Official Title of Study:

An Investigational Study to Evaluate Experimental Medication BMS-986165 Compared to Placebo in Participants With Plaque Psoriasis (POETYK-PSO-3) in Mainland China, Taiwan, and South Korea (POETYK-PSO-3)

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Statistical Analysis Plan

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Title:	A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Phase 3 Study to Evaluate the Efficacy and Safety of BMS-986165 in Subjects with Moderate-to-Severe Plaque Psoriasis
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SAP No.	2.0

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Approvals

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Abbreviations

Glossary of Abbreviations:	
AE	Adverse event
AEI	Adverse event of interest
[redacted]	[redacted]
ATC	Anatomic Therapeutic Classification
BID	Twice daily
BSA	Body surface area
CI	Confidence interval
CK	Creatine kinase
CMH	Cochran-Mantel-Haenszel
CRF	Case Report Form
CSP	Clinical Safety Program
CSR	Clinical Study Report
CTCAE	Controlled Terminology Criteria for Adverse Events
DLQI	Dermatology Life Quality Index
DMC	Data Monitoring Committee
EAIR	Exposure-adjusted incidence rate
ECG	Electrocardiogram
eC-SSRS	Electronic Columbia-Suicide Severity Rating Scale
[redacted]	[redacted]
FAS	Full Analysis Set
[redacted]	[redacted]
IL	Interleukin
IRS	Independent Reporting Statistician
IRT	Interactive Response Technology
ITT	Intention-to-treat
LOCF	Last observation carried forward
LS	Least-squares
[redacted]	[redacted]
MedDRA	Medical Dictionary for Regulatory Activities
mBOCF	Modified baseline observation carried forward

Glossary of Abbreviations:	
MI	Multiple imputation
[redacted]	[redacted]
NRI	Nonresponder imputation
PASE	Psoriatic arthritis screening and evaluation
PASI	Psoriasis Area and Severity Index
[redacted]	[redacted]
PGA-F	Physician Global Assessment-Fingernails
PHQ-8	Eight-Item Patient Health Questionnaire
[redacted]	[redacted]
PP	Per-protocol
[redacted]	[redacted]
pp-PGA	Palmoplantar Physician's Global Assessment
PPS	Per-protocol set
PSSD	Psoriasis Symptoms and Signs Diary
[redacted]	[redacted]
QD	Once daily
QoL	Quality of Life
QTcB	QT interval corrected using Bazett's formula
QTcF	QT interval corrected using Fridericia's formula
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
[redacted]	[redacted]
sPGA	static Physician Global Assessment
ss-PGA	Scalp specific Physician's Global Assessment
TEAE	Treatment-emergent adverse event
TFLs	Tables, figures, and listings
[redacted]	[redacted]

1.0 Purpose

The statistical analysis plan (SAP) describes the statistical methods to be used during the reporting and analyses of data collected under BMS Protocol IM011065.

The SAP outlines the following:

- Study design
- Study objectives
- Endpoints and assessments
- Analysis sets
- Statistical methodology
- Conventions and definitions

The SAP should be read in conjunction with the study protocol and case report form (CRF) according to the version on Page 1 of this document. Any further changes to the protocol or CRF may necessitate updates to the SAP. Changes following approval of the first version of the SAP will be tracked in the SAP Change Log and a final version of the updated SAP will be approved prior to final database lock.

2.0 Study Description

2.1 Study Design

This is a 52-week, multi-center, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of BMS-986165 vs placebo. A total of approximately 219 qualified subjects with moderate-to-severe plaque psoriasis in mainland China, Taiwan and South Korea will be randomized.

Day 1 activities
Following a screening period of up to 4 weeks, qualified subjects who have completed the screening procedures and have met the inclusion/exclusion criteria will be randomized in a blinded manner in a 2:1 ratio, stratified by country (mainland China, non-mainland China) and previous biologic use for psoriasis, psoriatic arthritis or other inflammatory diseases only (yes/no), via interactive response technology (IRT) to one of the following 2 treatment groups:

- BMS-986165 6 mg once daily (QD)
- Placebo

Dummy tablets (placebo to the BMS-986165 6 mg tablet) will be administered to the subjects to maintain blinding in a double-dummy fashion.

Week 16 activities
The coprimary endpoints, static Physician Global Assessment (sPGA) 0/1 and Psoriasis Area and Severity Index (PASI) 75 will be assessed at Week 16. Subjects receiving placebo will be switched in a blinded manner to BMS-986165 6 mg QD at Week 16. Subjects who are randomized to BMS-986165 6 mg QD will continue on their assigned treatment regimen in a blinded manner.

