Statistical Analysis Plan J4H-MC-FVAA Version 1

A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Investigate the Efficacy and Safety of LY3972406 in Adults With Moderate-to-Severe Plaque Psoriasis

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Title Page

Protocol Number: J4H-MC-FVAA

Compound Number: LY3972406

Short Title: A Study of LY3972406 in Adults with Moderate-to-Severe Plaque Psoriasis

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Version history

This Statistical Analysis Plan (SAP) for Study J4H-MC-FVAA (FVAA) is based on the protocol dated 31 October 2023.

SAP Version History Summary

SAP Version	Approval Date	Change	Rationale
1	See date on Page 1	Not Applicable	Original version

1. Introduction

Study J4H-MC-FVAA (FVAA) is a Phase 2, randomized, double-blind, placebo-controlled study to investigate the efficacy and safety of LY3972406 in adults with moderate-to-severe plaque psoriasis.

There are no changes to the analyses described in the protocol.

1.1. Objectives, Endpoints, and Estimands

Objectives	Endpoints
Primary	
• To compare the efficacy of LY3972406 versus placebo in the treatment of participants with moderate-to-severe plaque psoriasis	• Proportion of participants achieving PASI 75 at Week 12
Secondary	
• To compare the efficacy of LY3972406 versus placebo, as measured by improvement in clinical signs and symptoms	• Proportion of participants achieving the following at Week 12 o PASI 90 o PASI 100 o sPGA 0 (clear), or o sPGA 0 or 1 (clear or almost clear). • PASI percent change from baseline to Week 12 • BSA mean change from baseline to Week 12 • Proportion of participants who achieve a PSSI score of 0 at Week 12 • PSSI mean change from baseline to Week 12[a]
• To compare patient-reported outcomes from participants who received LY3972406 to those who received placebo	• Mean change from baseline to Week 12 for quality-of-life measures o DLQI o PatGA Psoriasis, and o PSS
• To characterize the PK of LY3972406	• Observed trough LY3972406 plasma concentration at Week 12
• To describe the safety of LY3972406 in participants with psoriasis	Summary of safety data, including number and incidence of • SAEs • TEAEs • Discontinuations due to AE

Objectives	Endpoints
Exploratory	
Exploratory objectives and endpoints may include, but are not limited to, evaluations of the following at various study time points in participants with moderate-to-severe plaque psoriasis: CCI	

Abbreviations: AE = adverse event; BSA = body surface area; DLQI = Dermatology Life Quality Index; IL = interleukin; PASI = Psoriasis Area and Severity Index; PatGA Psoriasis = Patient's Global Assessment of Psoriasis; CCI ; PK = pharmacokinetics; PSS = Psoriasis Symptoms Scale; PSSI = Psoriasis Scalp Severity Index; SAE = serious adverse event; sPGA = Static Physician's Global Assessment; TEAE = treatment-emergent adverse event.

[a] Only for participants with baseline scalp psoriasis involvement, defined as baseline PSSI >0.

Primary and secondary estimands

The primary clinical question of interest is

> What is the difference between each dosing regimen of LY3972406 and placebo in the target patient population in achieving a successful response without the use of prohibited concomitant medication or discontinuing the study intervention either due to lack of efficacy or due to an AE?

The efficacy estimands are described by the following attributes:

- Estimand strategy
  - Binary endpoints: hybrid of composite variable and treatment policy estimands (conditional)
  - Continuous endpoints: hypothetical (unconditional)
- Population: Adults with moderate-to-severe plaque psoriasis
- Endpoints
  - Binary: Psoriasis Area and Severity Index (PASI) 75 (primary), PASI 90, PASI 100, Static Physician's Global Assessment (sPGA) 0 (clear), sPGA 0 or 1 (clear or almost clear), and Psoriasis Scalp Severity Index (PSSI) 0
  - Continuous: PASI, body surface area, Dermatology Life Quality Index, Patient's Global Assessment of Psoriasis, PSSI, and Psoriasis Symptoms Scale
- Timepoints: Week 12 for all endpoints

- How to account for intercurrent events (ICEs):
    - ICEs related to study intervention include the use of prohibited concomitant medication and early discontinuation from the study or study intervention due to lack of efficacy or an adverse event (AE). Participants with ICEs related to study intervention will be considered as a treatment failure (binary endpoints) or missing at random (continuous endpoints) from the time of the ICE.
    - For all remaining ICEs, a treatment policy strategy will be used. That is, the observed data will be used regardless of whether ICEs unrelated to study intervention have occurred.
- Population-level summary:
    - Binary endpoints: Difference in proportion of participants achieving response between each dosing regimen of LY3972406 and placebo
    - Continuous endpoints: Mean difference between each dosing regimen of LY3972406 and placebo
- Rationale for the primary estimand:
    - If a participant used any prohibited concomitant medication for plaque psoriasis, the participant was not receiving sufficient benefits from the study intervention.
    - If a participant discontinued early from the study intervention due to lack of efficacy or an AE, the participant experienced a burden of the study intervention that outweighed its benefits.
    - All remaining ICEs are considered unrelated to the study intervention.

The safety estimand will be evaluated on each dosing regimen of LY3972406 and placebo on the safety analysis set. The estimand is described with the following attributes:

- Population: Adults with moderate-to-severe plaque psoriasis who had at least 1 dose of the study intervention
- Endpoints: serious adverse events (SAEs), treatment-emergent adverse events (TEAEs), and discontinuations due to AE
- Timepoints: All aggregated timepoints
- Population-level summary: Proportion of participants experiencing the safety endpoint

The occurrence of ICEs is irrelevant.

1.2. Study Design

Study FVAA is a Phase 2, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of LY3972406 in adults with moderate-to-severe plaque psoriasis.

The study duration will be approximately 29 weeks over 3 study periods:

- **Screening**: occurs within 35 days before the planned randomization visit (baseline; Visit 2, Week 0)
- **Double-blind treatment period**: lasts for 12 weeks from baseline
- **Posttreatment follow-up**: lasts for up to 12 weeks after last treatment visit (or last dose for early discontinuation)

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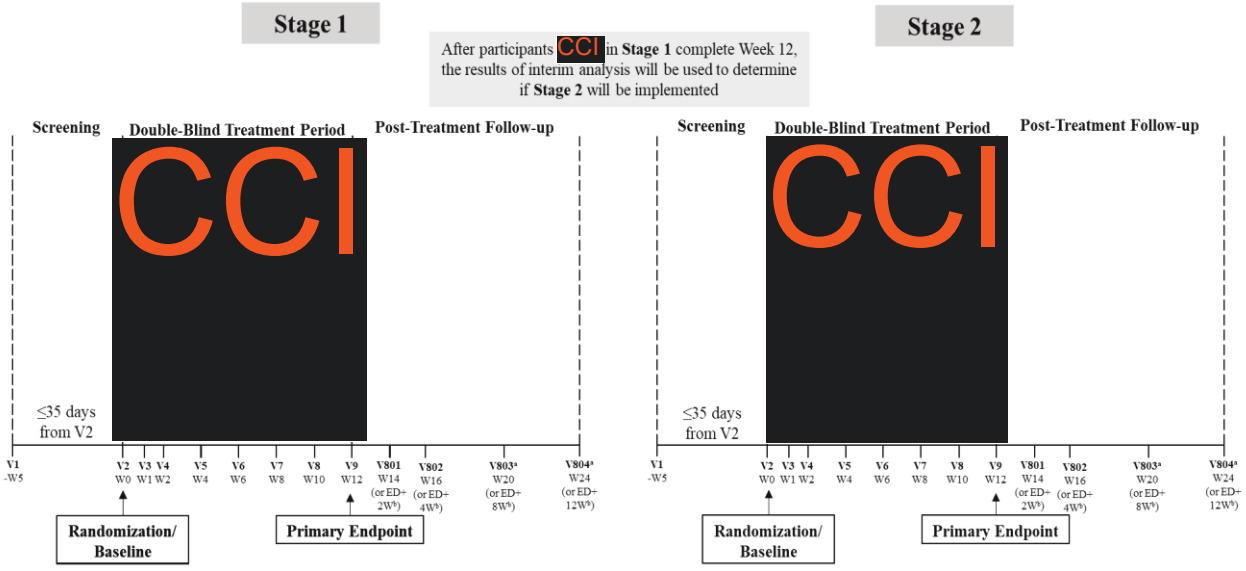
The study design is illustrated in Figure FVAA.1.1. The study will have 2 stages:

