PPD

Statistical Analysis Plan for Interventional Studies

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Sponsor Name: Meiji Pharma USA Inc.

Protocol Number: ME3183-3
Protocol Title: A Multi-center, Randomized, Double-blind, Placebo-controlled, Parallel Group, Phase 2a Study to Assess the Efficacy and Safety of ME3183 Administered Orally in Subjects with Moderate to Severe Plaque Psoriasis

Protocol Version and Date:
Version 1.0 (08-Oct-2021)
Version 2.0 (07-Dec-2021)

PPD **Project Code:** 7028898

Authors: PPD

Notice of Confidential and Proprietary Information:

Revision History

Version #	Date (DD-Mmm-YYYY)	Document Owner	Revision Summary
v0.1	18-Mar-2022	PPD	Initial Release Version
v0.2	19-Apr-2022		Revised draft addressing sponsor comments.
v1.0	13-Jun-2022		Finalized version.
v1.1	07-Jun-2023		Updated version with the following main updates: - screened set and randomized set are added in the analysis sets; clarifications are provided regarding defining safety analysis sets in the event of drug mis-dispensation; pharmacokinetic set and CCI [redacted] are updated to account for drug mis-dispensation. - estimands are updated for secondary efficacy points to allow for imputation (LOCF and NRI) for sPGA related secondary endpoint. - imputation rules for missing start dates are updated - additional analyses are added in the section of secondary efficacy endpoints and analysis - additional analysis of TEAEs by time of onset is added - additional outputs are added in the Index of Tables
v2.0	26-Jun-2023		Finalized version.
v3.0	11-Jul-2023		Finalized version.

I confirm that I have reviewed this document and agree with the content.

Approvals

PPD Approval

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1. Glossary of Abbreviations

Abbreviation	Description
AE	Adverse Event
AIC	Akaike's Information Criteria
ATC	Anatomical Therapeutic Chemical
BDRM	Blind Data Review Meeting
BID	Twice Daily
BLQ	Below the Limit of Quantification
BMI	Body Mass Index
BSA	Body Surface Area
CI	Confidence Interval
CMH	Cochran-Mantel-Haenszel
CS	Clinically Significant
C-SSRS	Columbia-Suicide Severity Rating Scale
CTMS	Clinical Trial Management System
C_{trough}	Trough Plasma Concentration
CV	Coefficient of Variation
DLQI	Dermatology Life Quality Index
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
FAS	Full Analysis Set
FSH	Follicle-Stimulating Hormone
GCP	Good Clinical Practice
GI	Gastrointestinal
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Council for Harmonisation
ID	Subject Identification

Abbreviation	Description
IL	Interleukin
IWRS	Interactive Web Response System
LLT	Lower Level Term
LOCF	Last Observation Carried Forward
LS	Least-square
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed-effect Model for Repeated Measures
NRI	Non-responder Imputation
NRS	Numerical Rating Scale
PASI	Psoriasis Area and Severity Index
PASI-50	≥ 50% Reduction from Baseline in the PASI score
PASI-75	≥ 75% Reduction from Baseline in the PASI score
PASI-90	≥ 90% Reduction from Baseline in the PASI score
PASI-100	100% Reduction from Baseline in the PASI score
CCI [redacted]	
PDE4	Phosphodiesterase 4
PK	Pharmacokinetic
PP	Patient Privacy
PPS	Per Protocol Set
PRO	Patient-reported Outcome
PT	Preferred Term
QD	Once Daily
QTc	Corrected QT Interval
QTcF	QT Interval Corrected using Fridericia's Formula
REML	Restricted Maximum Likelihood
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
SOP	Standard Operating Procedure
sPGA	Static Physician's Global Assessment

Abbreviation	Description
TEAE	Treatment-Emergent Adverse Event
TFL	Tables, Figures and Listings
TNF-α	Tumor Necrosis Factor-alpha
UV	Ultraviolet
UVB	Ultraviolet B
WHO	World Health Organization
WOCBP	Women of Childbearing Potential

2. Purpose

The purpose of this statistical analysis plan (SAP) is to ensure that the data listings, summary tables and figures which will be produced, and the statistical methodologies which will be used, are complete and appropriate to allow valid conclusions regarding the study objectives.

2.1. Responsibilities

PPD will perform the statistical analyses and is responsible for the production and quality control of all tables, figures, and listings.

2.2. Timings of Analyses

The primary analysis of safety, efficacy and pharmacokinetics/CCI is planned after all subjects complete the final study visit (Visit 8 at Week 16) or terminate early from the study. Database will be completely cleaned and locked prior to the primary analysis. No interim analyses are planned for the study.

3. Study Objectives

3.1. Primary Objective

- To evaluate the efficacy of oral ME3183 compared with placebo at Week 16 in subjects with moderate to severe plaque psoriasis as measured by the Psoriasis Area and Severity Index (PASI) score

3.2. Secondary Objectives

- To evaluate the safety and tolerability of oral ME3183 in subjects with moderate to severe plaque psoriasis
- To evaluate the efficacy of oral ME3183 in subjects with moderate to severe plaque psoriasis at various time points
- To evaluate the effect of oral ME3183 on patient-reported outcome (PRO) measures in subjects with moderate to severe plaque psoriasis
- To evaluate the pharmacokinetic (PK) of ME3183 and its metabolite (CCI) in subjects with moderate to severe plaque psoriasis who are treated with oral ME3183

3.3. Exploratory Objectives

CCI

4. Study Details/Design

4.1. Brief Description

This multi-center, randomized, double-blind, placebo-controlled, parallel group, Phase 2a study is designed to assess the efficacy and safety of ME3183 administered orally in subjects with moderate to severe plaque psoriasis. The study consists of a 4-week Screening Period (Day -28 to Day -1), a 16-week double-blind Treatment Period (Day 1 to Day 113), and a 4-week Follow-up Period (Day 114 to Day 141). The total duration of study participation for each subject is approximately 24 weeks.

Note: The study drug is administered from Day 1 to Day 112 in the Treatment Period and the end of Treatment Period assessments will be performed on Day 113.

The duration of the Follow-up Period is from Day 114 to Day 141 and the end of Follow-up Period assessments will be performed on Day 141.

A suitable number of subjects with moderate to severe plaque psoriasis will be screened to randomize approximately 125 subjects across approximately 30 study sites in the United States and Canada. Subjects will be centrally randomized (25 subjects per treatment group) in a 1:1:1:1:1 ratio to 1 of the following treatment groups to receive oral ME3183 or matching placebo for a duration of 16 weeks.

- Treatment Group 1: [redacted] mg ME3183 BID administered orally: [redacted] capsule of [redacted] mg ME3183 and [redacted] capsules of matching placebo in the morning and evening
- Treatment Group 2: [redacted] mg ME3183 QD administered orally: [redacted] capsules of [redacted] mg ME3183 and [redacted] capsule of matching placebo in the morning and [redacted] capsules of matching placebo in the evening
- Treatment Group 3: [redacted] mg ME3183 BID administered orally: [redacted] capsule of [redacted] mg ME3183 and [redacted] capsule of [redacted] mg ME3183 and [redacted] capsule of matching placebo in the morning and evening
- Treatment Group 4: [redacted] mg ME3183 QD administered orally: [redacted] capsules of [redacted] mg ME3183 in the morning and [redacted] capsules of matching placebo in the evening
- Treatment Group 5: Matching placebo BID administered orally: [redacted] capsules of matching placebo in the morning and evening

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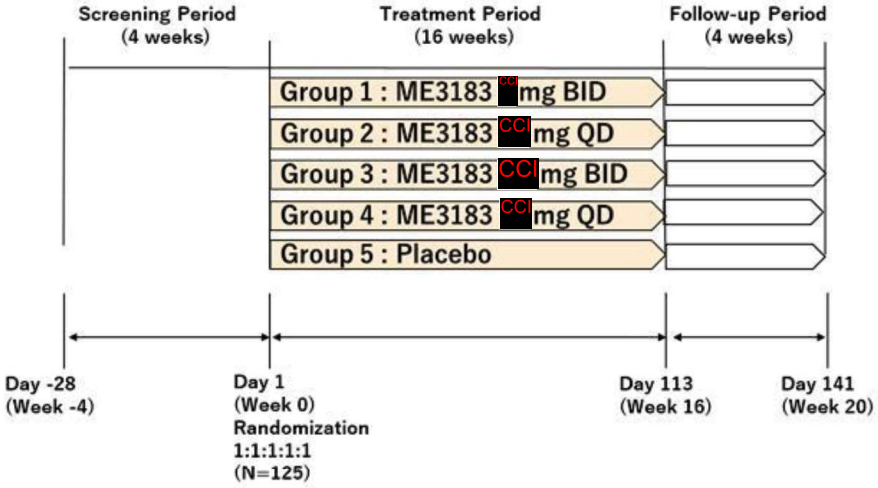
Figure 1. Study Design



Abbreviations: QD = once daily; BID = twice daily; N = approximate number of subjects to be randomized.

4.2. Subject Selection

4.2.1. Inclusion Criteria

Individuals must meet all of the following criteria to be included in the study:

1. Subject is willing and able to participate in the study and has read, understood, and signed the informed consent form (ICF) according to national regulations.

2. Subject is a male or female aged 18 to 75 years (inclusive) at the time of consent (i.e., Screening).

3. Subject has a body mass index (BMI) ≥ 18.5 to 40 kg/m^2 at Screening.

4. Subject has a diagnosis of plaque psoriasis for ≥ 24 weeks prior to Screening.

5. The subject's symptoms of plaque psoriasis are stable in the opinion of the investigator. Stable is defined as no acute deterioration (e.g., pustulation or erythroderma) within 12 weeks before Screening and no rebound of plaque psoriasis within 4 weeks before Screening.