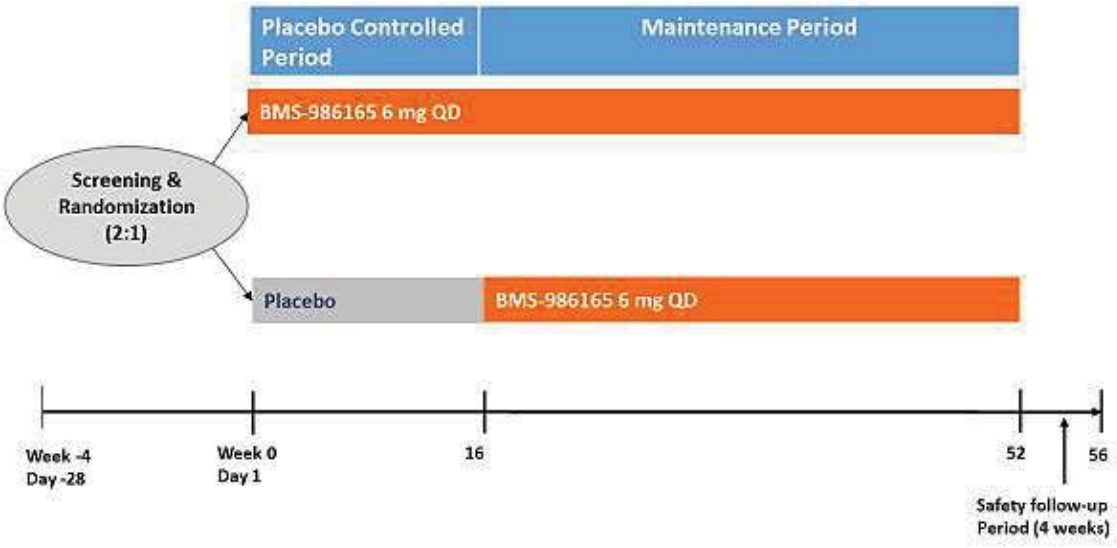
Week 24 activities

During the Week 24 assessment, a subject who has [redacted] may be treated with restricted topicals/shampoos as described in Section 6.7.1 of the protocol. These treatments may only be initiated at Week 24, and not at subsequent time points. A subject who is provided these treatments at Week 24 may use them as needed per the investigator's judgement through Week 52.

Study Design elements

The duration of study participation is approximately 60 weeks and will be divided into the following periods: Screening (up to 4 weeks), Treatment (52 weeks), and Follow-up (4 weeks). A schedule of assessments can be found in the protocol. A study design schematic is provided in Figure 1.

Figure 1: Study Design Schematic



[redacted]

2.3 Treatment Assignment and Randomization

At Week 0 (Day 1), subjects who have met all criteria for enrollment will be centrally randomized by a computer-generated randomization schedule in a 2:1 ratio to the following treatments:

- BMS-986165 6 mg QD
- Placebo

The randomization list was generated by the IRT vendor using a permuted block design within each stratum combination level. Randomization will be stratified by country (mainland China, non-mainland China) and previous biologic use for psoriasis, psoriatic arthritis or other inflammatory diseases only (yes/no).

A treatment group will be assigned by IRT based on the above-described randomization schedule and each subject will be assigned a unique randomization number. In addition, a kit (container) number will be assigned by the IRT to the subject corresponding to the treatment assignment. Dummy tablets (placebo to the BMS-986165 6 mg tablet) will be administered to the subjects to maintain blinding.

At Week 16, subjects receiving placebo treatment will be switched in a blinded manner to BMS-986165 6 mg QD. Subjects who are randomized to BMS-986165 6 mg QD will continue their treatment regimen through Week 52.

2.4 Unblinding Information

The Data Monitoring Committee (DMC) provides oversight of safety consideration throughout the study. A separate unblinded team, comprised of an unblinded Independent Reporting Statistician (IRS) and unblinded programmer(s), will produce output for the DMC using masked treatments. Treatment decodes may only be requested by DMC Chair and will be provided by the IRS. Data summaries and listings will be transmitted via a secure portal by IRS to only the DMC members. Additional details regarding the DMC process and unblinding are provided in the DMC charter.

An unblinded analysis of data through Week 16 will be performed after all subjects complete their Week 16 visit or have discontinued prior to Week 16. A select group of personnel who are not involved in the conduct of the study will review the results to write a clinical study report. Following the Week 16 analysis until the end of the study, the investigators, subjects, and clinical trial team members who directly cooperate with the site staff will continue to remain blinded to the initial treatment assignment. Details of maintaining the blind following the unblinded analysis will be finalized prior to the Week 16 database lock. A final analysis will be performed after all subjects complete the Week 52 visit or discontinue prior to the Week 52 visit, and a clinical study report will be written.

[redacted]

2.5 Changes in Statistical Considerations from the Protocol

The following is a list of the important changes in the SAP from the Statistical Considerations section in the protocol:

- Endpoints are revised and 2-point improvement from baseline criterion is added to endpoints Static Physician's Global Assessment (sPGA), Scalp specific Physician's Global Assessment (ss-PGA), Physician's Global Assessment-Fingernails (PGA-F) and Palmoplantar Physician's Global Assessment (pp-PGA)
- The hierarchical testing order for the key secondary endpoints has been updated. The hierarchy presented here supersedes the one that is in the protocol.
- The two endpoints were removed from the list of key secondary endpoints: Change from baseline in Psoriasis Symptom and Sign Diary (PSSD) symptom score and Palmoplantar Physician's Global Assessment (pp-PGA) 0/1 assessed as a proportion of subjects with a pp-PGA score of 0 or 1 among subjects with a baseline pp-PGA score ≥3.
- Imputation methods were updated to remove the prohibited medication/therapy criteria for binary and continuous endpoints.
- The list of relevant protocol deviations provided in the protocol was updated for determination of the Per Protocol population.
- Logistic regression analyses for binary endpoints were removed as these are similar to the CMH analyses.
- [redacted]
- [redacted]
- [redacted]

3.0 Objectives

3.1 Primary Objective

- Assess whether BMS-986165 is superior to placebo at Week 16 in the treatment of subjects with moderate-to-severe plaque psoriasis

3.2 Secondary [redacted] Objectives

- Assess whether BMS-986165 is superior to placebo over the first 16 weeks of treatment
- Assess whether BMS-986165 is superior to placebo in scalp psoriasis through week 16 in those subjects who have baseline scalp severity Physician's Global Assessment (ss-PGA) score ≥3

- Assess whether BMS-986165 is superior to placebo in nail psoriasis through week 16 in those subjects who have baseline Physician's Global Assessment of Fingernail Psoriasis (PGA-F) score ≥3
- Assess whether BMS-986165 is superior to placebo in palmoplantar psoriasis through week 16 in those subjects who have baseline palmoplantar Physician's Global Assessment (pp-PGA) score ≥3
- Evaluate improvement in patient-reported outcomes for BMS-986165 compared with placebo through Week 16
- [redacted]

4.0 Outcomes

The description of assessments for efficacy and safety can be found in Section 8 of the protocol. The calculation of key measures are provided in Section 8.2 of the SAP.