- In Stage 1, participants will be randomly assigned to receive LY3972406 CCI [redacted] or placebo.
- Stage 2 may be initiated at the sponsor's discretion after review of the interim analysis data from Stage 1 to collect additional safety and efficacy data at the CCI dose level. If Stage 2 is implemented, the participants will be randomly assigned to receive either
  - LY3972406 CCI [redacted] LY3972406 CCI [redacted] or placebo,

    OR
  - LY3972406 CCI [redacted] or placebo.



Abbreviations: ED = early discontinuation; n = number of participants; CCI [redacted] CCI V = Visit; W = Week.

a Visits 803 and 804 are not required for all participants.

b For the follow-up visits, the weeks in parentheses indicate weeks after the last dose.

Figure FVAA.1.1. Illustration of study design for clinical protocol J4H-MC-FVAA.

2. Statistical Hypotheses

The primary objective is to demonstrate that LY3972406 is superior to placebo in achieving PASI 75 at Week 12. Thus, the null hypothesis to be tested in relation to the primary estimand is as follows: LY3972406 is not different from placebo in achieving PASI 75 at Week 12.

2.1. Multiplicity Adjustment

Adjustment for multiple comparisons will not be employed in the analysis for this study.

3. Analysis Sets

For purposes of analysis, the following populations are defined:

Population	Description
Screening	All patients who signed informed consent.
Modified intent-to-treat (mITT)	All participants randomly assigned to study intervention and who take at least 1 dose of study intervention. Participants will be analyzed according to the study intervention to which they were assigned.
Per-protocol	All randomized participants who do not commit an important protocol deviation that could potentially compromise efficacy results. Participants will be analyzed according to the study intervention to which they were assigned.
Safety	All randomized participants who received at least 1 dose of study intervention. Participants will be analyzed according to the study intervention they received.
Pharmacokinetic (PK)	All participants randomly assigned to study intervention and who take at least 1 dose of study intervention and have PK data available.
Follow-up	All mITT participants who have entered the posttreatment follow-up period. Participants will be analyzed according to the study intervention to which they were assigned.

Note: In the context of this table and throughout the protocol, the terms “study intervention” and “treatment” may be used interchangeably.

4. Statistical Analyses

4.1. General Considerations

Statistical analysis of this study will be the responsibility of the sponsor or its designee.

This study has 2 stages. If Stage 2 is initiated, all data from Stage 1 will be combined with Stage 2 data for the primary outcome analysis. If Stage 2 is not initiated, the primary outcome analysis will occur at the end of Stage 1. The primary outcome lock will occur once all subjects have completed the double-blind period or discontinued study intervention and 100% of the primary endpoint data is available.

Primary and secondary hypotheses will be tested at a 1-sided 0.025 nominal level unless otherwise specified.

Unless otherwise specified, the modified intent-to-treat population will be used for all efficacy analyses.

ICEs will be summarized by the number of occurrences for each study intervention during the double-blind treatment period (through Visit 9).

Changes to the data analysis methods

Any change to the data analysis methods described in the protocol will require an amendment ONLY if it changes a principal feature of the protocol. Any other change to the data analysis methods described in the protocol, and the justification for making the change, will be described in the clinical study report. Additional exploratory analyses of the data will be conducted as deemed appropriate.

Continuous and categorical data analyses

Continuous data will be summarized in terms of the mean, standard deviation, minimum, maximum, median, and number of observations. Categorical data will be summarized as frequency counts and percentages. Comparisons between each LY3972406 dose and placebo will be performed for all analyses in the treatment period with no adjustment for multiple comparisons.

Baseline definitions

For the treatment period efficacy, health outcomes, quality-of-life, and safety analyses, baseline is defined as the last available value before the first drug administration, which in most cases will be the measure recorded at Week 0 (Visit 2). Change from baseline will be calculated as the visit value of interest minus the baseline value. For safety analyses using a baseline period, the baseline period is defined as the time from Visit 1 up through the date and time of the first dosing at Visit 2. Percent change from baseline will be calculated as 100 × (visit value – baseline value) / baseline value.

Data analysis methods

Treatment comparisons of categorical efficacy, patient-reported outcomes, and quality-of-life variables will be made using a Cochran-Mantel-Haenszel test stratified by prior exposure to biologic therapy for psoriasis (biologic naïve versus experienced). The 95% confidence intervals associated with the treatment response rate and treatment difference will be reported.

Treatment comparisons of continuous efficacy, patient-reported outcomes, and quality-of-life variables will be made using the mixed model for repeated measures (MMRM). The model will include the following as fixed factors: treatment, baseline value, visit, prior exposure to biologic therapy for psoriasis (biologic naïve versus experienced), and the interaction of treatment-by-visit. Type III sums of squares for the least squares means will be used for the statistical comparison; the 95% confidence interval will also be reported. The covariance structure to model the within-participant errors will be unstructured. If the unstructured covariance matrix results in a lack of convergence, the heterogeneous Toeplitz covariance structure, followed by the heterogeneous autoregressive covariance structure, will be used. In the event that none of the MMRM models converge, an analysis of covariance will be used with treatment, baseline value, and prior exposure to biologic therapy as fixed factors.

Fisher's exact test will be used for categorical safety data including AE, baseline, and discontinuations. Continuous vital sign, electrocardiogram (ECG), and laboratory values will be analyzed by analysis of covariance with treatment and baseline value in the model.

Handling of missing, unused, and spurious data

Handling of missing, unused, and spurious data is addressed prospectively in the overall statistical methods described in the protocol and in this document, where appropriate. Adjustments to the planned analyses are described in the final clinical study report.

Missing data imputation is not to be confused with estimand strategy. Missing data of categorical efficacy, patient-reported outcomes, and quality-of-life variables will be imputed using a nonresponder imputation (NRI) method, and the missing data will be considered as nonresponder. For continuous variables, missing data will not be imputed.

When NRI is applied, participants with missing data will be considered as nonresponders regardless of whether they have at least 1 postbaseline data.

