Statistical Analysis Plan: J2T-MC-KGBY

Study to Assess Lebrikizumab Pen Ease of Use in Patients with Atopic Dermatitis

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Statistical Analysis Plan (SAP)

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STUDY TO ASSESS LEBRIKIZUMAB PEN EASE OF USE IN PATIENTS WITH ATOPIC DERMATITIS

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STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

Statistical Analysis Plan V2.0; 16 Jul 2024 for Protocol #23037/J2T-MC-KGBY V1.0 12 Apr 2024.

The SAP signature page applies to both SAP text and SAP Templates (outputs shells or Table/ Listing/ Figure (TLF) shells). Templates must be sent to the client with the first draft SAP text.

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MODIFICATION HISTORY

Unique Identifier for this Version	Date of the Document Version	Author	Significant Changes from Previous Authorized Version
0.1	08MAY2024	PPD	Not Applicable – First draft
0.2	28MAY2024	PPD	As per Bios review comments, a listing of product complaints is added in Section 15.
1.0	03JUN2024	PPD	Not Applicable – First version
2.0	10JUL2024	PPD	Section 14.1.1: • Updated primary variable "Question 12" to "Question 11". • Added combined response of "Agree" or "Strongly agree"

TABLE OF CONTENTS

ABBREVIATIONS

AE	Adverse Event
AD	Atopic Dermatitis
CRF	Case Report Forms
ENR	Patients Enrolled Set
MedDRA	Medical Dictionary for Regulatory Activities
mSQAAQ	Modified Subcutaneous Administration Assessment Questionnaire
Q1	First Quartile
Q3	Third Quartile
REALM	Rapid Estimation of Adult Literacy in Medicine
SAP	Statistical Analysis Plan
SAS	Statistical Analysis Software
SD	Standard Deviation
SOC	System Organ Class

1. INTRODUCTION

This statistical analysis plan (SAP) describes the rules and conventions to be used in the presentation and analysis of the ease of use and confidence of lebrikizumab administrations via a prefilled pen. It describes the data to be summarized and analyzed, including specifics of the statistical analyses to be performed.

This statistical analysis plan (SAP) is based on protocol version 1.0, dated 12 APR 2024 and Case Report Forms (CRFs) version 1.0, dated 15 APR 2022.

2. STUDY OBJECTIVES

2.1 Primary Objective

The primary objective is to evaluate the ease of use and confidence of lebrikizumab administrations via a prefilled pen using the modified Subcutaneous Administration Assessment Questionnaire (mSQAAQ) following training on the pen.