4.1 Efficacy

4.1.1 Primary Endpoint(s)

The coprimary endpoints for BMS-986165 compared to placebo at Week 16 are defined as:

- sPGA 0/1 response assessed as a proportion of subjects with an sPGA score of 0 or 1 with at least 2-point improvement from baseline
- PASI 75 response assessed as a proportion of subjects who achieve a 75% improvement from baseline in the PASI score

4.1.2 Secondary Endpoint(s)

4.1.2.1 Key Secondary Endpoints for Comparisons to Placebo

The key secondary efficacy endpoints for BMS-986165 compared to placebo at Week 16 are defined as:

- PASI 90 response assessed as a proportion of subjects who achieve a 90% improvement from baseline in PASI score
- sPGA 0 response assessed as a proportion of subjects with an sPGA score of 0
- Scalp specific Physician's Global Assessment (ss-PGA) 0/1 assessed as a proportion of subjects with a ss-PGA score of 0 or 1 with at least a 2-point improvement from baseline among subjects with a baseline ss-PGA score ≥3
- PSSD symptom score of 0 assessed as a proportion of subjects with a PSSD symptom score of 0 among subjects with a baseline PSSD symptom score ≥1
- PASI 100 response assessed as a proportion of subjects who achieve a 100% improvement from baseline in PASI score
- Dermatology Life Quality Index (DLQI) 0/1 assessed as a proportion of subjects with a DLQI score of 0 or 1 among subjects with a baseline DLQI score ≥2

- Physician Global Assessment-Fingernails (PGA-F) 0/1 assessed as a proportion of subjects with a PGA-F score of 0 or 1 with at least a 2-point improvement from baseline among subjects with a baseline PGA-F score ≥3

[redacted]

[redacted]

4.2 Safety

The safety outcomes include the following:

- Adverse events (AEs)
    - Treatment-emergent adverse events (TEAEs) – defined as:
        - AEs which occur after the first dose of study treatment through 30 days after the final dose of the study treatment;
    - Treatment-emergent adverse events of interest (AEIs) for the following events:
        - Skin-related AEs
        - Infection AEs, including influenza
        - Creatine kinase (CK) elevation (evaluated as lab toxicity grade 2 or higher)
        - Malignancy
    - SAEs
    - Deaths
- Clinical laboratory parameters

- Absolute and change from baseline values
- Laboratory abnormalities (as determined by Controlled Terminology Criteria for Adverse Events [CTCAE v5.0] grading) presented as the worst postbaseline toxicity group
- Shifts from baseline to maximum postbaseline value
- Potential drug induced liver injury (DILI) is defined as a subject who meets the following criteria:
  - 1) ALT or AST elevation >3 times ULN

  AND
  - 2) Total bilirubin >2 times ULN, without initial findings of cholestasis (elevated serum alkaline phosphatase)

  AND
  - 3) No other immediately apparent possible causes of liver function test elevation and hyperbilirubinemia, including, but not limited to, viral hepatitis, preexisting chronic or acute liver disease, or the administration of other drug(s) known to be hepatotoxic.
- ALT or AST elevation >5 times ULN

- Vital signs
  - Absolute and change from baseline values
  - Marked abnormalities defined by the below categories:
    - Heart rate:
      - Value > 100 and change from baseline > 30
      - Value < 55 and change from baseline < -15
    - Systolic blood pressure:
      - Value > 140 and change from baseline > 20
      - Value < 90 and change from baseline < -20
    - Diastolic blood pressure:
      - Value > 90 and change from baseline > 10
      - Value < 55 and change from baseline < -10
- Electrocardiograms (ECGs)
  - Absolute and change from baseline values
  - Marked abnormalities defined by the below categories:
    - QT interval corrected using Fridericia's formula (QTcF):

- 450 -< 480 msec
- 480 -< 500 msec
- ≥ 500 msec
- 30 < change from baseline ≤ 60 msec
- Change from baseline > 60 msec
- Males: < 450 msec, ≥ 450 msec
- Females: < 470 msec, ≥ 470 msec

- PR interval ≥ 200 msec
- QRS interval ≥ 120 msec

In cases where the QT interval corrected using Bazett's (QTcB) formula is captured instead of QTcF, then the uncorrected QT will be converted to QTcF for analyses.

- Eight-Item Patient Health Questionnaire (PHQ-8) total score
  - Absolute and change from baseline values
  - Shifts from baseline scores
- Electronic Columbia-Suicide Severity Rating Scale (eC-SSRS)
  - Suicidal ideation and suicidal behavior responses by visit
  - Shifts from baseline to postbaseline value for suicidal ideation and suicidal behavior
  - Worst postbaseline value for suicidal ideation and behavior

[redacted]

5.0 Populations for Analyses

The following analysis sets will be used in the summary and analysis of study data:

- **Enrolled population**: All subjects who sign informed consent.
- **Full Analysis Set (FAS)**: All subjects who were randomized to receive assigned treatment. Following the intent-to-treat (ITT) principle, subjects will be analyzed according

to the treatment group assigned at randomization. The FAS will be the primary efficacy analysis population.

- **Per Protocol Set (PPS)**: A subset of the FAS who are compliant with study treatment and who do not have any relevant protocol deviations that may impact the coprimary efficacy endpoint assessments. The PPS will be analyzed according to the treatment assigned at randomization. The PPS will be a supportive efficacy analysis population and only the coprimary endpoints will be analyzed using this set.
- **As-treated population**: All randomized subjects who take at least one dose of study treatment. Subjects will be analyzed according to treatment received. The As-treated population will be used for safety analyses.