4.2. Participant Dispositions

A detailed description of participant disposition will be provided, including a summary of the number and percentage of participants entered into the study and randomized; the number and percentage of participants who complete the study or discontinue, both overall and by reason for discontinuation; and the frequency and percentage of patients who discontinued study treatment. A summary of important protocol deviations will be provided.

4.3. Primary Estimand Analysis

Treatment comparisons between each LY3972406 dose and placebo in the proportion of participants achieving PASI 75 at Week 12 will be analyzed using the Cochran-Mantel-Haenszel

test stratified by prior exposure to biologic therapy for psoriasis (biologic naïve versus experienced) with NRI, as described. Participants who fail to complete the 12-week treatment period due to an ICE related to study intervention or violate the concomitant medications rules will be treated as nonresponders. The 95% confidence intervals associated with the treatment response rate and treatment difference to placebo will be provided by treatment. The primary analysis will be conducted on the modified intent-to-treat analysis set when all participants reach Week 12 or have discontinued during the treatment period.

4.4. Secondary Estimands Analysis

Proportions of participants achieving the following scores will be analyzed using the Cochran-Mantel-Haenszel test stratified by prior exposure to biologic therapy for psoriasis (biologic naïve versus experienced) with NRI:

- PASI 90
- PASI 100
- sPGA 0 (clear)
- sPGA 0 or 1 (clear or almost clear)
- PSSI 0

Participants who fail to complete the 12-week treatment period due to an ICE related to study intervention or use prohibited concomitant medications will be treated as nonresponders. The 95% confidence intervals associated with the treatment response rate and treatment difference will be provided by treatment.

Treatment comparisons between each LY3972406 dose and placebo in the PASI percent change, body surface area mean change from baseline, PSSI mean change from baseline to Week 12, and patient reported outcomes will be analyzed using the MMRM model, as described in Section 4.1. No missing data imputation will be performed. The least squares mean and 95% confidence interval will be summarized by treatment.

4.5. Pharmacokinetic and Pharmacokinetic and Pharmacodynamic Methods

Plasma concentrations of LY3972406 will be summarized by time point and dosing regimen using descriptive statistics.

Additional analyses may be conducted as deemed necessary on review of the data. For example, graphical analyses, model-based pharmacokinetic (PK) analyses, or both may be conducted. Exposure-response analysis between LY3972406 concentrations and clinical efficacy endpoints, pharmacodynamic (PD) or biomarker endpoints, or both may be performed using population PK and PD nonlinear mixed-effects modeling techniques implemented in NONlinear Mixed Effects Modeling (NONMEM®) or Monolix® software.

Additionally, the impact of intrinsic and extrinsic factors, such as age, weight, gender, and renal function, on model parameters may be examined as needed.

4.6. Exploratory Analysis

The exploratory endpoints include

4.7. Safety Analyses

All safety data will be descriptively summarized by treatment groups (LY and placebo) and analyzed based on the safety population described in Section 3. The safety will be assessed by evaluating AEs, laboratory analytes, vital signs, ECGs, special safety topics, and the CCI . Additional analysis may be included if applicable. The duration of exposure will also be summarized.

The treatment period safety analyses will compare each and combined doses of LY3972406 to placebo; treatment group comparisons will be analyzed using the methods described in Section 4.1. Summaries of safety data collected during the follow-up period will be presented separately. Safety analyses will be conducted on the safety analysis set.

4.7.1. Extent of Exposure

Duration of exposure to study drug during the double-blind treatment period will be summarized by treatment arm. Duration of exposure on treatment will be calculated as the date of last dose of study drug (or date of discontinuation) minus the date of first dose of study drug plus 1 day. Total patient-years of exposure will be reported for each treatment group for overall duration of exposure. Descriptive statistics (number of participants in the analysis [subset] population, mean, standard deviation, minimum, maximum, first quartile, median, third quartile, and maximum) will be provided for patient-days of exposure.

Overall exposure will be summarized in total patient-years, which will be calculated as follows:

Exposure in patient years = Sum of duration of exposure (for all patients in treatment arm) / 365.25.

No inferential analysis for comparison between treatment arms will be performed.

4.7.2. Adverse Events

AEs are recorded in the electronic case report forms (eCRFs). Where changes in severity are recorded in the eCRF, each separate severity of the AE will be reported in the listings. Only the most severe will be used in the summary tables.

AEs will be coded according to the current version at the time of database lock of the Medical Dictionary for Regulatory Activities (MedDRA). The MedDRA lowest level term will be used in defining which events are treatment-emergent (TE). The severity of AEs is recorded as mild, moderate, or severe. The maximum severity for each lowest level term during the baseline period will be used as baseline. Baseline for the double-blind treatment period is defined as all preexisting conditions recorded at Visit 1 and any AEs recorded before the first dose of study intervention. The treatment period will be included as postbaseline for the analysis. For events with a missing severity during the baseline period, it will be treated as 'mild' in severity for determining treatment-emergence. Events with a missing severity during the postbaseline period will be treated as 'severe,' and treatment-emergence will be determined by comparing to baseline severity. For events occurring on the day of first taking study medication, the start times of the study treatment and AE will be used to determine whether the event was pre- versus posttreatment. If the start time for the AE is missing, it will be assumed to have started in the later period.

A TEAE is defined as an event that first occurred or worsened in severity after baseline and on or prior to the date of the last visit within the treatment period. For each event classification term, the number of participants experiencing a TEAE with that classification term will be tabulated. A follow-up emergent AE is defined as an event that first occurred or worsened in severity after Week 12 (Visit 9) or early discontinuation. For events that are gender-specific, the denominator and computation of the percentage will include participants only from the given gender. A preexisting condition is defined as a condition that starts before the participant has provided written informed consent and is ongoing at consent. A non-TEAE is defined as an AE that starts after informed consent but prior to the first dose. Further definitions and information for AEs can be found in FVAA Protocol in Section 8.3 and in Appendix 3, Section 10.3.

In an overview table, the number and percentage of subjects who experienced a TEAE or SAE, died due to an AE, or discontinued from the study due to an AE will be summarized by treatment.

An overall summary of AEs will be provided for the population, treatment period, severity, and relationship to the study drug. The number of TEAEs, the number of participants experiencing a TEAE, and the percentage of participants experiencing a TEAE will be summarized by population, treatment, and MedDRA system organ class (SOC) and preferred term (PT). The MedDRA version is documented in the Data Management Plan. This includes the number and percentage of participants who experienced TEAEs, TEAEs by maximum severity, deaths, SAEs, TEAEs related to study intervention, and AEs leading to discontinuation of study intervention. The summary and frequency AE tables will be presented for all causalities and

those considered related to the study drug by the clinician. Any serious AEs will be listed. AEs by day of onset will be presented.

The number and percentage of patients with TEAEs will be summarized by treatment group in the 2 formats listed below:

- by MedDRA PT nested within a SOC, with SOCs ordered alphabetically and events ordered within each SOC by decreasing frequency in the treatment group, and
- by MedDRA PT with events ordered by decreasing frequency in the treatment group.

AEs leading to permanent discontinuation of study drug and AEs leading to temporary interruption of study drug will also be summarized by treatment group using MedDRA PT nested within SOC.

Follow-up emergent AEs, SAEs including deaths, and AEs leading to study discontinuation will be summarized for the posttreatment follow-up period.

Listings will be presented for all AEs, all SAEs, all AEs leading to death, all AEs leading to study drug temporary interruption, and all AEs leading to discontinuation from the study.

