only baseline positive	ADA positive observed at baseline but not observed at any post-baseline
Only post-baseline positive (treatment-induced)	ADA positive not observed at baseline but observed at least once post-baseline
Both baseline and post-baseline positive	ADA positive observed at both baseline and at least once post-baseline
Incidence (treatment emergent ADA)	ADA positive post-baseline only or boosted their pre-existing ADA titer (≥ 4-fold increase) during the study period

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5 CHANGE FROM PREVIOUS VERSION

This is version 3 of the original approved SAP version 1 (version date 1-February-2024) and version 2 (version date 31-Oct-2024). The main change is to add missing data handling methods for Manual Muscle Testing and CDASI and also update calculation method for absolute % change for Manual Muscle Testing.

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6 REFERENCES

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APPENDIX 1 Approvals

Confirmation by the study biostatistician (or designee), biostatistics management (or designee), and the study clinical colleague or therapeutic lead (or designee) that the review of this statistical analysis plan is complete, and there is agreement on the content.

[redacted]
Sr Manager, Biostatistics
Name,
Title

Signed by: [redacted]
Signer Name: [redacted]
Signing Reason: I approve this document
Signing Time: 9/5/2025 | 4:24:16 PM GMT
16B1579CA828400CB16F704489ED6E62
Signature/Date

[redacted]
Director, Biostatistics
Name,
Title

Signed by: [redacted]
Signer Name: [redacted]
Signing Reason: I approve this document
Signing Time: 9/5/2025 | 4:17:05 PM GMT
4B204674B4E849ED84EF0BD3947644D2
Signature/Date

[redacted]
Medical Dir Global Development, Clinical Development
Name,
Title

Signed by: [redacted]
Signer Name: [redacted]
Signing Reason: I approve this document
Signing Time: 9/5/2025 | 4:15:39 PM GMT
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