[redacted]

5.1 Relevant Protocol Deviations

Relevant protocol deviations are deviations that can have an impact on the primary efficacy endpoints. The impact of relevant protocol deviations on the primary efficacy results will be assessed by excluding subjects from the FAS to define the PPS in supportive analyses of the primary efficacy endpoints. Relevant protocol deviations to be considered regarding exclusion of subjects from the FAS will include the following:

- Randomized but did not take any study treatment
- No postbaseline PASI or sPGA
- Baseline BSA involvement < 10%
- Baseline PASI score < 12
- Baseline sPGA < 3
- Did not have plaque psoriasis at baseline
- Poor compliance to study medication within the first 16 weeks of treatment, <75% compliant with study treatment
- Failure to adhere to prohibited concomitant medication restrictions as described below:
    - Investigational drug or placebo taken outside of the study any time between Day 1 and the Week 16 assessment
    - Phototherapy within 4 weeks prior to the Week 16 assessment
    - Biologic medications (eg, adalimumab, etanercept, infliximab, ustekinumab) any time between Day 1 and the Week 16 assessment
    - Oral psoriasis medications any time between Day 1 and the Week 16 assessment
    - Oral corticosteroids (unless for the treatment of an adverse event) within 4 weeks prior to the Week 16 assessment
    - Topical medications/treatments that could affect psoriasis evaluations within 2 weeks prior to the Week 16 assessment
    - Medicated shampoos within 2 weeks prior to the Week 16 assessment
- Subject received treatment that was different than intended treatment at any visit prior to Week 16.

All subjects with relevant protocol deviations will be identified prior to Week 16 database lock and unblinding of treatment assignment for the analysis of data through Week 16 with the exception of subjects where actual treatment received is different than randomized treatment which will be determined after treatment unblinding. Relevant protocol deviations will be summarized by treatment group and deviation category for the FAS population.

6.0 Statistical Analyses

Descriptive summaries and analyses outlined in Appendix 1 will be presented for data captured throughout the study using the following treatment groups.

For the comparison of endpoints collected during the first 16 weeks of treatment, summaries will be provided for the following treatment groups:

- BMS-986165 6 mg QD
- Placebo

After Week 16, data will be presented for the following treatments:

- BMS-986165 6 mg QD (starting from Week 16 through Week 52)
- Subjects who switched from placebo to BMS-986165 6 mg QD (including Week 16 through Week 52)
- All BMS-986165 6 mg QD (all subjects exposed to BMS-986165 6 mg QD; includes subjects on placebo that switched to BMS-986165 6 mg QD)

6.1 Efficacy Analyses

All efficacy analyses will be performed using the FAS, unless otherwise specified.

Tests to compare BMS-986165 6 mg QD vs. placebo for the coprimary endpoints will be two-sided with a significance level of 0.05. If both coprimary endpoints are statistically significant then testing will proceed for the secondary family of key secondary endpoints. In order to control for Type I error rate inflation within the secondary family of key secondary endpoints, a hierarchical testing method will be implemented for the key secondary endpoints.

The key secondary endpoints will be tested with a two-sided significance level of 0.05 to compare BMS-986165 6mg QD vs. placebo. A hierarchical testing approach will be used for testing of key secondary endpoints (see Section 6.1.3). If an endpoint fails at any step, then all subsequent p-values will be considered descriptive. Two-sided 95% confidence intervals (CIs) will be provided for all efficacy estimates. [redacted]

6.1.1 Primary Endpoints

6.1.1.1 Primary Analysis

Analysis Model

A stratified Cochran-Mantel-Haenszel (CMH) test will be used to compare the sPGA 0/1 response rates at Week 16 between BMS-986165 6 mg QD and placebo. The following stratification factors from IRT are included in the model: country (mainland China, non-mainland China) and prior biologic use (yes/no). The odds ratio (ratio of odds in BMS-986165 6 mg QD group to the odds in the placebo group) and the corresponding 2-sided 95% CIs and p-values

will be reported. Additionally, treatment differences in proportions and the 95% CI for the treatment difference will be provided. The common treatment difference in proportion with the confidence interval, common odds ratio with the 2-sided 95% confidence interval and p-value will be estimated by the Mantel-Haenszel method consistently.

Similar analyses will be performed to compare the PASI 75 response rates at Week 16 between BMS-986165 6mg QD and placebo.

Imputation Methodology

Non-responder imputation (NRI) will be used for coprimary efficacy endpoints for subjects who:

- Discontinue treatment or study prior to Week 16
- Have missing Week 16 endpoint data for any reason

NRI will be used as the primary method of imputation for the coprimary efficacy endpoints.

6.1.1.2 Sensitivity Analyses

As a method to assess the sensitivity of the primary imputation method for the coprimary endpoints, further imputation methods will be used to impute Week 16 data in subjects who:

- Discontinue treatment or study prior to Week 16
- Have missing Week 16 endpoint data for any reason

The coprimary endpoints will be analyzed using the primary analysis method for each sensitivity imputation method described below:

Last Observation Carried Forward (LOCF)

The last observed post-baseline value will be carried forward and used as the Week 16 value. Subjects without a post-baseline will be considered a nonresponder.

LOCF and NRI

Subjects randomized to the placebo group will have the endpoint value imputed using LOCF (post-baseline). If a placebo subject does not have a post-baseline values, they will be considered a nonresponder. Subjects randomized to BMS-986165 6 mg QD will have their endpoint value imputed using the NRI methodology.

Tipping Point Analysis

Tipping point analysis will further be used to assess the robustness of the primary study results. Different number of events between treatment groups will be assessed until the study conclusion is changed. Each imputed value is initially imputed as a responder. The imputed values in the placebo group will remain as responders while the BMS-986165 imputed values are replaced as a nonresponders one at a time, therefore changing the number of events between groups. Once all imputed values in the BMS-986165 group have been replaced with nonresponders values, the data will reset to where the BMS-986165 group imputed values are all responders and one by one the imputed values in the placebo group are replaced with a nonresponder until all placebo are nonresponders and all BMS-986165 are responders. Furthermore, every pair of imputations between the placebo and BMS-986165 groups will be assessed similarly, creating a matrix of possible patterns. Missing values in the placebo group will be imputed as responders while missing values in the BMS-986165 arm will be imputed as NRI as defined in 6.1.1.1.