4.7.3. Vital Signs, Laboratory Analytes and ECGs

Vital signs include systolic blood pressure, diastolic blood pressure, pulse, weight, and body mass index. Original-scale data will be analyzed. When these parameters are analyzed as continuous numerical variables, unplanned measurements will be excluded. When these parameters are analyzed as categorical outcomes, TE abnormalities, or both, planned and unplanned measurements will be included. The planned analyses described for the laboratory analytes in this section below will be used to analyze the vital signs, except for the inclusion of a threshold for change in addition to a limit for the definition of TE. Table FVAA 4.1 defines the low and high baseline values as well as the criteria used to define TE based on postbaseline values.

Table FVAA 4.1 Categorical Criteria for Abnormal Treatment-Emergent Blood Pressure and Pulse Measurement, and Categorical Criteria for Weight Changes for Adults

Parameter	Low	High
Systolic BP (mmHg) (Supine or sitting – forearm at heart level)	≤90 and decrease from baseline ≥20	≥140 and increase from baseline ≥20
Diastolic BP (mm Hg) (Supine or sitting – forearm at heart level)	≤50 and decrease from baseline ≥10	≥90 and increase from baseline ≥10
Pulse (bpm) (Supine or sitting)	<50 and decrease from baseline ≥15	100 and increase from baseline ≥15
Weight (kg) (Consistent clothing and timing in relationship to meals and voiding)	(Loss) decrease ≥7%	(Gain) increase ≥7%

Abbreviation: BP = blood pressure.

Laboratory analytes and vital signs will be summarized by population at each visit. For continuous data, change from baseline will also be summarized, where baseline is defined as the Visit 2 assessment for laboratory analytes and the Day 1 predose assessment for vital signs. Additionally, laboratory analytes data outside the reference ranges will be listed and flagged on individual participant data listings.

The ECG data will be obtained directly from the 12-lead ECG traces. These data include the PR, QT, QT interval corrected using Bazett's formula intervals, QRS duration, and heart rate (HR). In addition, QT interval corrected using Fridericia's formula (QTcF) will be calculated as follows:

$$QTcF = \frac{QT}{\sqrt[3]{\left(60/HR\right)}}$$

ECG data will be summarized at each timepoint for each treatment arm together with changes from baseline, where baseline is defined as the Day 1 predose triplicate assessment.

A table providing the counts and percentages of subjects with greater than 30 and greater than 60 maximum increase in QTcF intervals, as well as the frequency and percentages of maximum QTcF intervals greater than 450, greater than 480, and greater than 500, will be provided for each treatment arm.

4.7.4. Special Safety Topics

In addition to general safety parameters, safety information on specific topics will also be presented. Additional special safety topics may be added as warranted. In general, for topics regarding safety in special groups and circumstances, patient profiles, patient listings, or both, where applicable, will be provided when needed to allow medical review of the time course of cases or events, related parameters, patient demographics, study drug treatment, and meaningful concomitant medication use. In addition to the safety topics for which provision or review of patient data is specified, these will be provided when summary data are insufficient to permit adequate understanding of the safety topic.

4.7.4.1. Infections

Completion of the Infection eCRF page is required for each infection reported as an AE or SAE.

Infections will be defined using the PTs from the MedDRA Infections and Infestations SOC. TE infections will be analyzed for

- all infections: TE infections by PT (by maximum severity)
- serious infections: TE infections by PT (by maximum severity)
- opportunistic infections (OI): TE OI by narrow terms and broad terms separately, and
- infections resulting in permanent study drug discontinuation.

Potential opportunistic infections

The MedDRA terms used to identify infections considered to be OI in patients with immune mediated inflammatory conditions treated with immunomodulatory drugs are based on Winthrop et al. (2015) and are listed in the compound level safety standards. See also FVAA Protocol (Section 10.8, Appendix 8).

Potential opportunistic infections (POIs) will be identified in 2 ways:

1. POIs will be identified from TEAEs based on a Lilly-defined list of MedDRA PTs shown in Appendix 3, Section 6.3. The list is maintained outside the Study FVAA SAP and can be updated without an amendment to the Study FVAA SAP. These PTs are a subset of terms from the Infections and Infestations SOC, and
2. Medical will review the list of POIs, including the details captured on the infection-specific eCRF, and determine whether the infection is a 'confirmed opportunistic infection.'

The summary analysis of OIs identified using the 2 approaches above will be provided. Events will be ordered by decreasing frequency of pathogen nested under pathogen species (mycobacteria, bacteria, fungal, viral, and parasites). The order of frequency will be determined using the LY3972406 group.

4.7.4.2. Hepatic Safety

Hepatic laboratory parameters include alanine aminotransferase, aspartate aminotransferase, total bilirubin, serum alkaline phosphatase, and gamma-glutamyltransferase. The central laboratory reference ranges will be used for these laboratory assessments.

If a participant experiences elevated laboratory parameters, as detailed in Section 8.2.11 of the FVAA Protocol, additional tests will be performed to confirm the abnormality. Additional safety data may be collected if required, as defined in the FVAA Protocol. Where applicable, the following will be presented.

The participants' liver disease history and associated person liver disease history data will be listed. Use of acetaminophen during the study, which has potential for hepatotoxicity, will be listed. Results from any hepatic monitoring procedures, such as a magnetic resonance elastography scan, and biopsy assessments will be listed, if performed.

Hepatic risk factor assessment data will be listed. Liver related signs and symptoms data will be summarized by population and treatment, if deemed appropriate, and listed. Alcohol and recreational drug use data will also be listed.

All hepatic chemistry, hematology, coagulation, and serology data will be listed. Values outside the reference ranges will be flagged on the individual participant data listings.

The number and percentage of participants with the following abnormal elevations in hepatic laboratory tests at any time will be summarized between treatment groups:

- an alanine aminotransferase or aspartate aminotransferase measurement of at least 3-fold, at least 5-fold, and at least 10-fold the central laboratory upper limit of normal during the treatment period
- a total bilirubin measurement of at least 2-fold the central laboratory upper limit of normal during the treatment period, and
- an alkaline phosphatase measurement of at least 2.5-fold the central laboratory upper limit of normal during the treatment period.

The number and percentage of participants reporting hepatic events will be assessed using the MedDRA PTs contained in the following Standardized MedDRA Queries (SMQs):

- Broad and narrow terms in the Liver-related investigations, signs and symptoms SMQ
- Broad and narrow terms in the Cholestasis and jaundice of hepatic origin SMQ
- Broad and narrow terms in the Hepatitis noninfectious SMQ
- Broad and narrow terms in the Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions SMQ, and
- Narrow terms in the Liver-related coagulation and bleeding disturbances SMQ.

When criteria are met for hepatic evaluations, clinicians will complete a follow-up Hepatic Safety eCRF and listings will be provided.

4.7.6. Other Assessments

All other safety assessments not detailed in this section will be listed but not summarized or statistically analyzed.

4.8. Other Analyses

4.8.1. Endpoint Definitions

Primary and secondary endpoint definitions are provided in the table below.