6. The subject's severity of disease meets all of the following criteria:

   - Psoriatic plaques must cover ≥ 10% of body surface area (BSA) at Screening and Baseline
   - PASI score 12 to 40 at Screening and Baseline
   - Static Physician's Global Assessment (sPGA ≥ 3) at Screening and Baseline

7. Subject is deemed by investigator to be eligible for phototherapy or systemic therapy.

8. Subject agrees to avoid prolonged exposure to sunlight or use of artificial sunbathing (e.g., tanning

booths) or other ultraviolet (UV) light sources during the Treatment Period.

9. Subject, if female and of childbearing potential, must have a negative serum pregnancy test at Screening and negative urine pregnancy test at Baseline. Any women of childbearing potential (WOCBP) must agree to sexual abstinence or to use a highly effective contraceptive measure starting at Screening, continuing throughout the entire Treatment Period, and for at least 4 weeks after taking the last dose of study treatment. A female subject is considered to be a WOCBP after menarche and until she is in a postmenopausal state for 12 months or otherwise permanently sterile (for which acceptable methods include hysterectomy, bilateral salpingectomy, and bilateral oophorectomy). For the definition and a complete list of acceptable contraceptive measures see protocol APPENDIX 1.

10. Subject, if a fertile male, agrees to sexual abstinence or to use a condom during sexual activity with their female partner of childbearing potential starting at Screening, continuing throughout the entire Treatment Period, and for at least 4 weeks after taking the last dose of study treatment. A male subject is considered fertile after puberty unless permanently sterile by bilateral orchidectomy. Additionally, if their partner is a WOCBP, then their partner should be advised to use a highly effective contraceptive measure during sexual activity starting at Screening, continuing throughout the entire Treatment Period, and for at least 4 weeks after taking the last dose of study treatment. For the definition and a complete list of acceptable contraceptive measures see protocol APPENDIX 1.

11. Subject, if female, must agree to not donate, or retrieve for her own use, ova starting at Screening, continuing throughout the entire Treatment Period, and for at least 4 weeks after taking the last dose of study treatment.

12. Subject, if male, must agree to not freeze or donate sperm starting at Screening, continuing throughout the entire Treatment Period, and for at least 4 weeks after taking the last dose of study treatment.

4.2.2. Exclusion Criteria

Individuals meeting any of the following criteria at Screening or Baseline (as applicable) are ineligible to participate in this study:

1. Subject has a diagnosis of non-plaque psoriasis (predominantly guttate, pustular, inverse, or erythrodermic) or drug-induced psoriasis.

2. Subject has any unstable or clinically significant (CS) (as determined by the investigator) cardiac, endocrinologic, gastroenterologic, pulmonary, neurologic, psychiatric (such as major depression), hepatic, renal, hematologic, immunologic disease, or other disease (e.g., uncontrolled diabetes) that would place the subject at unacceptable risk if they were to participate in the study.

3. Subject has suicidal ideation or behavior in the past 12 months as indicated by a positive response (yes) to questions 3, 4, or 5 on the Columbia-Suicide Severity Rating Scale (C-SSRS) completed at Screening and/or at Baseline.

4. Subject has a present recurrent medical condition associated with significant gastrointestinal (GI) events (e.g., nausea, vomiting, constipation, abdominal pain, diarrhea).

5. Subject has any condition that would confound the ability to interpret data from the study (e.g., eczema, atopic dermatitis, lupus, inflammatory bowel disease).

6. Subject has any degree of dysphagia that may interfere with the oral dosing of the study treatment.

7. Subject has a history of allergy or hypersensitivity to any component of the study treatments.

8. Subjects who have had a prior laboratory confirmed COVID-19 test or have been in close physical contact (6 feet or closer for at least 15 minutes) with a person who is known to have laboratory confirmed COVID-19 or with anyone who has any symptoms consistent with COVID-19 within the past 14 days at Screening or Baseline.

9. Subjects experiencing any of the following symptoms at Screening or Baseline:

- Fever or chills
- Cough
- Shortness of breath or difficulty breathing
- Fatigue
- Muscle or body aches
- Headache
- New loss of taste or smell
- Sore throat
- Congestion or runny nose
- Nausea or vomiting
- Diarrhea

10. Subject has active or chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infection as per Screening viral serology tests. Exception: If the subject has received documented treatment which was curative for HCV and tests negative for HCV RNA at Screening, the subject may be considered for randomization.

11. Subject is positive for the Human Immunodeficiency Virus (HIV) antibodies (HIV-1 or HIV-2) at Screening or has a history of congenital or acquired immunodeficiency (e.g., common variable immunodeficiency disease).

12. Subject has a recent history of drug, substance, or alcohol abuse/dependence within 1 year prior to Screening as determined by the investigator.

13. Subject has an active infection (bacteria, viral, fungal, etc.) requiring treatment with systemic antibiotics within 4 weeks of Screening. Any treatment for such infections must be completed at least 4 weeks prior to Screening.

14. Subject has active tuberculosis or history of incompletely treated tuberculosis per medical history.

15. Subject has a malignancy or history of malignancy (except for treated [i.e., cured] basal cell or

squamous cell in situ skin carcinomas and treated [i.e., cured] cervical intraepithelial neoplasia or carcinoma in situ of the cervix with no evidence of recurrence).

16. Subject is pregnant or breastfeeding at Screening or at Baseline.

17. Subject has a history of lack of efficacy (inadequate efficacy when used in adequate dose and duration in accordance with the approved label) to any biological products for psoriasis. 18. Subject has received 2 or more biological products in the past for the treatment of psoriasis.

19. Subject has a history of lack of efficacy to 2 or more non-biologic systemic therapy due to inadequate efficacy when administered in adequate dose and duration in accordance with their label (approved in the subject's country) for psoriasis.

20. Subject has received any prior treatment with apremilast or any other Phosphodiesterase 4 (PDE4) inhibitor.

21. Subject has received ustekinumab, secukinumab, brodalumab, ixekizumab, guselkumab, risankizumab, tildrakizumab, or briakinumab (or any other therapeutic agent targeting Interleukin-12 [IL-12], IL-17, or IL-23) within 24 weeks of first administration of study treatment.

22. Subject has received Tumor Necrosis Factor-alpha (TNF-α) inhibitor(s)/blocker(s) within 8 weeks of first administration of study treatment.

23. Subject has received natalizumab (an integrin receptor antagonist), or agents that modulate B cells or T cells (e.g., alemtuzumab, abatacept, alefacept) within 12 weeks of first administration of study treatment.

24. Subject has received rituximab within 24 weeks of first administration of study treatment.

25. Subject has received any systemic immunosuppressants (e.g., methotrexate, azathioprine, cyclosporine, 6-thioguanine, mercaptopurine, mycophenolate mofetil, hydroxyurea, tacrolimus), any protein kinase inhibitor (e.g., tofacitinib, baricitinib, peficitinib, upadacitinib), or anakinra within 4 weeks of the first administration of study treatment.

26. Subject has received phototherapy (e.g., ultraviolet B including narrow band ultraviolet B, Goeckerman therapy, and excimer laser or psoralen ultraviolet A) or any systemic medications/treatments that could affect psoriasis or sPGA evaluation (including, but not limited to, oral or injectable corticosteroids, retinoids, 1,25-dihydroxy vitamin D3 and analogues, psoralens, sulfasalazine, or fumaric acid derivatives) within 4 weeks of the first administration of study treatment.

27. Subject has had a recent initiation of a drug that is known to potentially cause or exacerbate psoriasis (including, but not limited to, beta-blockers, lithium, and anti-malarials) within the 8 weeks prior to the first administration of study treatment; a subject who has been on a stable dose for at least 8 weeks prior to the first administration of study treatment without exacerbation of psoriasis may be randomized and does not need to discontinue these medications.

28. Subject has used topical medications/treatments that could affect psoriasis or sPGA evaluation (including, but not limited to, corticosteroids, anthralin, calcipotriene, topical vitamin D derivatives, retinoids, tazarotene, methoxsalen, trimethylpsoralen, pimecrolimus, tacrolimus, or PDE4 inhibitor) within 2 weeks of the first administration of study treatment.

29. Subject has received an investigational drug for biologic therapy within the previous 24 weeks prior to the first administration of study treatment or received any other non-biologic investigational therapy/drugs or device within 4 weeks or 5 half-lives (whichever is longer) prior to the first administration of study treatment.

30. Subject has received any prior treatment with ME3183.

31. Subject has any of the following abnormal laboratory test findings at Screening.

- Abnormal hepatic function
  - Aspartate aminotransaminase or alanine aminotransaminase ≥ 2×upper limit of normal or
  - Total bilirubin ≥ 2×upper limit of normal, unless the subject has a diagnosis of Gilbert's syndrome
- White blood cell count <3000/mm3(<3.0×109/L)
- Neutrophil count <1000/mm3(<1.0×109/L)
- Platelet count <100,000/μL (<100×109/L)
- Hemoglobin <8.0 g/dL
- Creatinine clearance estimated by Cockcroft-Gault formula <60mL/min
- Hemoglobin A1c >9.0%

32. Subject has a CS abnormality on a 12-lead Electrocardiogram (ECG) or QTcF > 450 msec at Screening or Baseline.

33. Subject has a systolic blood pressure ≥ 160 mmHg or a diastolic blood pressure ≥ 100 mmHg (based on at least 2 repeat measurements) at Screening.

34. Prisoners or subjects who are incarcerated for any reason.

35. Subject has any other factor constituting disqualification for study inclusion in the judgement of the investigator.

4.3. Determination of Sample Size

No formal sample size calculation was performed.

For the assessment of efficacy and safety of ME3183 in subjects with moderate to severe plaque psoriasis in this proof-of-concept study, approximately 125 eligible subjects will be enrolled. Twenty-five subjects will be randomized to each of the following treatment groups: ME3183 [redacted] mg BID, ME3183 [redacted] mg QD, ME3183 [redacted] mg BID; ME3183 [redacted] mg QD, and placebo. The number of planned subjects is considered adequate to assess safety and to provide efficacy estimates for in this Phase 2a study. The expected drop-out rate is assumed to be 10%.