At each iteration, the statistical analysis is assessed, and the direction of the analysis is recorded. A graph will be provided to identify at what point to which the difference in events cause a direction shift in study results. The tipping point analyses will be based on a two-sample chi-square test approach rather than a stratified CMH test approach for simplicity of the analysis.

Figure 1: Example of Tipping Point Analysis Direction Boundary

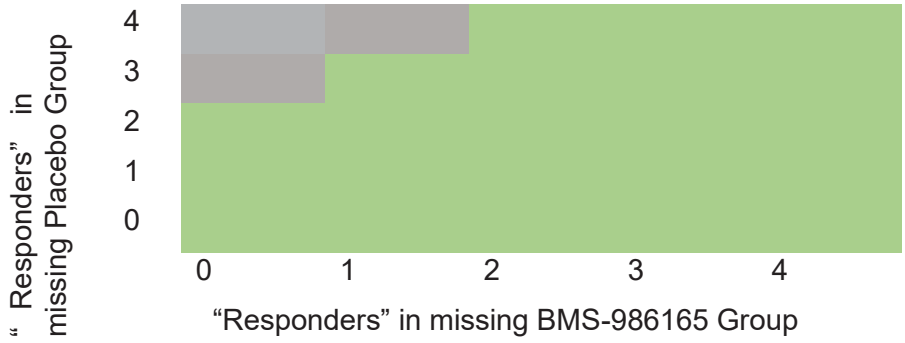


Figure 1 represents an example of the tipping-point analysis for all subjects with missing primary efficacy endpoint (responder/non-responder) in BMS-986165 group (N=5) and placebo group (n=5). Gray cells represent pairs where the statistical analysis resulted in non-significance. Green cells represent pairs where the statistical analysis resulted in significant difference between groups. The tipping-point boundary is where the green cells become gray.

Multiple Imputation

Multiple imputation (MI) will be used for sensitivity analyses for each of the coprimary efficacy endpoints, PASI 75 response at Week 16 and sPGA 0/1 response at Week 16. Multiple imputation of missing data for PASI 75 response and sPGA 0/1 response will be performed by fully conditional specification (FCS) using PROC MI in SAS with the FCS option. The FCS MI specifies the multivariate imputation model on a variable-by-variable basis by a set of conditional densities. For each missing value at Week X, the FCS MI will generate values from a conditional distribution for the missing data given the other data prior to Week X. The FCS MI model will include treatment group and stratification factors for randomization. A total of 1000 imputed (complete) datasets will be generated for the MI analysis. The same test procedure used for the main analysis (CMH test), will be used to analyze the responder endpoint from each imputed dataset. SAS PROC MIANALYZE will be used to pool the results from the CMH tests and generate an overall result by Rubin’s rules (1987).

6.1.1.3 Supportive Analysis

The coprimary endpoints will be analyzed for the PPS at Week 16 using the primary analysis methodology and primary imputation method.

6.1.2 Key Secondary Endpoints

Analysis Model

CMH tests will be used to compare response rates between BMS-986165 6mg QD and placebo. The following stratification factors from IRT are included in the model: country (mainland China, non-mainland China) and prior biologic use (yes/no). The odds ratio (ratio of odds in BMS-986165 6 mg QD group to the odds in the placebo group) and the corresponding 2-sided 95%

CIs and p-values will be reported. Additionally, treatment differences in proportions and the 95% CI for the treatment difference will be provided.

Imputation Methodology for Week 16 Endpoints

NRI will be used for key secondary efficacy endpoints for subjects who:

- Discontinue treatment or study prior to Week 16
- Have missing Week 16 endpoint data for any reason

Imputation Methodology for Week 52 Endpoints

The key secondary endpoints included in this analysis are the following:

- sPGA 0/1 response with at least a 2-point improvement from baseline at Week 52 and at Week 16
- PASI 75 response at Week 52 and at Week 16

Subjects must meet response criteria at both Weeks 16 and 52 in order to be considered a responder. Those who do not meet response criteria at both weeks will be considered a nonresponder.

NRI will be used for key secondary endpoints for subjects who:

- Discontinue treatment or study prior to Week 52
- Have missing Week 52 data

6.1.3 Adjustment for Multiplicity

The study hypothesis to be tested is to assess if the odds of achieving both sPGA 0/1 response and PASI 75 response at Week 16 in subjects receiving BMS-986165 6 mg QD are statistically greater than subjects receiving placebo. Each coprimary endpoint will be tested at a 2-sided Type I error = 0.05. Both endpoints need to demonstrate statistical significance to result in a successful study.

- sPGA 0/1 at Week 16: H_{01}: OR = 1 versus H_{11}: OR ≠ 1
- PASI 75 at Week 16: H_{02}: OR = 1 versus H_{12}: OR ≠ 1

Statistical analysis of the key secondary endpoints will be performed only if both coprimary endpoints are significant. The primary family of coprimary endpoints will be the serial gatekeeper for proceeding with testing of the key secondary endpoints.

In order to control for Type I error rate inflation within the key secondary endpoints, a hierarchical testing method will be implemented. A hierarchical test may only proceed to the next key secondary endpoint if the null hypothesis is rejected at the probability of making a Type I error of 0.05. If an endpoint fails at any step, then all subsequent p-values will be considered descriptive. See Table 1 for Ex-US submission hierarchy.

Table 1: Testing Order of Key Secondary Endpoints

- PASI 90

- ss-PGA 0/1 with at least a 2-point improvement from baseline among subjects with a baseline ss-PGA ≥3
- sPGA 0
- PASI 100
- PSSD symptom score of 0 among subjects with baseline PSSD symptom score ≥1
- DLQI 0/1 among subjects with baseline DLQI score ≥2
- PGA-F 0/1 with at least a 2-point improvement from baseline among subjects with a baseline PGA-F ≥3

No further multiplicity adjustments will be done for any additional time points or endpoints. Nominal p-values may be provided.