Measure	Description	Variable	Derivation and Comment	Imputation Approach if with Missing Components
PASI	PASI: Combines clinician-reported assessments of the extent of body-surface involvement in 4 anatomical regions (head and neck, trunk, arms, and legs) and the severity of scaling (S), redness (R), and plaque induration and infiltration (thickness, T) in each region, yielding an overall score of 0 for no psoriasis to 72 for the most severe disease (Fredriksson and Pettersson 1978). Severity is rated for each index (R, S, T) on a 0-4 scale (0 for no involvement up to 4 for very severe involvement): 0 = none 1 = slight 2 = moderate 3 = severe 4 = very severe The body is divided into 4 anatomical regions comprising the head (h), upper limb (u), trunk (t), and lower limb (l). In each of these areas, the fraction of total BSA affected is graded on a 0-6 scale (0 for no involvement; up to 6 for 90%-100% involvement): 0 = 0% (clear) 1 = >0% to <10% 2 = 10% to <30% 3 = 30% to <50% 4 = 50% to <70% 5 = 70% to <90% 6 = 90% to 100% The various body regions are weighted to reflect their respective proportion of BSA.	PASI score	The composite PASI score is calculated by multiplying the sum of the individual severity scores for each area by the weighted area-of-involvement score for that respective area, and then summing the 4 resulting quantities as follows: $PASI = 0.1(R_h + T_h + S_h)A_h + 0.2(R_u + T_u + S_u)A_u + 0.3(R_t + T_t + S_t)A_t + 0.4(R_l + T_l + S_l)A_l$ where, R_h, R_u, R_t, R_l = redness score of plaques on the head, upper limb, trunk, and lower limb, scored 0-4 respectively; T_h, T_u, T_t, T_l = thickness score of plaques on the head, upper limb, trunk, and lower limb, scored 0-4 respectively; S_h, S_u, S_t, S_l = scaliness score of plaques on the head, upper limb, trunk, and lower limb, scored 0-4 respectively; A_h, A_u, A_t, A_l = numerical value translation of percentage area of psoriatic involvement score for the head, upper limb, trunk, and lower limb, respectively. PASI scores are treated as a continuous score, with 0.1 increments within these values.	If any individual score is missing, the PASI score will not be calculated, hence missing.
		PASI change from baseline	Calculated as: observed PASI – baseline PASI.	Missing if baseline or observed value is missing.

Measure	Description	Variable	Derivation and Comment	Imputation Approach if with Missing Components
		PASI percent improvement from baseline	Calculated as: $Percent\ improvement\ from\ baseline = 100 \times \frac{Baseline\ PASI - Observed\ PASI}{Baseline\ PASI}$ If a patient has experienced an improvement, this measure will be positive. If a patient has experienced a worsening in the condition, this measure will be negative.	Missing if baseline or observed value is missing.
		PASI 75 (Primary)	A clinically meaningful response; at least a 75% improvement in PASI score from baseline.	Missing if baseline or observed value is missing.
		PASI 90	Higher level of clearance; at least a 90% improvement in PASI score from baseline.	Missing if baseline or observed value is missing.
		PASI 100	Complete resolution of plaque psoriasis; a 100% improvement in PASI score from baseline.	Missing if baseline or observed value is missing.
sPGA	sPGA: The physician's global assessment of the patient's psoriasis lesions at a given time point. Plaques are graded for plaque elevation, scaling, and erythema on a range of clear (0), almost clear (1), mild (2), moderate (3), and severe (4).	sPGA score	Range from 0 to 5: clear (0), almost clear (1), mild (2), moderate (3), severe (4).	Single item, missing if missing.
		sPGA (0,1)	An sPGA assessed as either 0 or 1, which represents a clinically meaningful response of minimal plaque severity or complete resolution of plaque psoriasis.	Missing if sPGA is missing.
		sPGA (0)	An sPGA assessed as 0, which represents a clinically important endpoint indicating complete resolution of plaque psoriasis.	Missing if sPGA is missing.

Measure	Description	Variable	Derivation and Comment	Imputation Approach if with Missing Components
BSA	Percentage of BSA: The investigator will evaluate the percentage involvement of psoriasis on each patient's BSA on a continuous scale from 0% (no involvement) to 100% (full involvement), in which 1% corresponds to the size of the patient's hand (including the palm, fingers, and thumb) (Van Voorhees et al. 2016)	BSA	Collected as a single scale as part of PASI electronic case report form eCOA. Range from 0% to 100%.	Single item, missing if missing.
		BSA change from baseline	Calculated as: observed BSA – baseline BSA.	Missing if baseline or observed value is missing.
PSS	The PSS is a patient-reported, 8-item scale used in adults. It is based on the assessment of • 4 symptoms: itch, pain, stinging, and burning • 3 signs: redness, scaling, and cracking • 1 item on the discomfort related to symptoms/signs (Armstrong et al. 2020). Respondents are asked to answer the questions based on their psoriasis symptoms in the past 24 hours.	PSS item scores	The PSS item scores will be collected during office visits.	The item is missing if it is not present in the data.
		PSS Symptoms Score	Calculated by summing the individual item scores as follows: itch NRS + pain NRS + stinging NRS + burning NRS.	If any of the 4 relevant item scores are missing, the score is missing.
		PSS Signs Score	Calculated by summing the individual item scores as follows: redness NRS + scaling NRS + cracking NRS.	If any of the 3 relevant item scores are missing, the score is missing.

Measure	Description	Variable	Derivation and Comment	Imputation Approach if with Missing Components
	The overall severity for each individual symptom from patient's psoriasis is indicated by selecting the number from an NRS of 0 to 10 that best describes the worst level of each symptom in the area in the past 24 hours, where 0 (no severity) and 10 (worst imaginable severity). The symptom severity scores, ranging from 0 to 10, are the values of the selected numbers indicated by the patient on the instrument's horizontal scale. Each of the 8 individual items will receive a score of 0 to 10 and will be reported as item scores for itch, pain, discomfort, stinging, burning, redness, scaling, and cracking.	PSS (Signs, Symptoms, items) Score change from baseline	Change from baseline = Observed PSS Score – Baseline PSS Score Here "PSS Score" could refer to the Signs, Symptoms, or an item Score. Negative change indicates improvement, and a positive change indicates deterioration of the condition.	Missing if either observed or baseline PSS score is missing.

Measure	Description	Variable	Derivation and Comment	Imputation Approach if with Missing Components
PSSI	PSSI is a clinician-reported assessment to be used if the patient has scalp psoriasis at baseline. The scalp will be assessed for erythema (redness), induration (hardness), and desquamation (shedding of skin) and percentage of area affected as follows: Erythema, Induration and Desquamation: 0 = Absent 1 = Slight 2 = Moderate 3 = Severe 4 = Severest Possible Percent of Scalp Involved: 0 = none 1 = <10% 2 = 10-29% 3 = 30-49% 4 = 50-69% 5 = 70-89% 6 = 90-100% (Thaçi et al. 2015)	PSSI score	The PSSI score is a composite score derived from the sum of the scores for erythema, induration, and desquamation multiplied by the score for the extent of scalp area involved (percent of scalp involved). The range is 0 to 72.	If any individual score is missing, the PSSI score will not be calculated, hence missing.
		PSSI score change from baseline	Calculated as: observed PSSI – baseline PSSI.	Missing if baseline or observed value is missing.
		PSSI score of 0	A PSSI response is defined as a PSSI score of 0, which is also referred to as scalp clearance.	Missing if PSSI score is missing.
DLQI	The DLQI is a validated, dermatology-specific, patient-reported outcomes assessment that evaluates patient's health-related QoL. This questionnaire has 10 items that are grouped in 6 domains, including symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. The recall period of this scale is over the "last week." Response categories and corresponding scores are Very much = 3 A lot = 2 A little = 1 Not at all = 0 Not relevant = 0	DLQI total score	A DLQI total score is calculated by summing all 10 question responses and has a range of 0 to 30 (less to more impairment) (Finlay and Khan 1994; Basra et al. 2015).	If 2 or more questions are missing, the total score is missing. Note: #7B could be a valid missing when #7A is not "No." That is, #7 should be considered as 1 question.
		DLQI total score and domain scores change from baseline	Calculated as: observed DLQI (total score or domain scores) – baseline DLQI (total score or domain scores).	Missing if baseline or observed value is missing.