4.4. Treatment Assignment and Blinding

4.4.1. Method of Study Treatment Assignment

Prior to dosing on Day 1, all the eligible subjects will be randomly assigned to 1 of the 5 treatment groups in a 1:1:1:1:1 ratio. Subjects will be assigned a randomization number through interactive web response system (IWRS), in accordance with the randomization code generated by the authorized personnel at PPD designated by PPD. An unblinded, independent study statistician will be assigned to produce the randomization schedule. Once a randomization number is allocated to 1 subject, same number may not be assigned to another subject even if the former discontinued the study.

To promote balanced allocation, randomization will be stratified by the subject's receipt (yes/no) of previous treatment with a biologic drug for psoriasis. Bio-naïve subjects will be randomized above 50% of the planned total subject randomization.

4.4.2. Blinding

This is a double-blind study.

An IWRS will be used for subject randomization and a unique subject identification number will be assigned automatically. According to the randomization schedule as indicated in the Schedule of Assessments (Table 1), the investigator or designee will obtain the study drug kit number from the IWRS for the subject, and the number will be provided to the pharmacist or designee at the study center who is responsible for handling the study drugs. This pharmacist or designee will dispense the study drug to the subject based on the study drug kit number generated from the IWRS. An unblinded, independent study statistician will be assigned to produce the randomization schedule. No other study site personnel, subjects, Sponsor personnel, or Sponsor designees will be unblinded to treatment assignment throughout the duration of the study unless unblinding is required. If an investigator becomes unblinded to a given subject's study treatment, that subject will be discontinued from the study unless there are ethical reasons for that subject not to be discontinued; approval from the Medical Monitor must be obtained in such instances.

In the event that emergency unblinding is required for a given subject because of adverse events (AEs) or concerns for the subject's safety or wellbeing, the investigator may break the randomization code for the subject via the IWRS, by which system the unblinding will be captured. The investigator is responsible for notifying the Medical Monitor and/or Sponsor of such an event as soon as possible. The unblinding and its cause will also be documented in the electronic case report form (eCRF).

The bioanalytical laboratory will receive a copy of the randomization schedule for PK analysis, as the Sponsor does not intend to analyze the samples from the placebo group. The blinding procedure will be documented in a separate document.

4.5. Administration of Study Medication

ME3183 (CCI mg, CCI mg, CCI mg, and CCI mg) and a matching placebo will be prepared using the following ME3183 and placebo capsules:

- ME3183 Capsule CCI mg
- ME3183 Capsule CCI mg

- ME3183 Placebo Capsule

Refer to the investigator's brochure (IB) for complete details on the study treatment.

A designated pharmacist will dispense the study drugs at each visit. Additional details on dispensing of the study drugs will be provided in the pharmacy manual.

4.6. Study Procedures and Flowchart

Table 1 outlines the timing of procedures and assessments to be performed throughout the study. Protocol Section 12.5 specifies safety laboratory assessment samples to be obtained. See Protocol Sections 11, 12, and 13 for additional details regarding efficacy assessments, safety assessments, and PK assessments, respectively. Details of other assessments such as CCI are provided in Protocol Section 14.

In case a randomized subject is not able to attend scheduled study visit on-site due to restrictions related to SARS-CoV-2, a remote visit may be conducted instead (a phone call or a televisit).

It is strongly recommended to conduct the study assessments for the applicable visit as per protocol Schedule of Assessments (see Table 1) as much as possible. If possible and if local regulations allow and the subject agrees, trained and authorized members of the site staff are encouraged to collect study assessments, including samples for scheduled laboratory tests at subject's home or at a local facility. Alternatively, the subject could have the hematology, coagulation, chemistry, urinalysis, and pregnancy testing at a local laboratory and the laboratory reports will be provided to the investigator. The local laboratory results should be entered in the eCRF.

Subjects with signs and symptoms of infection, including SARS-CoV-2 infection should immediately contact the investigator, who should inform the Medical Monitor or designee as soon as possible to discuss subject's continuation of study treatment. In case of suspicions for SARS-CoV-2 infection, relevant testing should be performed local site procedures. In case study visits or assessments are not performed for reasons related to SARS-CoV-2 restrictions, this should be documented in the source documents and eCRF.

Table 1. Schedule of Assessments

Study Procedures	Screening Period	Treatment Period							Follow-up Period[b]
	Screening (Visit 1)	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8[a]	Follow-up Visit (Visit 9)
	Week -4	Week 0	Week 1	Week 2	Week 4	Week 8	Week 12	Week 16	Week 20
	Days -28 to -1	Day 1 (Baseline)	Day 8 (±1 day)	Day 15 (±1 day)	Day 29 (±3 days)	Day 57 (±3 days)	Day 85 (±3 days)	Day 113* (±3 days)	Day 141** (±3 days)
Eligibility Assessments									
Informed consent	X	-	-	-	-	-	-	-	-
Inclusion/exclusion criteria	X	X	-	-	-	-	-	-	-
Demographics	X	-	-	-	-	-	-	-	-
Dermatologic and medical history[c]	X	-	-	-	-	-	-	-	-
Prior and concomitant medications/therapies and procedures	X	X	X	X	X	X	X	X	X
History of previous treatment with a biologic drug for psoriasis	-	X	-	-	-	-	-	-	-
C-SSRS	X	X	-	-	-	-	-	-	-
Safety Assessments									
Physical examination (complete)	X	-	-	-	-	-	-	-	-
Physical examination (targeted)	-	X	X	X	X	X	X	X	X
Height and weight[d]	X	-	-	-	-	-	-	-	-
blood pressure (systolic and diastolic), heart rate, respiratory rate, body temperature, and body weight	X	X	X	X	X	X	X	X	X
12-lead ECGs[e]	X	X	-	-	X	X	X	X	X

Study Procedures		**Screening Period**	**Treatment Period**							**Follow-up Period[b]**
		Screening (Visit 1)	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8[a]**	**Follow-up Visit (Visit 9)**
		Week -4	**Week 0**	**Week 1**	**Week 2**	**Week 4**	**Week 8**	**Week 12**	**Week 16**	**Week 20**
		Days -28 to -1	**Day 1 (Baseline)**	**Day 8 (±1 day)**	**Day 15 (±1 day)**	**Day 29 (±3 days)**	**Day 57 (±3 days)**	**Day 85 (±3 days)**	**Day 113* (±3 days)**	**Day 141** (±3 days)**
Safety Laboratory Tests										
Viral serology[g]		X	-	-	-	-	-	-	-	-
Hematology and Coagulation[h]		X	Xi	X	X	X	X	X	X	X
Blood chemistry[j]		X	Xi	X	X	X	X	X	X	X
Urinalysis		X	X	X	X	X	X	X	X	X
Pregnancy test (serum β-hCG) (WOCBP only)		X[k]	-	-	-	-	-	-	-	-
Pregnancy test (urine β-hCG) (WOCBP only)		-	X[l, m]	-	-	X[m]	X[m]	X[m]	X[m]	X[m]
Serum FSH (postmenopausal women only)		X	-	-	-	-	-	-	-	-
AE Monitoring										
Monitor for AEs and SAEs		X	X	X	X	X	X	X	X	X
Pharmacokinetic Assessments										
PK sample (blood)[n]		-	-	X	-	X	X	-	X	-
Efficacy Assessments										
PASI score		X	X[o]	X	X	X	X	X	X	X
BSA		X	X[o]	X	X	X	X	X	X	X
sPGA		X	X[o]	X	X	X	X	X	X	X
PRO assessments	Itch NRS	-	X	X	X	X	X	X	X	X
	DLQI	-	X	X	X	X	X	X	X	X
CCI										
Other Assessments										

Study Procedures	**Screening Period**	**Treatment Period**							**Follow-up Period[b]**
	Screening (Visit 1)	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8[a]**	**Follow-up Visit (Visit 9)**
	Week -4	**Week 0**	**Week 1**	**Week 2**	**Week 4**	**Week 8**	**Week 12**	**Week 16**	**Week 20**
	Days -28 to -1	**Day 1 (Baseline)**	**Day 8 (±1 day)**	**Day 15 (±1 day)**	**Day 29 (±3 days)**	**Day 57 (±3 days)**	**Day 85 (±3 days)**	**Day 113* (±3 days)**	**Day 141** (±3 days)**
Medical photography (target skin lesion)[p]	-	X	-	X	X	-	-	X	-
Clinical Drug Supplies									
Subject randomization	-	X	-	-	-	-	-	-	-
Dispense study drug	-	X	X	X	X	X	X	-	-
Administration of study drug[q]	-	X	X	X	X	X	X	-	-
Subject to return back unused study treatment for compliance check	-	-	X	X	X	X	X	X	-
Schedule the date/time for the next visit	X	X	X	X	X	X	X	X	-
Discharge the subject from the study site[r]	X	X	X	X	X	X	X	X	X

Abbreviations: β-hCG = β-human chorionic gonadotropin; AE = adverse event; BMI = body mass index; BSA = body surface area; C-SSRS = Columbia-Suicide Severity Rating Scale; DLQI = Dermatology Life Quality Index; ECG = electrocardiogram; FSH = follicle-stimulating hormone; HBV = hepatitis B virus; HCV = hepatitis C virus; PASI=Psoriasis Area and Severity Index; CCI [redacted]; PK=pharmacokinetic; PRO=patient-reported outcome; QTcF = QT interval corrected using Fridericia's formula; SAE = serious adverse event; sPGA = Static Physicians Global Assessment; WOCBP = women of childbearing potential; NRS = numerical rating scale.

* The duration of the Treatment Period is from Day 1 to Day 112 and the end of Treatment Period assessments will be performed on Day 113.