6.1.4 Subgroup Analyses

Subgroup analyses will be performed on the coprimary endpoints using the FAS. The primary imputation method will be applied for these analyses. The CMH test using the stratification factors from IRT will be the analysis method used. The following subgroups will be considered:

- Country (Mainland China, Taiwan, South Korea)
- Sex (male, female)
- Age group (<65 y, ≥65 y)
- Body weight (<90 kg, ≥90 kg)
- Prior biologic use (yes, no) – from case report form
- Prior systemic treatment of psoriasis (Yes/No)
- Prior phototherapy (Yes/No)
- sPGA (3, 4)
- PASI score (≤20, >20)
- BSA involvement (10-20, >20)
- Duration of disease (< 10 y, ≥ 10 y)
- Age at disease onset (<18, 18-39, ≥40)

[redacted]

[redacted]

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[redacted]

6.2 Safety

Summaries of safety data will be presented by period and treatment group, as applicable, for the As-treated population.

6.2.1 Adverse Events

Adverse events will be presented for the number and percentage of subjects and the number of events. Treatment-emergent will be provided in listings. Summary tables will be reported in decreasing frequency based on the total column. Counting for frequency analysis will be by subject and not by AEs, and subjects are only counted once for recurring AEs within each system organ class (SOC) or preferred term (PT); however, the number of total AEs per subject, including multiple occurrences of individual AEs, will also be presented. For summaries of severity, AEs will be reported only at their maximum severity in each subject. Subjects with multiple AEs within a particular SOC or PT will be counted under the category of their most severe event within that SOC or PT.

AE (including deaths) dates will be imputed according to algorithms detailed in Section 8.0. The imputed date of AE onset will be used to assess whether AEs should be considered as treatment-emergent and included in the safety summaries. The original, partial dates will be included in data listings. No imputation will be performed on missing AE seriousness, severity, or relationship; they will be reported as missing.

AEs will be included in a period if the start date of the AE is after the first dispensation date within a period.

An overall summary for the following categories will be presented:

- Deaths
- SAEs
- Related SAEs
- AEs
- Related AEs
- Discontinued treatment due to AEs

The following summaries will also be provided for the following:

- TEAEs by SOC and PT
- Treatment-related TEAEs by SOC and PT

- TEAEs by PT reported in ≥ 5% of subjects
- TEAEs by PT reported in ≥ 1% of subjects
- Treatment-related TEAEs by PT reported in ≥ 5% of subjects
- TEAEs categorized by severity by SOC and PT
- Exposure-adjusted incidence rate (EAIR) for TEAEs by SOC and PT – EAIR is defined in Section 8.1 of the SAP.

6.2.1.1 Adverse Events of Interest (AEI) and Other Important AEs

Summaries for treatment-emergent AEIs events will be provided by PT for each AEI category.

- Skin-related events
- Infection events
- Malignancy events

Creatine kinase (CK) elevation for CK elevation > 2.5 upper limit of normal will be summarized as CTCAE grade 2 or higher in the clinical laboratory summaries.

Additional information collected for some events as part of the clinical safety program and adjudicated events will also be summarized.

6.2.1.2 Serious Adverse Events

Summaries for treatment-emergent SAEs will be provided for the following:

- Treatment-emergent SAEs by SOC and PT

6.2.1.3 Adverse Events Leading to Discontinuation of Study Treatment or Study Treatment Interruption

Summaries for TEAEs leading to discontinuation of study treatment will be provided for the following:

- TEAEs by SOC and PT

Summaries for TEAEs leading to study treatment interruption will be provided for the following:

- TEAEs by SOC and PT

6.2.2 Deaths

All adverse events with an outcome of death will be listed.

6.2.3 Clinical Laboratory Data

Laboratory parameters will be summarized using the International System (SI) of Units. Data will be summarized by time point, as applicable. The following summaries will be provided for each parameter:

- Absolute, change from baseline values for continuous parameters
- Number and percentage of subjects for the following:
    - Maximum postbaseline CTCAE grade for each applicable laboratory parameter

- Shifts from baseline based on maximum postbaseline CTCAE grade

- Drug-induced Liver Injury (DILI) and Hy's Law summaries

6.2.4 Vital Signs and Physical Findings

Vital signs, including weight, will be summarized by time point, as applicable. The following summaries will be provided for each parameter:

- Absolute and change from baseline values
- Number and percentage of subjects for the following:
  - Marked abnormality for each abnormality category as defined in Section 4.2

6.2.5 ECGs

ECG parameters will be summarized by time point, as applicable. The following summaries will be provided for each parameter:

- Absolute, change from baseline values and change from baseline in maximum post-baseline value for continuous parameters
- Number and percentage of subjects for the following:
  - Marked abnormality for each abnormality category as defined in Section 4.2

6.2.6 Other Safety Data

6.2.6.1 PHQ-8

PHQ-8 total score will be summarized by time point, as applicable. The following summaries will be provided:

- Absolute and change from baseline values
- Number and percentage of subjects:
  - Shifts from none, mild, moderate, moderately severe and severe scores at baseline and at each time point

6.2.6.2 eC-SSRS

Suicidal ideation and behavior individual item responses will be summarized by time point, as applicable. The following summaries will be provided:

- Number and percentage of subjects with positive responses on suicidal ideation and/or suicidal behavior questions for each question and overall all questions within suicidal ideation and suicidal behavior
- Shifts from baseline based on maximum postbaseline response
- Worst postbaseline value for suicidal ideation and behavior

6.3 General Methodology

The following standards/ methods will be used:

- Statistical package(s) planned to be used
  - All analyses will use SAS version 9.4 or higher.