Measure	Description	Variable	Derivation and Comment	Imputation Approach if with Missing Components
PatGA	The PatGA is a patient reported, single item scale on which patients are asked to rank, by selecting a number on a 0-to-5 NRS, the severity of their psoriasis "today" from 0 (clear), no psoriasis, to 5 (severe).	Change from baseline	Change from baseline = Observed Item PatGA score – Baseline Item PatGA score.	Missing if baseline or observed value is missing.

Abbreviations: BSA = body surface area; DLQI = Global Assessment Dermatology Life Quality Index; eCOA = electronic Clinical Outcome Assessment; NRS = numeric rating scale; PASI = Psoriasis Area and Severity Index; PatGA = Patients Global Assessment of Psoriasis; PSS = Psoriasis Symptoms Scale; PSSI = Psoriasis Scalp Severity Index; QoL = quality of life; sPGA = Static Physician Global Assessment.

4.8.2. Subgroup Analyses

Subgroup analyses of the primary endpoint and secondary endpoints will be made to assess consistency of the intervention effect across the following subgroups:

- age group: younger than 65 versus 65 years or older
- sex: female versus male
- ethnicity: Hispanic or Latino versus Non-Hispanic or Latino
- race: White versus Black versus Other
- prior exposure to biologic therapy: biologic naïve versus biologic experienced, and
- body mass index: less than 30 versus 30 or greater.

If the number of participants is too small (less than 10%) within a subgroup, then the subgroup categories may be redefined prior to unblinding the study.

4.9. Interim Analyses

Analyses for the primary database lock will be conducted as described in Section 9.3 of the protocol. If Stage 2 is not initiated, the primary outcome database lock will occur when all the participants from Stage 1 have completed the Week 12 visit or have discontinued the study intervention. If Stage 2 is initiated, the primary outcome database lock will occur when all the participants from Stage 2 have completed the Week 12 visit or have discontinued the study intervention.

Two interim analyses may be conducted during Stage 1 prior to the primary database lock at the sponsor's discretion. One interim may occur when approximately 50% to 90% of participants from Stage 1 have completed the Week 12 visit or have discontinued the study intervention. Another interim analysis may be conducted when approximately 90% to 100% of participants from Stage 1 have completed the Week 12 visit or have discontinued the study intervention. The results of either interim analysis can be used by the sponsor's internal assessment committee (IAC) to recommend if Stage 2 should be initiated.

The interim analyses may include safety, PK, PD, and efficacy data. The data may be used for internal decision making, development of PK and PD modeling, or both. An assessment of unblinded interim data will be conducted by an IAC with a limited number of individuals who do not have direct site contact or data entry or validation responsibilities. Study sites will receive information about interim results only if they need to know for the safety of their participants.

The study will not be stopped early due to efficacy.

Unblinding details are specified in the blinding unblinding document.

At the discretion of the sponsor, prespecified interim analyses may not be conducted.

4.9.1. Data Monitoring Committee or Other Review Board

There will be no Data Monitoring Committee for this study. An assessment of unblinded interim data will be conducted by an IAC with a limited number of prespecified team members who do not have direct site contact or data entry or validation responsibilities. An IAC charter provides details on IAC membership and the governing processes.

4.10. Changes to Protocol-Planned Analyses

There is no change to protocol-planned analyses.

5. Sample Size Determination

For the primary outcome database lock at the end of Stage 1, approximately CCI participants will be randomly assigned to receive LY3972406 CCI or placebo in a CCI ratio. With approximately CCI participants per treatment group, this study will have more than CCI power to detect a difference between LY3972406 and placebo of CCI or greater in PASI 75 response rates at Week 12. The sample size was determined based on a CCI [redacted] PASI 75 placebo response rate. If Stage 2 is initiated (with or without the CCI arm), this study will have more than CCI power to detect a difference between each LY3972406 arm and placebo of CCI or greater in PASI 75 response rates at Week 12 under the same assumptions.

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6. Supporting Documentation

6.1. Appendix 1: Demographic and Baseline Characteristics

The patient's year of birth, sex, weight, height, prior exposure to biologic therapy for psoriasis (biologic naïve versus experienced), and other demographic characteristics are collected at the screening visit. Age and body mass index will be calculated.

Only the year of birth is collected at screening. For the purpose of age calculation, the month and day of birth will be imputed as July 01, of the year of birth. Age is computed as follows:

Age = (Informed Consent Date – Date of Birth +1)/365.25.

Demographic and baseline characteristics, including age, gender, race, and ethnicity, will be summarized for each treatment group.

Certain characteristics that are collected at baseline or after baseline but not summarized in the demographic summary will be reported as a listing.

No inferential analysis for the comparability of baseline covariates across treatment groups will be performed.

6.2. Appendix 2: Treatment Compliance

Study treatment administration and compliance will be listed for all entered patients. The number and percentage of patients who are treatment compliant by visit will be summarized by treatment group.

No patient will be excluded from the modified intent-to-treat population as a consequence of significant noncompliance.

No analyses are planned to assess treatment compliance.

6.3. Appendix 3: Lilly-Defined MedDRA Preferred Terms for POIs

Preferred Term (MedDRA Version 26.1)
Mycobacterial infection
Pneumonia fungal
Herpes simplex virus urethritis
Varicella zoster viraemia
Osteoarticular sporotrichosis
Cardiac tuberculosis
Device related fungaemia
Fusarium endocarditis
Chagas' gastrointestinal disease
Tuberculoma
Cutaneous blastomycosis
BK polyomavirus test positive

Preferred Term (MedDRA Version 26.1)
JC polyomavirus test positive
JC virus CSF test positive
Cutaneous listeriosis
Urinary tract candidiasis
Pulmonary mucormycosis
Rhinocerebral mucormycosis
Disseminated aspergillosis
Disseminated blastomycosis
Disseminated coccidioidomycosis
Cytomegalovirus infection reactivation
Hepatitis C virus core antigen
Herpes simplex reactivation
Herpes zoster reactivation
Varicella zoster sepsis
Disseminated leishmaniasis
Disseminated mycobacterium avium complex infection
Mycobacterium haemophilum infection
Disseminated mucormycosis
Disseminated paracoccidioidomycosis
Disseminated sporotrichosis
Disseminated strongyloidiasis
Cryptococcal meningoencephalitis
Laryngeal cryptococcosis
Hepatitis A
Herpes simplex bronchitis
Herpes simplex test positive
Lung diffusion test decreased
JC polyomavirus test
JC polyomavirus test positive
Parasitic pneumonia
Lung diffusion test
Herpes zoster disseminated
WU virus infection
Cerebral nocardiosis
Fungal myositis
Mastoiditis fungal
Pulmonary blastomycosis
Varicella encephalitis
Varicella meningitis
Elsberg syndrome
Oral herpes zoster