** The duration of the Follow-up Period is from Day 114 to Day 141 and the end of Follow-up Period assessments will be performed on Day 141.

[a] or Early Termination Visit.

[b] Subjects who discontinued or withdrew early from study treatment should return after 4 weeks of last dose of study treatment for follow-up safety assessments.

[c] Must include history of drug, substance, or alcohol abuse/dependence within 1 year prior to Screening as determined by the investigator.

[d] Record height at Screening only.

[e] 12-lead ECG must include QTcF measurement.

[g] All subjects must have the following viral serology tests completed at Screening: anti-HCV antibody, HBV surface antigen, HBV core antibody, HIV-1 antibody, and HIV-2 antibody. If the subject tests positive for anti-HCV antibody, then HCV RNA via polymerase chain reaction should be performed to confirm

or rule out active infection. If the subject has received documented treatment which was curative for HCV and tests negative for HCV ribonucleic acid (RNA) at Screening, the subject may be considered for enrollment.
[h] Includes complete full and differential blood count, platelet count, hemoglobin, hemoglobin A1c (only at Screening), fibrinogen and prothrombin time. See Protocol Section 12.5 for a complete list of tests to be performed.
[i] To be obtained predose (subjects are required to fast for at least 10 hours prior to the collection of specimens for safety laboratory tests).
[j] See Protocol Section 12.5 for a list of tests to be performed.
[k] All WOCBP must have a negative serum pregnancy test at Screening to be eligible for the study.
[l] All WOCBP must have a negative urine pregnancy test prior to randomization and dosing on Day 1.
[m] A serum pregnancy test should be performed for confirmation of any positive urine pregnancy test. The subject will be withdrawn from the study treatment if the confirmatory serum pregnancy test is positive. The subject must not receive any further doses of the study drug and will be asked to return for the follow-up visit 4 weeks after the last dose of study drug.
[n] The PK and CCI blood samples will be collected predose at all scheduled visits as per Schedule of Assessments.
[o] To be performed prior to randomization.
[p] Medical photography of the target skin lesion will be obtained at selected sites in a selected number of subjects for documentation and publication purposes only.
[q] Subjects will take the first dose of the study drug upon returning to their home after all Day 1 (Visit 2) assessments are completed.
[r] Subjects will be discharged from the study site after all the postdose study procedures are completed.

5. Endpoints

5.1. Primary Efficacy Endpoint

The primary efficacy endpoint is the proportion of subjects achieving ≥ 75% reduction from baseline in the PASI score (PASI-75) at Week 16.

5.2. Secondary Efficacy Endpoints

- The percent change from baseline in PASI score at all visits from Week 1 to Week 16
- The proportion of subjects achieving PASI-50, PASI-75, PASI-90, PASI-100 at all visits from Week 1 to Week 16
- Time to PASI-50 and PASI-75
- The proportion of subjects achieving a Static Physicians Global Assessment (sPGA) score of “0” (“clear”) or “1” (“almost clear”) combined with 2-point reduction on the 5-point sPGA scale at all visits from Week 1 to Week 16
- The change from baseline in affected body surface area (BSA) at all visits from Week 1 to Week 16
- The change from baseline in the itch numerical rating scale (NRS) at all visits from Week 1 to Week 16
- The change from baseline in the Dermatology Life Quality Index (DLQI) score at all visits from Week 1 to Week 16
- Percentage of subjects with at least a 5-point reduction from baseline in the DLQI score at all visits from Week 1 to Week 16

5.3. Exploratory Endpoints

CCI

5.4. Pharmacokinetic Endpoints

The PK endpoint is the trough plasma concentration (C_{trough}) of ME3183 and its metabolite (CCI).

CCI

5.6. Safety Endpoints

The safety endpoints are as follows:

- The incidence, severity, and seriousness of AEs reported over the 16-week Treatment Period and the 4-week Follow-up Period
- Changes from baseline in CS physical examination findings and vital sign measurements (blood pressure, heart rate, respiratory rate, body temperature, and body weight) over the 16-week Treatment Period and the 4-week Follow-up Period
- Changes from baseline in ECG findings over the 16-week Treatment Period and the 4-week Follow-up Period
- Changes from baseline in safety laboratory values (hematology, coagulation, blood chemistry, and urinalysis) over the 16-week Treatment Period and the 4-week Follow-up Period

6. Analysis Sets

6.1. Screened Set

All subjects who have signed ICFs will be included in the screened set.

6.2. Randomized Set

All subjects who have signed ICFs and have received a randomization number within the IWRS will be included in the randomized set.

6.3. Safety Analysis Set

All randomized subjects who received at least 1 dose of study drug will be included in the safety analysis set. Analyses in the safety analysis set will be based on the study treatment actually received by each subject.

In the event of drug mis-dispensation, the following guidelines will be followed:

- For subjects randomized to the placebo group but received any active study drug, they will be included in the active treatment group corresponding to the largest number of kits dispensed.
- For subjects randomized to any one of the four active treatment groups, they will be included in the active treatment corresponding to the largest number of kits dispensed.

The Safety Analysis Set will be used for all analyses of safety endpoints.

6.4. Full Analysis Set

All subjects who have been randomized, received at least 1 dose of study drug, and have at least 1 evaluable post-baseline time point for primary endpoint will be included in the full analysis set (FAS). Analyses in the FAS will be based on the subject's randomized treatment group.

The FAS will be used for all analyses of efficacy endpoints.

6.5. Per Protocol Set

The per protocol set (PPS) is a subset of the FAS; the PPS will exclude subjects with protocol deviations that may significantly impact the assessment of the primary objective of the study. Analyses in the PPS will be based on the study treatment actually received by each subject. All decisions to exclude subjects from the PPS will be made prior to the unblinding of the study.

6.6. Pharmacokinetic Set

The PK analysis set will consist of all subjects who were correctly administered at least 1 ME3183 dose and where ME3183 or CCI concentration data is available without any protocol deviation interfering with these results. Analyses in the PK analysis set will be based on the study treatment actually received by each subject. In the event of drug mis-dispensation when a subject has received more than one active study drug, the subject will be excluded from the PK analysis set.

PK concentrations are listed for all subjects in PK analysis set.

CCI

[redacted]

6.8. Protocol Deviations

All subject data will be reviewed for the occurrence of protocol deviations. Identified protocol deviations will be recorded into the Clinical Trial Management System (CTMS) by the Site Monitor. The detail on the types of Protocol deviation criteria is made in the BDRM Preparation Plan. Final decisions of subjects to be included in the PPS will be made at the BDRM. All deviations will be categorized as major or minor. Significant protocol deviations are defined as those with major severity.

Deviation type will be recorded as one of the following categories:

- Concomitant Medication / Administration of prohibited medication
- Inclusion or Exclusion Criteria
- Informed Consent / ICF not signed or signed late
- Informed Consent / Other
- Investigational Product / Incorrect IP kit given to subject
- Investigational Product / IP
- Investigational Product / IP Storage
- Investigational Product / Other
- Met Withdrawal Criteria but was not Withdrawn
- Randomization / Mis-stratification
- Randomization / Multiple Randomizations
- Randomization / Other
- Randomization / Randomized not Treated
- Randomization / Treated and not Randomized
- SAE not reported or reported late
- Study Procedure / Missed procedure

- Study Procedure / Other
- Study Procedure / Site Staff Authorization, Delegation, Training
- Study Procedure / Subject compliance
- Study Procedure / Unmasking (not per protocol)
- Study Procedure / Visit Missing
- Visit Window

7. Estimands

7.1. Estimand for Primary Efficacy Endpoint

The main estimand for the primary efficacy endpoint 'proportion of subjects achieving ≥ 75% reduction from baseline in the PASI score (PASI-75) at Week 16' is defined as follows:

- Population: Subjects with moderate to severe plaque psoriasis defined by the study inclusion/exclusion criteria in Section 4.2. The analysis population for the primary efficacy endpoint will be full analysis set as defined in Section 6.2 and per protocol set as defined in Section 6.3.
- Variable: Binary variable indicating whether the subject has achieved ≥ 75% reduction from baseline in the PASI score (PASI-75) at Week 16.
- Population-level summary: Numbers and proportions of subjects achieving ≥ 75% reduction from baseline in the PASI score (PASI-75) at Week 16, and differences in these proportions between each ME3183 treatment group and placebo group.
- Intercurrent events:
    - Withdrawals or early terminations will be handled using hypothetical strategy, where Last Observation Carried Forward (LOCF) and Non-responder Imputation (NRI) will be applied as sensitivity analyses in addition to complete-case analysis.
    - All other intercurrent events will be handled using treatment policy strategy.

7.2. Estimands for Secondary Efficacy Endpoints

The estimands for secondary efficacy endpoints are defined as below:

- Population: Subjects with moderate to severe plaque psoriasis defined by the study inclusion/exclusion criteria in Section 4.2. The analysis population for the secondary efficacy endpoints will be full analysis set as defined in Section 6.2.
- Variables:
    - Continuous variables measuring the percent changes from baseline in PASI score at all visits from Week 1 to Week 16
    - Binary variables indicating whether the subject has achieved ≥ 50%, 75%, 90% and 100% reduction from baseline in the PASI score at all visits from Week 1 to Week 16
    - Time to event variable measuring the time from baseline to the time achieving ≥ 50% and 75% reduction in PASI score in days respectively, censored by the date of last PASI assessment date for subjects who never achieves ≥ 50% or 75% reduction
    - Binary variables indicating whether the subject has achieved a sPGA score of "0" ("clear") or "1" ("almost clear") combined with a 2-point reduction on the 5-point sPGA scale at all visits from Week 1 and Week 16
    - Continuous variables measuring the changes from baseline in BSA at all visits from Week 1 to Week 16
    - Continuous variables measuring the changes from baseline in NRS at all visits from Week 1 to Week 16
    - Continuous variables measuring the changes from baseline in DLQI score at all visits from Week 1 to Week 16

  - Binary variables indicating whether a subject achieves at least a 5-point reduction from baseline in the DLQI score at all visits from Week 1 to Week 16
- Population-level summary:
  - Binary variables will be summarized using numbers and proportions of subjects achieving that outcome of interest, then differences in the proportions between each ME3183 treatment group and placebo group will be calculated.
  - Continuous variables will be summarized using descriptive statistics by treatment group and overall. Mixed-effect model for repeated measures will be used to estimate the least-square (LS) mean differences between each ME3183 treatment group and placebo group.
  - Time to event variables will be summarized using medians and 95% CIs, Kaplan-Meier estimates, and hazard ratios estimated Cox proportional hazard models.
- Intercurrent events:
  - Withdrawals or early terminations will be handled via while-on-treatment policy, where no missing data will be imputed, except for analyses listed below where intercurrent events will be handled via hypothetical strategy and missing data will be imputed using LOCF and NRI methods in addition to complete case analysis: percent change from baseline for PASI scores at all visits from Week 1 to Week 16, the numbers and percentages of subjects achieving ≥ 50%, 75%, 90% and 100% reduction from baseline in the PASI score at all visits from Week 1 to Week 16, the numbers and percentages of subjects achieving an sPGA score of “0” (“clear”) or “1” (“almost clear”) and a 2-point reduction from baseline.