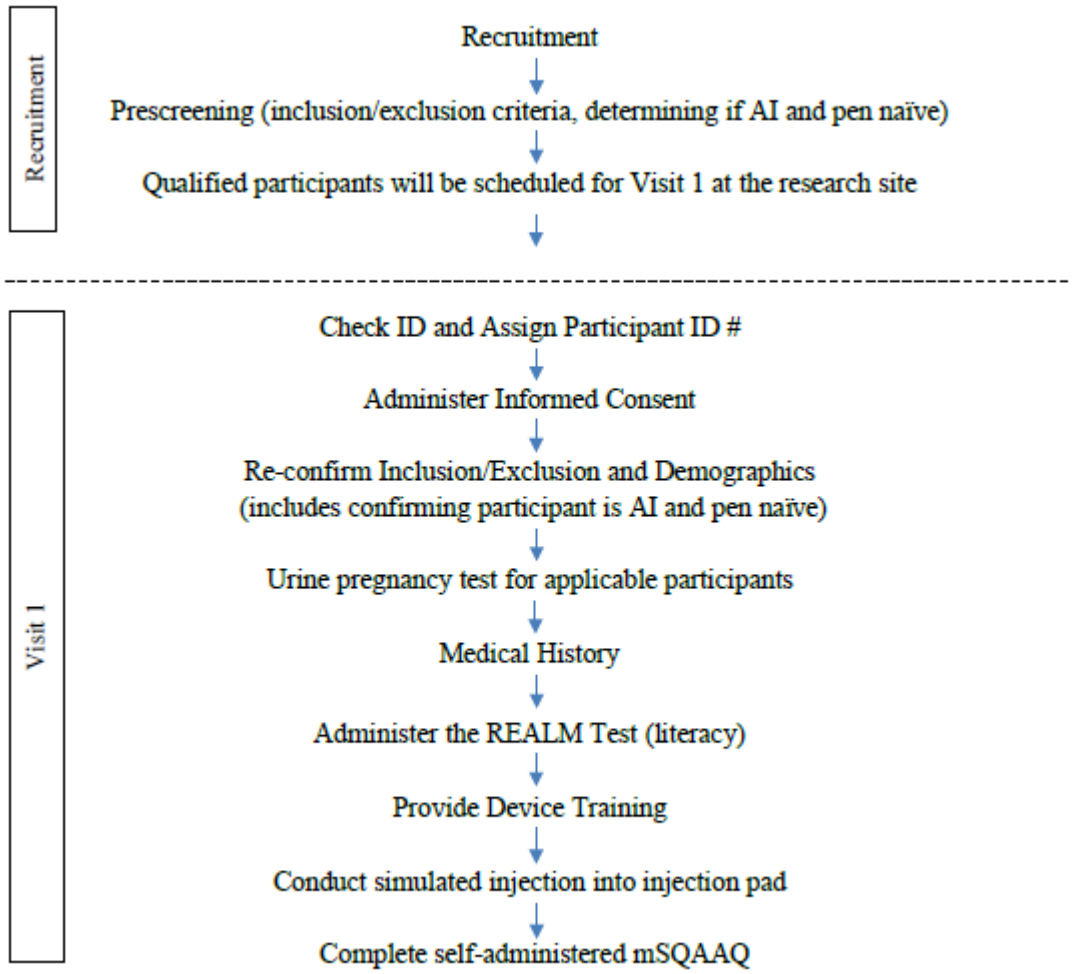
3. STUDY DESIGN

3.1 General Description

This study is an open-label, single site ease of use study of the lebrikizumab pen and consists of a single study visit for approximately 56 adult participants. All participants will receive training and perform mock injections on a practice pad using the pen. Participants will be under the supervision of a study interviewer when handling the pen and will complete the mSQAAQ following the simulated injection.

No treatment will be administered to the participants. A Study Flowchart can be found in Figure 1.

Figure 1 Study Flowchart



3.2 Schedule of Events

The schedule of events can be found in Table 2 of the protocol.

3.3 Changes to Analysis from Protocol

No changes from protocol.

4. PLANNED ANALYSES

4.1 Interim Analysis

There are no interim analyses planned for this study.

4.2 Final Analysis

The final analysis described in this SAP will be performed by IQVIA Real World (RW) Biostatistics following the database lock. The corresponding TLFs will form the basis for the clinical study report.

5. ANALYSIS SETS

5.1 All Patients Screened [SCR]

All Patients Screened (SCR) set will contain all patients screened for the study.

5.2 All Patients Enrolled Set [ENR]

All Patients Enrolled (ENR) set will contain all patients who provide informed consent for this study.

6. GENERAL CONSIDERATIONS

6.1 Sample Size

The planned final sample size of 51 participants with full data is sufficient to provide descriptive insights about the study population. Given the nature of the study it is expected that CCI%+ of participants enrolled will complete the study and provide full analyzable data.

As defined in the protocol, under the assumption that CCI% of the participants will respond "agreed" or "strongly agreed" to the device being "easy to use" and "they are confident they can use the device" we will have 95% confidence that the response rate is located in this range of proportions: [CCI% - CCI%]. Table 1 shows a variety of possible sample sizes. For the purpose of the intended claims the 95% CI lower bound should remain above CCI%, preferably above CCI%, and the parameters for the calculation of sample size have been selected for that.

Table 1 Sample Size Calculation

Proportion	Margin	Lower CI	Upper CI	Sample Size
95.0%	CCI			
95.0%				
90.0%				
85.0%				
80.0%				

6.2 Baseline

This is a single center, single visit simulated use study. All participants will complete the study at the end of Visit 1. For the purpose of this study, baseline refers to Visit 1. Day 1 is also referred to as Visit 1.

6.3 Baseline Data

Baseline data is defined as data collected at Visit 1.

6.4 Windowing Conventions

This study will require one visit. Subjects will be enrolled and completed at Visit 1.

6.5 Software Version

All analyses will be conducted using Statistical Analysis Software® (SAS) version 9.3 or higher.

7. STATISTICAL CONSIDERATIONS

7.1 Statistical Tests and Confidence Intervals

Continuous variables will be summarized using descriptive statistics, i.e., by the number of non-missing and missing observations, mean, standard deviation (SD), first quartile (Q1), median, third quartile (Q3), minimum, and maximum.

Categorical variables will be summarized by frequency counts (n) and percentages (%). Percentages will not include the missing category and are calculated over the number of patients with available (non-missing) data. Counts of missing data will be provided in the tables for information only.

For reporting conventions, percentages will be reported to 1 decimal place unless greater precision is deemed appropriate, except for cases when 100% is presented. In cases of a count of 0, the percentage will not be presented. The 95% confidence interval (CI) for the response rates will be calculated using Clopper-Pearson method.

7.2 Missing data

Missing data will not be imputed. All analysis will be conducted based on the observed data. Any participants who attend a study visit but do not complete the simulated injection will be excluded from the analysis. Partial completion of the mSQAAQ will be analyzed per the instrument instructions.