- Standard summary statistics for continuous and categorical variables:
  - Unless otherwise noted, categorical variables will be summarized using counts and percentages. Percentages will be rounded to one decimal place, except 100% will be displayed without any decimal places and percentages will not be displayed for zero counts.
  - Continuous variables will be summarized using the number of observations (n), mean, standard deviation (SD), median, minimum and maximum. The median, minimum and maximum values will be displayed to the same level of precision as the raw data, the mean to a further decimal place and the SD to two additional decimal places.
  - Variables will be summarized by period, treatment group, and time point, as applicable.

6.3.1 Subject Populations and Disposition

The number of subjects enrolled/screened and the number and percentage of subjects randomized, treated, and in each analysis population will be presented. The number and percentage of subjects randomized in each country and site will be presented.

Additionally, the following summaries will be provided for the FAS by treatment group and overall:

- Number and percentage of subjects who completed 16 weeks of treatment
- Number and percentage of subjects who discontinued treatment prior to Week 16 and reason for treatment discontinuation
- Number and percentages of subjects who completed 52 weeks of treatment, who discontinued treatment prior to Week 52 and post Week 16, and who discontinued treatment at any time and reason for treatment discontinuation. Denominator will be the number of subjects in the FAS.

6.3.2 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized by treatment group for the FAS. Demographic characteristics include the following:

- Sex
- Race
- Ethnicity
- Age (in years, at time of signing informed consent) and age category (<65 vs ≥65)
- Weight (in kg, at baseline) and weight category (<90 kg vs ≥90 kg)
- Body mass index (BMI in kg/m^2, at baseline)
- Country (Mainland China, Taiwan, South Korea)
- Prior biologic use for psoriasis, psoriatic arthritis and other inflammatory diseases only (yes, no)
- Reason for discontinuation of prior biologic use

- Prior systemic treatment use (yes/no)
- Prior phototherapy use (yes/no)
- Stratification factors obtained from IRT: country (mainland China, non-Mainland China) and prior biologic use
- Stratification factors obtained from database: country (mainland China, non-Mainland China) and prior biologic use
- sPGA (3, 4)
- PASI score (≤20, >20)
- BSA involvement (10-20, >20)
- Duration of disease (< 10 y, ≥ 10 y)
- Age at disease onset (<18, 18-39, ≥40)

Additional demographics or baseline data may be added to summary tables.

General medical history and medical history related to psoriasis will be coded using the Medical Dictionary for Regulatory Activities (MedDRA 23.1 or later). General medical history data will be summarized for each SOC and PT by treatment group and overall for the FAS. Separate tables will be provided for psoriasis medical history.

6.3.3 Prior and Concomitant Medications

Prior and concomitant medications will be coded according to World Health Organization-Drug Dictionary WHO-DD (version at the time of DBL) and will be summarized by Anatomic Therapeutic Classification (ATC) and preferred term (PT) by treatment group for the As-treated population. The number and percentage of subjects using at least one medication and each medication will be displayed by treatment group. Subjects taking more than one medication within the same ATC or PT will be counted once.
Prior medications are defined as medications that started prior to first study treatment, but no longer being taken at the time of the study. i.e. start and stop prior to the first study treatment.

Concomitant medications are defined as medications that were ongoing at the time of first dose of study treatment, or started on or after the first dose of study treatment but before the last dose of study treatment.

Post study medications are defined as medications that started after the last dose of study treatment.

Summaries will be provided for prior medications as well concomitant medications.

Medication dates will be imputed according to algorithms detailed in Section 8.0. The imputed dates will be used to assess whether medications should be included in the summaries as prior or concomitant, however the original, partial dates will be included in data listings.

6.3.3.1 Psoriasis, Psoriatic Arthritis and Other Inflammatory Disease Related Systemic Medications

Prior medications that started and stopped prior to first treatment start date for systemic biologic and non-biologic medications will be summarized as described above for the number and percentage of subjects using each reported medication.

6.3.4 Exposure

6.3.4.1 Duration of Treatment

Duration by Group

Overall duration of each treatment, in days, will be calculated for each subject in each treatment group. Subjects are dispensed study treatment at each visit, starting with Day 1 (Week 0) and at each subsequent visit. The date of first dose of study treatment is the Week 0 [redacted] dosing date and is recorded on the eCRF. If this date is missing, then the earliest drug dispensation date will be used. The last dose date is recorded on the end of treatment page in the eCRF. If this date is missing, then the latest date from the [redacted] page or drug accountability return date will be used.

Duration of treatment will be summarized descriptively by treatment group.

BMS-986165:

Subjects randomized to BMS-986165 will have their duration of treatment derived as:

- Date of last dose – date of first dose +1

Placebo:

For subjects randomized to placebo, duration is defined as:

- Placebo = Date of last dose of placebo – date of first dose +1
- BMS-986165 = Date of last dose of BMS-986165 – date of first dose of BMS-986165 +1

Duration by Period

Overall duration (in days) of each treatment received within each study period will be calculated. Duration within each period is defined for each treatment group as:

$$Last\ dose\ date - first\ dose\ date + 1$$

6.3.4.2 Summary of Dosing

The number of doses taken for each subject for each period will be determined using the eCRF drug accountability data and is defined as:

$$Doses\ Taken = (number\ of\ tablets\ dispensed - number\ of\ tablets\ returned)$$

The number of doses taken will be summarized descriptively by treatment group within each period and overall.

6.3.4.3 Compliance

Treatment compliance will be determined from data captured on the Drug Accountability eCRF.

$$Number\ of\ expected\ doses = (date\ of\ next\ visit - date\ of\ current\ visit)$$

Treatment compliance will be derived for each period. Compliance is defined as:

$$\left(\frac{Number\ of\ doses\ taken}{Number\ of\ expected\ doses}\right) x100$$

Period compliance will be calculated by summing over all visits within the period using descriptive statistics by treatment group. The number and percentage of subjects with <75%, 75% to 100%, and >100% compliance will be provided by treatment group for each period. If a subject does not return the container, then this dispensation event will be excluded in the calculation for the total number of doses taken, total number of expected doses, and total compliance.