Preferred Term (MedDRA Version 26.1)
Pulmonary histoplasmosis
Septic cardiomyopathy
Tuberculosis of uterine cervix
Tuberculous pelvic inflammatory disease
Campylobacter bacteraemia
Disseminated varicella
Disseminated varicella zoster virus infection
Aspergillosis oral
Aspergillus infection
Aspergillus test
Aspergillus test positive
Bronchopulmonary aspergillosis
Cerebral aspergillosis
Meningitis aspergillus
Oro-pharyngeal aspergillosis
Sinusitis aspergillus
Bacillary angiomatosis
Bartonella test
Bartonella test positive
Bartonellosis
Peliosis hepatis
Splenic peliosis
Systemic bartonellosis
Trench fever
Blastomycosis
Epididymitis blastomyces
Osteomyelitis blastomyces
Campylobacter infection
Campylobacter sepsis
Campylobacter test positive
Candida endophthalmitis
Candida infection
Candida osteomyelitis
Candida pneumonia
Candida retinitis
Candida sepsis
Candida test
Candida test positive
Cerebral candidiasis
Endocarditis candida

Preferred Term (MedDRA Version 26.1)
Fungal oesophagitis
Gastrointestinal candidiasis
Hepatic candidiasis
Hepatosplenic candidiasis
Meningitis candida
Mucocutaneous candidiasis
Oesophageal candidiasis
Oral candidiasis
Oral fungal infection
Oropharyngeal candidiasis
Peritoneal candidiasis
Respiratory moniliasis
Splenic candidiasis
Systemic candida
Coccidioides encephalitis
Coccidioidomycosis
Cutaneous coccidioidomycosis
Meningitis coccidioides
Cryptococcal cutaneous infection
Cryptococcal fungaemia
Cryptococcosis
Cryptococcus test
Cryptococcus test positive
Disseminated cryptococcosis
Gastroenteritis cryptococcal
Meningitis cryptococcal
Neurocryptococcosis
Osseous cryptococcosis
Pneumonia cryptococcal
Biliary tract infection cryptosporidial
Cryptosporidiosis infection
Gastroenteritis cryptosporidial
Cytomegalovirus chorioretinitis
Cytomegalovirus colitis
Cytomegalovirus duodenitis
Cytomegalovirus enteritis
Cytomegalovirus enterocolitis
Cytomegalovirus gastritis
Cytomegalovirus gastroenteritis
Cytomegalovirus gastrointestinal infection

Preferred Term (MedDRA Version 26.1)
Cytomegalovirus gastrointestinal ulcer
Cytomegalovirus hepatitis
Cytomegalovirus infection
Cytomegalovirus mononucleosis
Cytomegalovirus mucocutaneous ulcer
Cytomegalovirus myelomeningoradiculitis
Cytomegalovirus myocarditis
Cytomegalovirus nephritis
Cytomegalovirus oesophagitis
Cytomegalovirus pancreatitis
Cytomegalovirus pericarditis
Cytomegalovirus syndrome
Cytomegalovirus test
Cytomegalovirus test positive
Cytomegalovirus urinary tract infection
Cytomegalovirus viraemia
Disseminated cytomegaloviral infection
Encephalitis cytomegalovirus
Pneumonia cytomegaloviral
Asymptomatic viral hepatitis
Chronic hepatitis B
HBV-DNA polymerase increased
Hepatitis B
Hepatitis B antigen
Hepatitis B antigen positive
Hepatitis B core antigen
Hepatitis B core antigen positive
Hepatitis B DNA assay
Hepatitis B DNA assay positive
Hepatitis B DNA increased
Hepatitis B e antigen
Hepatitis B e antigen positive
Hepatitis B reactivation
Hepatitis B surface antigen
Hepatitis B surface antigen positive
Hepatitis B virus test
Hepatitis B virus test positive
Hepatitis post transfusion
Hepatitis viral
Withdrawal hepatitis

Preferred Term (MedDRA Version 26.1)
Chronic hepatitis C
Hepatitis C
Hepatitis C RNA
Hepatitis C RNA fluctuation
Hepatitis C RNA increased
Hepatitis C RNA positive
Hepatitis C virus test
Hepatitis C virus test positive
Colitis herpes
Eczema herpeticum
Gastritis herpes
Herpes oesophagitis
Herpes ophthalmic
Herpes sepsis
Herpes simplex
Herpes simplex colitis
Herpes simplex encephalitis
Herpes simplex gastritis
Herpes simplex hepatitis
Herpes simplex meningitis
Herpes simplex meningoencephalitis
Herpes simplex meningomyelitis
Herpes simplex necrotising retinopathy
Herpes simplex oesophagitis
Herpes simplex pneumonia
Herpes simplex sepsis
Herpes simplex viraemia
Herpes simplex visceral
Herpes virus infection
Herpes virus test abnormal
Meningitis herpes
Meningoencephalitis herpetic
Meningomyelitis herpes
Ophthalmic herpes simplex
Pneumonia herpes viral
Disseminated varicella zoster vaccine virus infection
Encephalitis post varicella
Genital herpes zoster
Herpes zoster
Herpes zoster cutaneous disseminated

Preferred Term (MedDRA Version 26.1)
Herpes zoster infection neurological
Herpes zoster meningitis
Herpes zoster meningoencephalitis
Herpes zoster meningomyelitis
Herpes zoster meningoradiculitis
Herpes zoster necrotising retinopathy
Herpes zoster oticus
Herpes zoster pharyngitis
Necrotising herpetic retinopathy
Ophthalmic herpes zoster
Varicella keratitis
Varicella virus test
Varicella virus test positive
Varicella zoster virus infection
Acute pulmonary histoplasmosis
Chronic pulmonary histoplasmosis
Endocarditis histoplasma
Histoplasmosis
Histoplasmosis cutaneous
Histoplasmosis disseminated
Meningitis histoplasma
Pericarditis histoplasma
Presumed ocular histoplasmosis syndrome
Retinitis histoplasma
Anti-JC virus antibody index
BK virus infection
Human polyomavirus infection
JC polyomavirus test
JC virus granule cell neuronopathy
JC virus infection
Polyomavirus test
Polyomavirus test positive
Polyomavirus viraemia
Polyomavirus-associated nephropathy
Progressive multifocal leukoencephalopathy
Legionella infection
Legionella test
Legionella test positive
Pneumonia legionella
Pontiac fever

Preferred Term (MedDRA Version 26.1)
Leishmaniasis
Visceral leishmaniasis
Listeraemia
Listeria encephalitis
Listeria sepsis
Listeria test
Listeria test positive
Listeriosis
Meningitis listeria
Microsporidia infection
Cutaneous nocardiosis
Nocardia sepsis
Nocardia test positive
Nocardiosis
Pulmonary nocardiosis
Abscess fungal
Alternaria infection
Arthritis fungal
Biliary tract infection fungal
Central nervous system fungal infection
Cerebral fungal infection
Encephalitis fungal
Erythema induratum
Eye infection fungal
Fungaemia
Fungal abscess central nervous system
Fungal endocarditis
Fungal labyrinthitis
Fungal peritonitis
Fungal pharyngitis
Fungal retinitis
Fungal sepsis
Hepatic infection fungal
Meningitis fungal
Mycotic endophthalmitis
Myocarditis mycotic
Oropharyngitis fungal
Osteomyelitis fungal
Otitis media fungal
Pancreatitis fungal