7.3 Examination of Subgroups

Subgroup analyses will be performed descriptively without comparisons between subgroups. The following subgroup analyses will be performed for this study:

- Injection experience (Yes, No) as defined in Section 10.

- Literacy (Limited literacy, Normal literacy) as defined in Section 10.
- Any comorbidity that involves joints (Yes, No) as defined in Section 11.

If there are fewer than 5 patients in a given subgroup, that data will not be summarized. Given that the sample size calculations did not consider subgrouping, the analyses will be exploratory in nature.

7.4 Randomization Schedule

No randomization will be performed for this study.

8. OUTPUT PRESENTATIONS

TLFs shells will be developed by IQVIA RWS Biostatistics using the standard processes. The format and content of the statistical analysis is illustrated in the TLF shells provided with this SAP.

9. DISPOSITION AND WITHDRAWALS

All patients who provide informed consent will be accounted for in this study. Subject disposition will be summarized in terms of number and percentages (n, %) for the below variables (see Section 7.1 for more details). Unless specified otherwise, percentages will be calculated using the number of patients from ENR as denominator.

- Patients in SCR.
- Patients in ENR.
- Patients not meeting eligibility criteria.
- Patients who completed the study.
- Patients who discontinued the study.
- Reason for study discontinuation.
    - Adverse Event or Serious Adverse Event
    - Noncompliance with Protocol
    - Withdrew consent
    - Screen Failure
    - Other

For the variables “Patients in ENR” and “Patients not meeting eligibility criteria”, percentages are calculated based on SCR as denominator.
A listing will also be provided for the above disposition data.

10. DEMOGRAPHIC AND OTHER PATIENT CHARACTERISTICS

Demographic data and patient characteristics will be presented for the ENR. No statistical testing will be carried out for demographic or patient characteristics. The following demographic characteristics will be presented as described in Section 7.1:

- Age at enrollment (years)
- Sex (Male, Female)
- Race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Pacific Islander, White, Other, Multiple, Refused to answer)
- Ethnicity (Hispanic, Non-hispanic)
- Education (Less than High School, Completed High School/GED, Some College/Technical School, Graduated College/Technical School or more, refused to answer)
- Employment status (Employed Full-Time, Employed Part-Time, Unemployed, Student, Retired, Other, refused to answer)
- Total annual household income ($0 to $14,999, $15,000 to $24,999, $25,000 to $34,999, $35,000 to $44,999, $45,000 to $64,999, $65,000 to $74,999, $75,000 or more, refused to answer)

A listing will also be provided for the above demographic characteristics.

Descriptive statistics (see Section 7.1) will be provided for the following patient characteristics:

Injection Experience:

- Number of subjects with any previous injection experience (Yes, No)
- Number and percentage of injection tool used (pre-filled syringe (PFS), Vial/Syringe, Other)

- Number and percentage of previous injection experience (Perform injections frequently on self, perform injections frequently on others, perform injections rarely on self, perform injections rarely on others)

A listing of injection experience will be provided for each term as collected in the eCRF, including the data listed above, the drug and/or device used for injection, and the last time they performed an injection.

Pregnancy:

- Number and percentage of participants who are individuals not of childbearing potential (INOCBP]) (Yes, No)
- Number and percentage of Reason for being INOCBP (Surgically sterilized, Tubal Ligation, not capable of producing ova or embryo due to congenital anomaly)
- Number and percentage of pregnancy test completed (Yes, No)
    - Number and percentage of reason for pregnancy test not performed (Refused, unable to urinate, other)
    - Participants who read Instructions for Use (Yes, No)
    - Participant given the opportunity to have their questions about the injection simulation process answered (Yes, No)
    - Injection simulation observation for correct demonstration of below tasks:
        - Task 1: Uncap the pen (Yes, No, Not assessed).
        - Task 2: Place and unlock (Yes, No, Not assessed).
        - Task 3: Press and hold for 15 seconds (Yes, No, Not assessed). Note that “Press and hold for 15 seconds" means that you should either press and hold for 15 seconds or wait for the second click as outlined in task 3 of the Instructions for Use (IFU).

11. MEDICAL HISTORY

A brief medical history will be conducted to gather information about the approximate date of participants’ AD diagnosis and any previous or current AD treatments. Data will be captured during

the enrollment visit and will be presented for the ENR. Medical History and Comorbidities will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). The MedDRA version used for a given output will be added in the footnote.