7.3. Estimands for Secondary Safety Endpoints

The estimands for the secondary safety endpoints are defined as below:

- Population: Subjects with moderate to severe plaque psoriasis defined by the study inclusion/exclusion criteria in Section 4.2. The analysis population for the secondary safety endpoints will be the safety analysis set as defined in Section 6.1.
- Variables:
  - Binary variables indicating whether a subject experiences any AEs over the 16-week treatment period and the 4-week follow-up period, along with information regarding severity and seriousness
  - Continuous variables measuring the change from baseline in CS physical examination findings and vital sign measurements (blood pressure, heart rate, respiratory rate, body temperature, and body weight) over the 16-week treatment period and the 4-week follow-up period
  - Continuous variables measuring the change from baseline in ECG findings over the 16-week treatment period and the 4-week follow-up period
  - Binary variable indicating whether the subject has any abnormal ECG findings at all visits over the 16-week treatment period and the 4-week follow-up period
  - Continuous variables measuring the change from baseline in safety laboratory values (hematology, coagulation, blood chemistry and urinalysis) over the 16-week treatment period and the 4-week follow-up period
  - Binary variables indicating whether subject has any abnormal safety laboratory findings (hematology, coagulation, blood chemistry and urinalysis) over the 16-week treatment period and the 4-week follow-up period

- Population-level summary:
    - Binary variables will be summarized using numbers and proportions of subjects achieving that outcome of interest.
    - Continuous variables will be summarized using descriptive statistics.
- Intercurrent events:
    - Withdrawals or early terminations will be handled via while-on-treatment policy, where no missing data will be imputed.

8. General Aspects for Statistical Analysis

8.1. General Methods

- Unless otherwise specified, summaries will be presented for each treatment group and overall.
- Continuous variables will be summarized using the number of subjects (N), mean, standard deviation (SD), median, minimum, and maximum. Categorical variables will be tabulated with the number and percentage of subjects for each category.
- All relevant subject data will be included in listings. All subject data will be included in listings. The listings will be generally sorted by treatment and subject identification (ID), unless otherwise specified.

8.2. Key Definitions

- Age will be collected in the eCRF and the derivation is defined as follows:

  Age = year of informed consent – year of birth

- BMI will be calculated using weight at baseline and height at screening using the formula below:

  BMI (kg/m^2) = weight (kg) / [height (m)]^2

- Baseline

  Baseline is defined as the last non-missing assessment before the date/time of first dose of any study drug and includes assessments taken on Day 1, unless otherwise specified.

  For PK analysis, the baseline values are those collected predose at all scheduled visits per Schedule of Assessments in Table 1.

- Change from baseline

  The change from baseline will be calculated for each post-baseline assessment as:

  Change from baseline = Post-baseline value – baseline value

- Percent change from baseline

  The percent change from baseline will be calculated for each post-baseline assessments as:

  Percent change from baseline =

  (Post-baseline value – baseline value) * 100 / baseline value

8.3. Missing Data

For the purposes of assessing treatment emergence for AEs or classifying medications into prior/concomitant, the following algorithms will be used for partially missing dates. However, the assessment times (start date, stop date) without imputation will be presented in the listings.

For start dates of events:

- Only the year is reported:
    - If the participant did not receive any study drug (i.e., study intervention start date is missing), then start date will be set to 'January 1'
    - If the participant received the study drug (i.e., study intervention start date is not missing):
        - If the year of the start date is identical to that of the study intervention start date and the stop date contains a full date and earlier than the study intervention start date, then start date will be set to 'January 1', otherwise the start date will be set to the study intervention start date.
        - If the year of the start date is not identical to that of the study intervention start date, then the start date will be set to 'January 1'.
- Only the month and year are reported:
    - If the participant did not receive any study drug, then the start date will be set to the 1st day of the month.
    - If the participant received any study drug:
        - If the month and year are identical to the month and year of the study intervention start date, and the stop date contains a full date earlier than the study intervention start date, then the start date is set to the 1st day of the month, otherwise set start date to the study intervention start date.
        - If the month and year are not identical to the month and year of the study intervention start date, the start date will be set to the 1st day of the month.

For stop dates of events:

- Only the year is reported: if the last visit is in the reported year, the date of last visit will be used as the stop date; otherwise, '31 December' will be used as the stop date.
- Only the month and year are reported: if the last visit is in the reported month and year, the date of last visit will be used as the stop date; otherwise, the last day of the reported month and year will be used as the stop date.

If an AE has the start date completely missing, this AE will be considered as treatment-emergent, unless the stop date is before first dose of randomized study drug.

If a medication has the stop date completely missing, this medication will be considered as ongoing and concomitant.

There is no imputation for missing values in the safety analysis. The imputation of efficacy data is described in Section 10.

8.4. Visit Windows

The visits recorded in database will be used for all analyses. There is no plan to re-assign visits based on actual visit dates.

8.5. Pooling of Centers

This study will be conducted at approximately 28 sites. All data will be combined for summaries and analyses.

8.6. Subgroups

Selected analysis will be carried out further stratified by prior receipt of any biologics for psoriasis (bio-naïve vs non-bio-naïve, where bio-naïve is defined as not receiving any biologics for psoriasis previously and non-bio-naïve is defined otherwise), including primary efficacy analysis and selective secondary efficacy analysis for PASI scores (actual values, percent change from baseline at post-baseline visits, proportions of subjects achieving PASI-50, PASI-75, PASI-90 and PASI-100 at post-baseline visits).

9. Demographic, Other Baseline Characteristics and Medication

9.1. Subject Disposition and Withdrawals

This section describes subject disposition for both subject study status and the subject analysis populations.

The number of subjects screened, the number and percentage of subjects randomized and not randomized among all subjects screened, and the reasons for not being enrolled will be summarized. The above percentages will be calculated using the number of subjects screened as the denominator.

The number of subjects randomized and the number and percentage of subjects included in the safety analysis population, FAS, PPS, PK analysis set and CCI will be summarized by treatment group and overall. Subjects withdrawing early and primary reason for withdrawal will be summarized. The above percentages will be calculated using the number of subjects enrolled as the denominator. The completion status and the reason for discontinuation will be listed.

A frequency table will be provided to summarize the number and percentages of randomized subjects excluded from the Safety Analysis Set, FAS, PPS, PK Set and CCI. Additionally, reasons for exclusion will be summarized for each analysis set, where numbers and percentages for each CCI category will be displayed. All percentages are based on the number of subjects randomized within each treatment group and overall. Listings of subjects excluded from the analysis populations, with the reasons for exclusions, will be provided.

9.2. Protocol Deviation

Major protocol deviations, as determined in the Blind Data Review Meeting (BDRM) prior to database lock, may result in the removal of a subject from the PPS.

The number and percentage of subjects with at least one major protocol deviation by type of deviation category will be presented by treatment group and overall. In addition, all protocol deviations (including both major and minor deviations) will be provided in a by-subject listing.

9.3. Demographic and Baseline Characteristics

Demographics and baseline characteristics will be summarized descriptively by treatment group and overall using Safety Analysis Set, FAS and PPS. The comparability of the treatment groups for each relevant characteristic will be assessed descriptively in table format; no statistical hypothesis tests will be performed on these characteristics.

For summaries (number and percentage) of categorical variables in demographics and baseline disease characteristics, a “missing” or “not applicable” level may be added (in addition to the levels specified below) to account for missing or not applicable data as appropriate.

9.3.1. Demographics and Baseline Characteristics

Summary statistics will be provided by treatment group and overall for the following variables:

- Age (years)
- Sex (Male, Female)
- Child bearing potential for female subjects only (No, Yes)

- Race (White, Black or African American, Asian, Native Hawaiian or Pacific Islander, American Indian or Alaska Native)
- Ethnicity (Hispanic or Latino, Not Hispanic or Latino)
- Height (cm) at screening. Conversion to cm: Height (in inch) * 2.64
- Weight (kg) at baseline. Conversion to kg: Weight (in lbs.) * 0.4536
- BMI (kg/m^2)
- Previously Treated with Any Biologics for Psoriasis (Yes, No)
- Allergy or Toxicity of Previous Treatment (Yes, No)
- History of Substance Abuse (Yes, No)
- Smoking
    - Yes (Light, Moderate, Heavy, Other)
    - No (Past Smoker, Never Smoker)
- Alcohol Intake
    - Yes (Beer, Wine, Spirits, Other)
    - No

9.3.2. Baseline Clinical Characteristics

Baseline clinical characteristics will be summarized descriptively by treatment group and overall and will include the following:

- Age at initial diagnosis of psoriasis (years)
- Duration of plaque psoriasis (from date of initial diagnosis to the date of informed consent; year, presented with one decimal of accuracy)
- Type of psoriasis at initial diagnosis (Plaque, Guttate, Pustular, Inverse, Erythrodermic, Nail psoriasis, Psoriatic arthritis, Not known)
- Severity of psoriasis at initial diagnosis (Mild, Moderate, Severe, Unknown)
- Prior treatment for psoriasis (Yes, No)
- Any associated types of psoriasis other than plaque at screening (Yes, No)
- Other associated types of psoriasis at screening (Guttate, Pustular, Inverse, Erythrodermic, Nail psoriasis)

9.4. Medical History

Medical history terms will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) dictionary Version 24.1 or later. A frequency table (with number and percentage) of medical history will be presented by treatment group and overall in terms of system organ class (SOC) and preferred term (PT) for the Safety Analysis Set.