Preferred Term (MedDRA Version 26.1)
Parasitic pneumonia
Pericarditis fungal
Phaeohyphomycosis
Pneumonia fungal
Pulmonary trichosporonosis
Sinusitis fungal
Splenic infection fungal
Systemic mycosis
Atypical mycobacterial infection
Atypical mycobacterial lower respiratory tract infection
Atypical mycobacterial lymphadenitis
Atypical mycobacterial pneumonia
Atypical mycobacterium pericarditis
Atypical mycobacterium test positive
Borderline leprosy
Bovine tuberculosis
Indeterminate leprosy
Lepromatous leprosy
Leprosy
Mycobacterial disease carrier
Mycobacterial peritonitis
Mycobacterium abscessus infection
Mycobacterium avium complex immune restoration disease
Mycobacterium avium complex infection
Mycobacterium chelonae infection
Mycobacterium fortuitum infection
Mycobacterium kansasii infection
Mycobacterium leprae test positive
Mycobacterium marinum infection
Mycobacterium test
Mycobacterium test positive
Mycobacterium ulcerans infection
Superinfection mycobacterial
Tuberculoid leprosy
Type 1 lepra reaction
Type 2 lepra reaction
Allescheriosis
Fusarium infection
Mucormycosis
Phaeohyphomycotic brain abscess

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Preferred Term (MedDRA Version 26.1)
Pseudallescheria infection
Pseudallescheria sepsis
Scedosporium infection
Paracoccidioides infection
Pulmonary paracoccidioidomycosis
Penicillium infection
Penicillium test positive
Blood beta-D-glucan
Blood beta-D-glucan abnormal
Blood beta-D-glucan increased
Gomori methenamine silver stain
Pneumocystis jirovecii infection
Pneumocystis jirovecii pneumonia
Pneumocystis test positive
Epstein Barr virus positive mucocutaneous ulcer
Epstein-Barr viraemia
Epstein-Barr virus associated lymphoma
Epstein-Barr virus associated lymphoproliferative disorder
Epstein-Barr virus infection
Lymphoproliferative disorder
Lymphoproliferative disorder in remission
Oral hairy leukoplakia
Post transplant lymphoproliferative disorder
Aortitis salmonella
Arthritis salmonella
Meningitis salmonella
Osteomyelitis salmonella
Paratyphoid fever
Pneumonia salmonella
Salmonella bacteraemia
Salmonella sepsis
Salmonella test positive
Salmonellosis
Typhoid fever
Shigella infection
Shigella sepsis
Shigella test positive
Cutaneous sporotrichosis
Pulmonary sporotrichosis
Sporotrichosis

Preferred Term (MedDRA Version 26.1)
Strongyloidiasis
Cerebral toxoplasmosis
Disseminated toxoplasmosis
Eye infection toxoplasmal
Meningitis toxoplasmal
Myocarditis toxoplasmal
Pneumonia toxoplasmal
Toxoplasma serology
Toxoplasma serology positive
Toxoplasmosis
American trypanosomiasis
Chagas' cardiomyopathy
Meningitis trypanosomal
Trypanosoma serology positive
Trypanosomiasis
Adrenal gland tuberculosis
Bone tuberculosis
Choroid tubercles
Conjunctivitis tuberculous
Cutaneous tuberculosis
Disseminated Bacillus Calmette-Guerin infection
Disseminated tuberculosis
Ear tuberculosis
Epididymitis tuberculous
Extrapulmonary tuberculosis
Immune reconstitution inflammatory syndrome associated tuberculosis
Interferon gamma release assay
Interferon gamma release assay positive
Intestinal tuberculosis
Joint tuberculosis
Lymph node tuberculosis
Male genital tract tuberculosis
Meningitis tuberculous
Mycobacterium tuberculosis complex test
Mycobacterium tuberculosis complex test positive
Oesophageal tuberculosis
Oral tuberculosis
Pericarditis tuberculous
Peritoneal tuberculosis

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Preferred Term (MedDRA Version 26.1)
Prostatitis tuberculous
Pulmonary tuberculoma
Pulmonary tuberculosis
Renal tuberculosis
Salpingitis tuberculous
Silicotuberculosis
Spleen tuberculosis
Thyroid tuberculosis
Tuberculid
Tuberculin test
Tuberculin test false negative
Tuberculin test positive
Tuberculoma of central nervous system
Tuberculosis
Tuberculosis bladder
Tuberculosis gastrointestinal
Tuberculosis liver
Tuberculosis of central nervous system
Tuberculosis of eye
Tuberculosis of genitourinary system
Tuberculosis of intrathoracic lymph nodes
Tuberculosis of peripheral lymph nodes
Tuberculosis ureter
Tuberculous abscess central nervous system
Tuberculous endometritis
Tuberculous laryngitis
Tuberculous pleurisy
Tuberculous tenosynovitis
Vibrio test positive
Vibrio vulnificus infection

Abbreviations: HBV = hepatitis B virus; MedDRA = Medical Dictionary for Regulatory Activities.

7. References

Armstrong AW, Edson-Heredia E, Naegeli AN, et al. Development of the Psoriasis Symptoms Scale (PSS) in patients with moderate-to-severe psoriasis: qualitative and quantitative analyses. *J Dermatolog Treat*. 2020;31(5):452-459. https://doi.org/10.1080/09546634.2019.1623370

Basra MKA, Salek MS, Camilleri L, et al. Determining the minimal clinically important difference and responsiveness of the Dermatology Life Quality Index (DLQI): further data. *Dermatology*. 2015;230(1):27-33. https://doi.org/10.1159/000365390

Finlay AY, Khan GK. Dermatology Quality of Life Index (DLQI)--a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994;19(3):210-216. https://doi.org/10.1111/j.1365-2230.1994.tb01167.x

Fredriksson T, Pettersson U. Severe psoriasis--oral therapy with a new retinoid. *Dermatologica*. 1978;157(4):238-244. https://doi.org/10.1159/000250839

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Thaçi D, Unnebrink K, Sundaram M, et al. Adalimumab for the treatment of moderate to severe psoriasis: subanalysis of effects on scalp and nails in the BELIEVE study. *J Eur Acad Dermatol Venereol*. 2015;29(2):353-360. https://doi.org/10.1111/jdv.12553

Van Voorhees AS, Feldman SR, Lebwohl MG, et al. *The Psoriasis and Psoriatic Arthritis Pocket Guide: Treatment Algorithms and Management Options*. 4th ed. National Psoriasis Foundation; 2016.

Winthrop KL, Novosad SA, Baddley JW, et al. Opportunistic infections and biologic therapies in immune-mediated inflammatory diseases: consensus recommendations for infection reporting during clinical trials and postmarketing surveillance. *Ann Rheum Dis*. 2015;74(12): 2107-2116. https://doi.org/10.1136/annrheumdis-2015-207841

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