The following will be presented:

- Number and percentage of participants who normally wear corrective lenses, contacts, or glasses to read? (Yes, No)
- Number and percentage of participants who have any difficulty, even with glasses, reading small print, such as labels on medicine bottles, a telephone book, or food label? (No difficulty, A little difficulty, A moderate amount of difficulty, A great deal of difficulty, Unable to perform the activity, Not applicable).
- Number and percentage of any of the following conditions:
    - Osteoarthritis
    - Rheumatoid Arthritis
    - Carpal Tunnel Syndrome
    - Neuropathy
    - Other
- Number and percentage of, how difficult was it for you during the last 48 hours to unlock your door with a key because of finger joint problems? (Not at all difficult, A little difficult, Moderately difficult, Very difficult, I am unable to perform this activity, Not applicable).
- Number and percentage of, how difficult was it for you during the last 48 hours to zip up or unzip a zipper because of finger joint problems? (Not at all difficult, A little difficult, Moderately difficult, Very difficult, I am unable to perform this activity, Not applicable).

A listing by patient including each term as collected in the eCRF.

12. CONCOMITANT MEDICATION

A listing by patient including each medication term, indication, start and end date, ongoing condition (Yes/No), infected body system, dose, unit, dose form, route, and frequency will be included as collected in the eCRF.

13. STUDY MEDICATION EXPOSURE

No study medication will be given in this study.

14. PRIMARY OUTCOME

14.1 Primary Endpoint

The primary endpoints are the ease of use and confidence of lebrikizumab administrations via a prefilled pen using the modified Subcutaneous Administration Assessment Questionnaire (mSQAAQ) following training on the pen.

14.1.1 Primary Variables

The SQAAQ is an innovative, 12-item, self-administered questionnaire designed to evaluate the user-friendliness of the device and the patient's confidence during the administration of a subcutaneous injection of a medication. In this study, evaluation of the subject's experience will be based on the mSQAAQ, a self-administered questionnaire that assesses the ease of use and confidence in using the lebrikizumab pen. This tool is comprised of 10 questions (of which 2 questions were removed in the eCRF). Responses are scored on a 7-point Likert scale ranging from 'strongly disagree' to 'strongly agree' as follows:

1 - Strongly disagree

2 - Disagree

3 - Slightly Disagree

4 - Neither agree nor disagree

5 - Slightly agree

6 – Agree*

7 - Strongly agree*

*A combined response of "Agree" or "Strongly agree" will also be presented for all questions.

The following are the questions were removed in the eCRF:

- Question 6: Easy to store device in refrigerator

- Question 10: Device is stable against skin during injection

The primary variables are the results reported for each element of the mSQAAQ, which are as follows:

- Question 9: Overall, easy to use
- Question 11: I am confident in my ability to use the device

The other variables are the results reported for each element of the mSQAAQ, which are as follows:

- Question 1: Easy for me to learn how to use
- Question 2: Easy for me to unlock
- Question 3: Easy to hold in my hand when I inject my dose
- Question 4: Easy to inject my dose
- Question 5: Easy to know that my dose is complete
- Question 7: Easy to remove needle shield/cover
- Question 8: Easy to pick up
- Question 12: I am confident my dose is complete

Number, percentage, and 95% confidence interval of partial responders will also provide, overall.

14.1.2 Analysis of Primary Variables

The primary analysis will be performed on the ENR. Each element will be summarized using descriptive statistics (see Section 7.1).

15. SAFETY OUTCOMES

All outputs for safety outcomes will be based on the ENR. AE/SAE/Product complaints will be coded using the latest version of MedDRA at the time of data analysis. The MedDRA version used for a given output will be added in the footnote.

A listing by patient including each verbatim term, preferred term, start and end date, ongoing status (Yes/No), action taken, outcome, severity, seriousness, relationship to the device, and relationship to drug will also be provided.

A listing of adverse events, medications and product complaints will be provided. It will include patient responses to whether the participant experienced any adverse events during this study, whether the participant is currently taking any medication or therapy, whether the participant identified any product complaints, and whether a product complaint form was submitted to the study sponsor.

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16. REFERENCES

1. Davis, T. C., Long, S. W., Jackson, R. H., Mayeaux, E. J., George, R. B., Murphy, P. W., and Crouch, M. A. Rapid Estimate of Adult Literacy in Medicine: A Shortened Screening Instrument. Family Medicine 1993;25:391-396.

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ELI_LILLY_JAB94256_Auto_inj_SAP_v2.0_16JUL2024

Final Audit Report 2024-07-19

Created:	2024-07-18
By:	PPD
Status:	Signed
Transaction ID:	PPD

"ELI_LILLY_JAB94256_Auto_inj_SAP_v2.0_16JUL2024" History

Document created by PPD
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Document emailed to PPD
2024-07-18 - 4:12:10 PM GMT

Document emailed to PPD for signature
2024-07-18 - 4:12:11 PM GMT

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Challenge: The user clicked on the signature field: 'Signature 1'.
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Challenge: The user opened the agreement.

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2024-07-19 - 8:25:27 AM GMT

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Signing reason: Approved

Signature Date: 2024-07-19 - 8:25:29 AM GMT - Time Source: server

Agreement completed.

2024-07-19 - 8:25:29 AM GMT