9.5. Prior and Concomitant Medications and Procedures

Medications will be coded using the World Health Organization (WHO) Drug Dictionary Version September 2021 or later, and subject incidence will be tabulated by Anatomic Therapeutic Class (ATC) Level 2 and preferred term (PT) for the Safety Analysis Set. The systemic medication of psoriasis will be summarized and listed separately.

Prior procedures will be collected with medical history, coded using MedDRA Version 24.1 or later and summarized by SOC and PT for the Safety Analysis Set.

See Section 8.3 for handling of partial dates for medications/procedures, in the case where it is not possible to define a medication/procedures as prior, concomitant, or post treatment.

- Prior medications/procedures are the medications/procedures which started and stopped prior to the first dose of study drug.
- Concomitant medications/procedures are medications/procedures which started prior to, on or after the first dose of study drug and before or on the date of last dose of study drug.
- Post medications/procedures are medications/procedures which started after the last dose of study drug.

9.6. Prior Treatment for Psoriasis

Prior systemic treatment for psoriasis is collected from the eCRF page “Prior Systemic Treatment for Psoriasis”. The medications will be coded using WHO Drug Dictionary version September 2021 or later and summarized by ATC and PT for the Safety Analysis Set.

9.7. Extent of Exposure

Treatment duration will be summarized by treatment and overall using the Safety Analysis Set.

Subject data listings of study drug dispensation records will be provided.

Treatment duration (in days) is calculated as the date of the last dose of study drug – the date of the first dose of study drug + 1.

The specific definitions of the first dose and last dose dates of study drug are given below:

- First dose date: The date of the first dose of study drug that is dispensed at Week 0/Visit 2 obtained from the study drug exposure eCRF page.

- Last dose date: The date of the last dose of study drug obtained from the end of treatment eCRF page for subjects who have completed the treatment or discontinued early.

Summary statistics for treatment duration (in days), as well as a frequency summary of treatment duration categories (<7 days, 7 - <14 days, 14 - <28 days, 28 - <56 days, 56 - <84 days, 84 – ≤112 days, > 112 days), will be provided.

9.8. Treatment Compliance

As part of the routine recording of the amount of study drug taken by each subject, the numbers of capsules dispensed and returned, as well as the number of planned and actual capsules taken will be recorded at each visit during treatment period, starting at Visit 2.

The overall study drug compliance is collected from eCRF page “Study Drug Accountability”. The derivation is defined as below:

- Overall compliance (percent): calculated as actual number of actual capsules taken / planned number of actual capsules taken x 100%

Treatment compliance will not be calculated for subjects (if existent) who have only the tablet dispensed record at Week 0/Visit 2 and no other drug accountability records. A frequency summary of compliance

will also be presented with the following categories: < 70%, 70% - ≤ 85%, 85% - ≤100%, and >100% by treatment group and overall.

10. Efficacy

Unless otherwise specified, all efficacy analyses will be performed using the FAS. The analysis of the primary efficacy endpoint and selective analysis for the secondary endpoints will also be performed using the PPS.

10.1. Primary Efficacy Endpoint and Analysis

The primary efficacy endpoint is the proportion of subjects achieving ≥ 75% reduction from baseline in the PASI score at Week 16. Baseline is defined as the PASI score on Day 1 pre-dose.

For each ME3183 treatment group, the difference in the proportion of subjects achieving the difference in PASI-75 (ME3183 – placebo) and its 95% confidence interval (CI) will be estimated and tested for superior treatment effect using the Cochran-Mantel-Haenszel (CMH) test with prior receipt of any biologics for psoriasis (bio-naïve vs non-bio-naïve) as adjustment factor at a 1-sided significance level of $\alpha = 0.025$.

Analysis will be conducted using observed data at Week 16 only (complete-case analysis). In the presence of missing data, additional sensitivity analysis will be conducted using both LOCF and NRI. Under LOCF, the last non-missing PASI score will be carried forward to Week 16, based on which the subject will be considered as responder or non-responder and summarized accordingly. Under NRI, subjects with missing PASI scores at Week 16 will be considered non-responders.

Subgroup analysis will be carried out stratified by the prior receipt of any biologics for psoriasis (bio-naïve vs non-bio-naïve), where Fisher's exact test will be used instead of CMH for superiority.

10.2. Secondary Efficacy Endpoints and Analyses

The binary variables for secondary endpoints include the following:

- The proportion of subjects achieving PASI-50, PASI-75, PASI-90, PASI-100 at all visits from Week 1 to Week 16
- The proportion of subjects achieving an sPGA score of "0" ("clear") or "1" ("almost clear") combined with 2-point reduction on the 5-point sPGA scale at all visits from Week 1 to Week 16
- The proportion of subjects with at least a 5-point reduction from baseline in the DLQI score at all visits from Week 1 to Week 16

The binary secondary endpoints will be analyzed using similar methods as described in Section 10.1. Analysis of PASI-related secondary endpoints will be based on both FAS and PPS using complete case analysis, LOCF and NRI. In addition, analysis will be performed stratified by receipt of any biologics for psoriasis based on FAS. Analysis of the secondary endpoint of achieving an sPGA score of "0" ("clear") or "1" ("almost clear") combined with a 2-point reduction on the 5-point sPGA scale will be based on both FAS and PPS using complete analysis, LOCF and NRI. Analysis of the secondary endpoint of at least 5-point reduction from baseline in the DLQI score will be based on both FAS and PPS using complete case analysis only.

The continuous variables for secondary endpoints include the following:

- The percent change from baseline in PASI score at all visits from Week 1 to Week 16
- The change from baseline in affected BSA at all visits from Week 1 to Week 16
- The change from baseline in the itch NRS at all visits from Week 1 to Week 16
- The change from baseline in the DLQI score at all visits from Week 1 to Week 16

Descriptive statistics for the continuous secondary endpoints described above will be provided at each schedule visit by treatment group. Additionally, the secondary continuous efficacy endpoints (including percent changes for PASI, changes for DLQI, BSA and NRS) will be analyzed using a mixed-effect model for repeated measures (MMRM) with the change or percent change from baseline as the response variable, treatment group, visit, treatment-by-visit interaction as fixed effects, and the baseline value as a covariate. An unstructured covariance matrix will be used to model the correlation among repeated measurements. The Kenward-Roger adjustment will be used with restricted maximum likelihood (REML) to make proper statistical inference. The LS mean differences between ME3183 treatment groups and placebo at each scheduled visits along with the 2-sided 95% CIs and 2-sided p-values will be estimated from the MMRM model. In the event that MMRM with unstructured covariance matrix fails to converge, alternative covariance structures will be explored, including Toeplitz, heterogeneous Toeplitz, variance components, compound symmetry, heterogeneous compound symmetry, autoregressive and heterogeneous autoregressive covariance matrices, where the optimal covariance matrix structure will be selected based on Akaike's Information Criteria (AIC), where smaller values of AIC indicate better overall fit. MMRMs will be estimated for the secondary continuous efficacy endpoints using complete case analysis only.

Kaplan-Meier method will be used for summarizing the time to the first response of PASI-50 and PASI-75 in days. The time to the first response of PASI-50 and PASI-75 is defined as the number of days from the first dose of the study drug to the first response. If a subject does not achieve PASI-50 and PASI-75, the variable will be censored on the last PASI assessment date. Median time to response and 95% CI will be provided, when estimable. The CI will be based on log-log transformation. The reverse Kaplan-Meier plots of PASI-50 and PASI-75 will be presented by treatment group. The comparison of the time to PASI-50 and PASI-75 between each ME3183 treatment group and placebo will be performed using the log-rank test.

The Cox proportional hazard model will be used for analyzing the time to PASI-50 and PASI-75, where time to the first response of PASI-50 or PASI-75 will be used as outcome variables and treatment group will be included as covariates. Estimated hazard ratios along with 95% CIs and p-values between each ME3183 treatment group and placebo will be provided.

For the secondary endpoints of proportions of subjects achieving PASI-50, PASI-75, PASI-90, PASI-100 at all visits from Week 1 to Week 16 and percent change in PASI scores from baseline at all visits from Week 1 to Week 16, any missing PASI scores arising from intercurrent events will be imputed via LOCF and NRI, similar to the methods described in Section 10.1 for the primary efficacy endpoints, in addition to the complete case analysis.

For PASI and DLQI, in addition to the total score, the region specific PASI scores (head, upper limbs, trunk, lower limbs) and the numerical responses for each of the ten questions in DLQI questionnaire will be summarized descriptively at each study visit for the actual values and changes from baseline for all post-baseline visits.

10.3. Exploratory Efficacy Endpoints and Analyses

CCI

[redacted]

11. Pharmacokinetics

The PK analysis set will be used for the PK analysis.

11.1. PK Sampling Schedule

Blood samples for quantitation of ME3183 and its metabolite (CCI) will be collected at the time points indicated in Section 4.6 Table 1 Schedule of Assessment. The actual date and time of each blood sample collection will be recorded in the subject's eCRF and will be reported in the PK listing. The plasma samples will then be sent for bioanalysis using a validated method.

11.2. Plasma PK Endpoint

The C_{trough} in plasma of ME3183 and its metabolite (CCI) will be summarized descriptively by treatment group in the Tables, Figures and Listings (TFLs).

11.3. Presentation of Concentration Data

11.3.1. Handling of Missing Data

Missing concentration data for all subjects who are administered study drug will be considered as non-informative missing and will not be imputed. No concentration estimates will be provided for missing sample values.

For individual plasma concentration vs. time curves, the following rules will apply:

- Concentration values below the limit of quantification (BLQ) of the corresponding analyte (ME3183 or CCI) in samples will be treated as zero, with the exception of calculation of geometric mean and geometric coefficient of variation% (CV%), for which these assessments will be excluded.

11.3.2. Listing and Presentation of Individual PK Data

The following presentations of individual PK concentrations will be produced:

- Listing of PK sampling times including nominal and actual time elapsed from dose with the deviation from the nominal time and measured concentrations of the drug.

Individual C_{trough} concentrations in linear scale for all subjects by treatment combined on one graph and plotted for each day.

11.4. PK Parameters Derivation

No PK parameters derivation is planned for ME3183 and its metabolite (CCI) concentrations.

11.4.1. PK Parameters Summarization

For summarization of PK data for ME3183 and its metabolite (CCI), the following data handling measures will be employed:

- The mean/median value at a time point where 1 or more samples have BLQ values will be reported even if the mean/median value is BLQ.
- Zero mean or median values will be included in summary tables.
- SD will not be displayed if more than 30% of values are missing or BLQ.

- Tables of summary statistics for concentration-time data will be reported as per below table.

The following summary presentations of mean PK concentrations for ME3183 and its metabolite (CCI) will be produced:

- Table of PK concentrations summarized by nominal time for each treatment separately.
- Mean C_{trough} profiles in linear scale for both treatments vs. nominal time.

Variable	Summarized with:
plasma concentration at each time point	n, number and % BLQ, arithmetic mean, SD, coefficient of variance (CV) %, Geometric mean and CV%, minimum, median and maximum

CV% = SD/mean in %.

%BLQ = 100 * (total number of subjects who have BLQ values/total number of exposed subjects within treatment group, with a PK assessment at each time point).

11.5. Planned Statistical Models for PK Parameters and Concentrations

No formal statistical analysis is planned for ME3183 and its metabolite (CCI) concentrations.

11.6. Interim Analyses

No formal interim analysis is planned.

11.7. Deviation from Analyses Planned in Protocol

Not applicable.

CCI

13. Safety

All safety analyses will be performed using the safety analysis set.

13.1. Adverse Events

An AE is any symptom, physical sign, syndrome, or disease that either emerges during the study or, if present at Screening, worsens during the study, regardless of the suspected cause of the event. AEs will be collected from the time the subject signs the ICF through 4 weeks after the last dose of study drug.

AEs will be coded according to the MedDRA Version 24.1 or higher. Unless otherwise specified, AEs will be summarized by SOC and PT by treatment group and overall, with SOCs presented in the standard international order and PTs within SOCs presented in descending order of subject incidence.

Adverse events are summarized by subject incidence rates. In any tabulation, a subject contributes only once to the count for a given SOC or PT. If a subject experiences more than 1 occurrence of the same AE, the occurrence with the greatest severity and the closest association with the study drug will be used in the summary tables.

For the purposes of this study, any AEs classified as 'Unrelated' or 'Unlikely' will be considered as 'Not Related' and 'Possibly', 'Probably', or 'Definitely' as 'Related' to the study treatment. Missing relationship will be considered related to study product.

All AEs will be listed by subject, along with information regarding onset, duration, relationship and severity to study drug, seriousness, action taken with study drug, and outcome.

13.1.1. Treatment-Emergent Adverse Events

A Treatment-Emergent Adverse Event (TEAE) is an AE that occurred during the study after the first dose of study drug or that was present prior to dosing and exacerbates after the first dose of study drug.

If the treatment-emergent status of an AE is unclear due to a missing/incomplete start date, it will be considered treatment-emergent. Date imputation rules for missing AE start dates are described in Section 8.3.

13.1.2. Overall summary of AEs

An overall summary of the following AE categories will be provided for all subjects in the Safety Analysis Set:

- Any AEs
- Any TEAEs
- Any drug-related TEAEs
- Any severe TEAEs
- Any serious TEAEs
- Any serious drug-related TEAEs
- Any TEAEs leading to treatment discontinuations
- Any serious TEAEs leading to treatment discontinuation
- Any TEAEs leading to death
- Any deaths

13.1.3. TEAEs by Maximum Severity/Relationship

All TEAEs will be summarized by maximum severity (mild, moderate, severe, and, if needed, missing). If a subject reports multiple occurrences of a specific event within a specific analysis period, the subject will be counted only once by the maximum severity. If the severity is missing for one or more but not all of the occurrences of the same event, the maximum severity of the remaining occurrences with non-missing severities will be used. If the severity is missing for all of the occurrences, the subject will be counted only once in the "missing" category of severity.

Similarly, all TEAEs will be summarized by maximum relationship to the study drug (unrelated, unlikely, possibly, probably, definitely related, and missing if needed). If a subject reports multiple occurrences of a specific event within a specific analysis period, the subject will be counted only once by the maximum relationship. If the relationship is missing for one or more but not all of the occurrences of the same event, the maximum relationship of the remaining occurrences with non-missing relationships will be used. If the relationship is missing for all of the occurrences, the subject will be counted only once in the "missing" category of relationship to the study drug.

13.1.4. TEAEs by Time of Onset

All TEAEs will be summarized by time of onset (Day 1 – 3, Day 4 – 7, Day 8 – 14, Day 15 – 21, Day 22 – 28, Day 29 – 56, Day 57 – 84, Day 85 – 113, Day 114+), where an overall summary of the numbers and percentages of subjects with any TEAEs within a particular time of onset period will be calculated along with further breakdown by SOC and PT.

13.2. Laboratory Evaluations

Laboratory tests include the following:

- Viral serology (HBV, HCV, and HIV)
- Hematology and coagulation
- Blood chemistry
- Urinalysis (Dipstick)
- Pregnancy tests (WOCBP only; serum or urine β-human chorionic gonadotropin)
- Serum follicle-stimulating hormone (FSH) (postmenopausal women only)

Summary statistics of actual values and changes from baseline will be provided for each laboratory parameters by treatment group at each study visit if the results of the laboratory are continuous. Frequencies tables, including numbers and percentages of subjects with normal and abnormal (low vs high), will be presented for laboratory parameters with categorical results by treatment group at each study visit. Shift tables will also be provided displaying the numbers and percentages of subjects with normal and abnormal results compared with the results at baseline.

Viral serology and pregnancy test results will be summarized in listings only. Subject data listings of all laboratory data will be provided.

13.3. Vital Signs

Vital signs (body temperature, body weight, respiratory rate, heart rate, systolic and diastolic blood pressure measurements) will be evaluated at the visits indicated in the Schedule of Assessments (Table 1). Summary statistics for actual values and changes from baseline in vital signs will be provided for each

vital sign parameter at each scheduled visit by treatment group and overall. A subject data listing of all vital sign data will be provided.

13.4. ECG

A 12-lead, resting ECG will be obtained at the visits indicated in the Schedule of Assessments (Table 1). Summary statistics for actual values and changes from baseline will be provided for each of the ECG parameters at each scheduled visits, including ventricular rate (bpm), PR (msec), QRS (msec), QT (msec), and QTcF (msec) measurements will be obtained. A frequency table with number of percentage of patients with normal, abnormal and clinically significant abnormal ECG results will be provided. The clinically noteworthy QT/QTc interval (>450, >480, or >500 msec) or clinically noteworthy change from baseline (>30 or >60 msec) will also be summarized using frequency tables by treatment group at each scheduled visit.

13.5. Physical Examination

A complete physical examination including height and weight will be performed at Screening (Visit 1). A targeted physical examination to verify continued subject eligibility and to follow-up regarding any change in medical history will be performed at the study visits indicated in Schedule of Assessments (Table 1). Symptom-driven, targeted physical examinations will be performed as clinically indicated at any study visit. Any CS physical examination finding should be reported as an AE. All physical examination data will be summarized in data listings.

14. Changes from Analysis Planned in Protocol

There are no changes from analysis planned in the study protocol.

15. Reference List

None.

16. Programming Considerations

- All TFLs, and statistical analyses will be generated using SAS Version 9.4 (SAS Institute Inc., Cary, NC, USA). Computer-generated TFL outputs will adhere to the following specifications.

16.1. General Considerations

- One SAS program can create several outputs, or a separate SAS program will be created for each output.
- One output file can contain several outputs or each output will be stored in a separate file.
- Output files will be delivered in Word format or portable document format pdf.
- Numbering of TFLs will follow International Council for Harmonisation (ICH) E3 guidance.

16.2. Table, Figure, and Listing Format

16.2.1. General

- All TFLs will be produced in landscape format on <American letter size / A4 paper size>, unless otherwise specified.
- All TFLs will be produced using the Courier New font, size 8 which is the smallest acceptable point size for the Regulatory Authorities.
- The data displays for TFLs will have a minimum blank 1-inch margin on all 4 sides.
- Headers and footers for figures will be in Courier New font, size 8 which is the smallest acceptable point size for the Regulatory Authorities.
- Legends will be used for all figures with more than one variable, group, or item displayed.
- TFLs will be in black and white (no color), unless otherwise specified.
- Specialized text styles, such as bolding, italics, borders, shading, and superscripted and subscripted text, will not be used in the TFLs, unless otherwise specified. On some occasions, superscripts 1, 2, or 3 may be used.
- Only standard keyboard characters will be used in the TFLs. Special characters, such as non-printable control characters, printer-specific, or font-specific characters, will not be used. Hexadecimal-derived characters will be used, where possible, if they are appropriate to help display math symbols (e.g., µ). Certain subscripts and superscripts (e.g., cm2, Cmax) will be employed on a case-by-case basis.
- Mixed case will be used for all titles, footnotes, column headers, and programmer-supplied formats, as appropriate.

16.2.2. Headers

All outputs will have the following header at the top left of each page:

- Meiji Pharma USA Inc.

- Protocol ME3183-3 (PPD Study Number 7028898)
- Draft/Final Run: <ddmmmyyyy>
- All outputs will have Page n of N at the top or bottom right corner of each page. TFLs are internally paginated in relation to the total length (i.e., the page number will appear sequentially as page n of N, where N is the total number of pages in the table).
- The date the output was generated will appear along with the program name as a footer on each page.

16.2.3. Display Titles

- Each TFL will be identified by the designation and a numeral (i.e., Table 14.1.1). A decimal system (x.y and x.y.z) are used to identify TFLs with related contents. The title will be centered. The analysis set will be identified on the line immediately following the title and will be enclosed in parenthesis. The title and table designation will be single spaced. A solid line spanning the margins will separate the display titles from the Column headers. There will be one blank line between the last title and the solid line.

Table x.y.z
First Line of Title
Second Line of Title if Needed
(ITT Analysis Set)

16.2.4. Column Headers

- Column headings will be displayed immediately below the solid line described above in initial upper-case characters.
- In the case of efficacy tables, the variable (or characteristic) column is on the far left followed by the treatment group columns and total column (if applicable). P-values may be presented under the total column or in separate p-value column (if applicable). Within-treatment comparisons may have p-values presented in a row beneath the summary statistics for that treatment.
- For numeric variables, include ‘unit’ in column or row heading when appropriate.
- Analysis set sizes will be presented for each treatment group in the column heading as (N=xx) (or in the row headings, if applicable). This is distinct from the ‘n’ used for the descriptive statistics representing the number of subjects in the analysis set.
- The order of treatments in the tables and listings will be Placebo first in the case of placebo controlled studies and Active comparators first in the case of active comparator trials, followed by a total column (if applicable).

16.2.5. Body of the Data Display

16.2.5.1. General Conventions

Data in columns of a table or listing are formatted as follows:

- Alphanumeric values will be left-justified;
- Whole numbers (e.g., counts) will be right-justified; and
- Numbers containing fractional portions will be decimal aligned.

16.2.5.2. Table Conventions

- Units will be included where available.
- For categorical parameters, all categories will be presented in the table, even if n=0 for all treatment groups in a given category. For example, the frequency distribution for symptom severity would appear as:

Severity Rating	N
severe	0
moderate	8
mild	3

Where percentages are presented in these tables, zero percentages will not be presented and so counts of 0 will be presented as 0 and not as 0 (0%).

- An Unknown or Missing category will be added to each parameter for which information is not available for 1 or more subjects.
- Unless otherwise specified, the estimated mean and median for a set of values will be printed out to 1 more significant digit than the original values, and standard deviations will be printed out to 2 more significant digits than the original values. The minimum and maximum will report the same significant digits as the original values. For example, systolic blood pressure will be presented as follows:

N	XX
Mean	XXX.X
Std Dev	X.XX
Median	XXX.X
Minimum	XXX
Maximum	XXX

- P-values will be output in the format: '0.xxx', where xxx is the value rounded to 3 decimal places. Every p-value less than 0.001 will be presented as <0.001. If the p-value are less than 0.0001, then present as <0.0001. If the p-value is returned as >0.999, then present as >0.999.
- Percentage values will be printed to one decimal place, in parentheses with no spaces, one space after the count (e.g., 7 (12.8%), 13 (5.4%)). Unless otherwise noted, for all percentages, the number of subjects in the analysis set for the treatment group who have an observation will be the denominator. Percentages after zero counts will not be displayed and percentages equating to 100% will be presented as 100%, without decimal places.

- Tabular display of data for medical history, prior/concomitant medications, and all tabular displays of adverse event data will be presented by the body system, treatment class, or SOC with the highest occurrence overall in decreasing order, assuming all terms are coded. Within the body system, drug class and SOC, medical history (by preferred term), drugs (by ATC1 code), and adverse events (by preferred term) will be displayed in decreasing order. If incidence for more than 1 term is identical, they will then be sorted alphabetically. Missing descriptive statistics or p-values which cannot be estimated will be reported as '-'.

- The percentage of subjects will normally be calculated as a proportion of the number of subjects assessed in the relevant treatment group (or overall) for the analysis set presented. However, careful consideration is required in many instances due to the complicated nature of selecting the denominator, usually the appropriate number of subjects exposed. Details will be described in footnotes or programming notes, as necessary.

- For categorical summaries (number and percentage of subjects) where a subject can be included in more than one category, a footnote or programming note will be added describing whether the subject is included in the summary statistics for all relevant categories or just 1 category as well as the selection criteria.

- Where a category with a subheading (such as SOC) has to be split over more than one page, output the subheading followed by '(cont)' at the top of each subsequent page. The overall summary statistics for the subheading should only be output on the first relevant page.

16.2.5.3. Listing Conventions

- Listings will be sorted for presentation in order of treatment groups as above, subject number, visit/collection day, and visit/collection time.

- Missing data will be represented on subject listings as either a hyphen ('-') with a corresponding footnote ('- = unknown or not evaluated'), or as 'N/A', with the footnote 'N/A = not applicable', whichever is appropriate.

- Dates will be printed in SAS DATE9.format ('DD_MMM_YYYY': 01JUL2000). Missing portions of dates will be represented on subject listings as dashes (--JUL2000). Dates that are missing because they are not applicable for the subject will be output as 'N/A', unless otherwise specified.

- All observed time values will be presented using a 24-hour clock HH:MM or HH:MM:SS format (e.g., 11:26:45, or 11:26). Time will only be reported if it was measured as part of the study.

- Units will be included where available.

16.2.5.4. Figure Conventions

- Unless otherwise specified, for all figures, study visits will be displayed on the X-axis and endpoint (e.g., treatment mean change from baseline) values will be displayed on the Y-axis.

16.2.6. Footnotes

- A solid line spanning the margins will separate the body of the data display from the footnotes.

- All footnotes will be left justified with single-line spacing immediately below the solid line underneath the data display.
- Footnotes will always begin with 'Note:' if an informational footnote, or 1, 2, 3, etc. if a reference footnote. Each new footnote will start on a new line, where possible.
- Subject specific footnotes are avoided, where possible.
- Footnotes will be used sparingly and add value to the TFL. If more than six lines of footnotes are planned, then a cover page is strongly recommended to be used to display footnotes, and only those essential to comprehension of the data will be repeated on each page.
- The last line of the footnote section will be a standard source line that indicates the name of the program used to produce the data display, the date the program was run, and the listing source (i.e., 'Program : myprogram.sas Listing source: 16.x.y.z').
- Sources and/or cross-references in footnotes will use the keyword prefix (Listing or Table) for each type of reference and will be separated by a comma when multiple cross-references of the same type are displayed where the prefix will be displayed in plural forms. When multiple types of references are involved, they would be separated by ";".
  Example
  Listing source: Table 14.2.4.1; Listings 16.2.4.1.1, 16.2.4.1.2, 16.2.4.2.1

17. Quality Control

SAS programs are developed to produce output such as analysis data sets, summary tables, data listings, figures or statistical analyses. An overview of the development of programs is detailed in PPD Developing Statistical Programs SOP (3907).

PPD Developing Statistical Programs SOP (3907), Conducting the Transfer of Biostatistical Deliverables SOP (3908) and the SAS Programming and Validation Plan describes the quality control procedures that are performed for all SAS programs and output. Quality control is defined here as the operational techniques and activities undertaken to verify that the SAS programs produce the output by checking for their logic, efficiency and commenting and by review of the produced output.

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16.2.5.2	Study Drug Compliance	(Full Analysis Set)
16.2.6.1	Psoriasis Area and Severity Index (PSAI)	(Full Analysis Set)
16.2.6.2	Static Physician's Global Assessment (sPGA)	(Full Analysis Set)
16.2.6.3	Dermatology Life Quality Index (DLQI)	(Full Analysis Set)
16.2.6.4	Body Surface Area (BSA)	(Full Analysis Set)
16.2.6.5	Numerical Rating Scale (NRS)	(Full Analysis Set)
16.2.7.1	Treatment-Emergent Adverse Events	(Full Analysis Set)
16.2.7.2	Non-Treatment-Emergent Adverse Events	(Full Analysis Set)
16.2.8.1.1	Laboratory Reference Ranges	
16.2.8.1.2	Hematology and Coagulation	(Full Analysis Set)
16.2.8.1.3	Blood Chemistry	(Full Analysis Set)
16.2.8.1.4	Urinalysis (Dipstick)	(Full Analysis Set)
16.2.8.2.1	Vital Signs	(Full Analysis Set)
16.2.8.2.2	Electrocardiogram (ECG)	(Full Analysis Set)
16.2.8.2.3	Physical Examination	(Full Analysis Set)
16.2.8.2.4	Serology at Screening	(Full Analysis Set)
16.2.8.2.5	Serum Pregnancy Test and FSH at Screening	(Full Analysis Set)
16.2.8.2.6	Urine Pregnancy Test	(Full Analysis Set)
16.2.8.2.7	Individual Ctrough Concentrations	(Full Analysis Set)
CCI	[redacted]	

21. Shells

Tables, Figures and Listings mock shells are documented in a separate document.

22. Appendices

None.

Meiji_ME3183-3_SAP_v3.0_11Jul2023_CLEAN

Final Audit Report 2023-07-12

Created:	2023-07-11
By:	PPD
Status:	Signed
Transaction ID:	PPD

"Meiji_ME3183-3_SAP_v3.0_11Jul2023_CLEAN" History

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