[redacted]

6.5.2 Impact on Safety Endpoints

No modifications will be made for the presentations of safety data due to COVID-19. There will not be additional safety data handling considerations for missing data or treatment interruptions due to COVID-19.

6.6 Country Specific Analyses

Country or region specific analyses may take place to support submissions to regional health authorities. In general these would consist of repeating a subset of the analyses described in this SAP for subjects from a specific country, which would potentially be used for evaluation of consistency between the country and the overall population.

Unless otherwise noted, the same analysis methods will be used as for the global population. Also, unless otherwise noted, no formal hypothesis testing will be performed and descriptive summary statistics and estimates will be provided for evaluation of consistency of the population. No adjustment for multiplicity will be made. Stratification factors may or may not be used in analyses as appropriate, taking into account the size of the population.

Country specific analysis will be performed for the Greater China subgroup. This population contains subjects that are Chinese by race and enrolled at sites within mainland China and National Medical Products Administration certified sites withinTaiwan.

7.0 Sequence of Planned Analyses

7.1 Interim Analyses

No interim analysis is planned for this study.

7.2 Final Analyses and Reporting

An unblinded analysis of the data collected up to Week 16 will be conducted once all randomized subjects have either completed the placebo-controlled treatment period (ie, through Week 16) or have discontinued prior to Week 16. A final database lock and analysis will occur after all subjects complete Week 52 or discontinue prior to Week 52. See Section 2.4 for detailed information about unblinding and analysis and reporting at Week 16 and Week 52.

All final, planned analyses identified in this statistical analysis plan will be performed only after the last subject has completed the study and the database has been locked. The randomization codes for all subjects will remain blinded until after the database has been locked.

[redacted]

8.0 Conventions

8.1 General Definitions

The following data definitions and handling conventions will be used for general analysis:

Term	Definition
Study Day	For dates prior to the first dose date, assessment date – first dose date For dates on or after the first dose date, assessment date – first dose date + 1 day
Baseline	Unless otherwise stated, Baseline is defined as the last measurement at the randomization visit (Week 0). If the measurement on Day 1 is missing, then a prior measurement during the screening period may be used as baseline. Baseline assessments must be performed per protocol and standard of care assessments may not be used for baseline. Baseline for each PSSD question will be calculated as the average value over the 7 days prior to the randomization visit. In the event of missing values in the 7 days prior to the randomization visit, daily scores from at least 4 days out of the 7 days can be used to calculate the average score. If > 3 daily scores in the last 7 days are missing for a particular question, then the baseline value for that question will be missing. If any questions are missing baseline after using the described rule, then the baseline value for the subscore using that question and the baseline value for the total score will be missing.
Change from Baseline	Change from baseline is defined as (value at post-baseline visit – value at baseline).
Change from baseline to the maximum post-baseline value or change from baseline to the worst post-baseline value	The maximum/worst post-baseline value is defined as highest/worst observed post-baseline value. The change from baseline is calculated using this maximum/worst value - baseline value.
Concomitant and Prior Medication	Prior medications are defined as medications that started prior to first study treatment, but no longer being taken at the time of the study. i.e. start and stop prior to the first study treatment. Concomitant medications are defined as any medications ongoing at the start of study treatment or with a start date on or after the first dose date and prior to the last dose date. Post study medications are defined as medications that started after the last dose of study treatment.
End of Study (EOS) Date	The EOS date is the date recorded on the eCRF that a randomized subject either discontinued or completed the study. If the subject is lost to follow-up, the EOS date will be the date of the last visit assessment obtained.
Exposure-adjusted incidence rate (EAIR)	EAIR = 100*365.25*(total number of subjects with the AE)/total exposure time for the selected AE under each

	treatment that a subject is exposed. Where total exposure time for each AE within a treatment is calculated as follows: • If a subject has at least 1 treatment emergent event while on a particular treatment, then the exposure time for that subject and AE on that treatment is: o First AE onset date – treatment start date (of that particular treatment) +1 • If a subject does not have an event, exposure time for that AE is: o Treatment stop date (of that particular treatment) – Treatment start date (of that particular treatment) + 1 + 30 days (if subject discontinued or subject completed but is not rolling into IM011075 study) o Treatment stop date (of that particular treatment) – Treatment start date (of that particular treatment) + 1 (if subject completed and is rolling into IM011075 study) Total exposure time = sum of exposure time for each AE within a treatment
First Dose Date – Study	The date a subject received their first dose on Day 1 as recorded in the eCRF Week 0 [redacted] dosing date or the earliest drug dispensation date.
Last Dose Date – Study	The date of last recorded dose on the End of Treatment eCRF for a randomized subject. If this date is missing, the latest date from the [redacted] exposure page or drug accountability return date will be used.
First Dose Date – Period	The date a subject received their first dose as recorded in the eCRF Week 0 [redacted] dosing date or the earliest drug dispensation date for Treatment Period 1 and the earliest drug dispensation date for Treatment Period 2.
Last Dose Date – Period	The date of the last visit in the periods – 1. If a subject prematurely discontinues study treatment within a period, the date of last recorded dose on the eCRF will be used as the last dose date for the period.
Percent Change from Baseline	Percent change from baseline is defined as ([value at post-baseline visit – value at baseline]/value at baseline) x 100. If the baseline value is 0 and the post-baseline value is also 0, then the percent change from baseline is set to 0. If the baseline value is 0 and the post-baseline is >0, then the percent change from baseline value will be missing.

8.2 Calculation of Key Measures

The following efficacy assessments will be used to assess subjects' disease activity and severity during the study. Outcomes are reported via an eCOA tool at various times throughout the study as described in the protocol Schedule of Activities. At study visits, assessments by the investigator or subjects and results/responses will be reported directly into the eCOA tool at the time of the visit. The tool will open assessments in a sequential manner, meaning that the full assessment is to be completed prior to moving forward to the next assessment. This limits the possibility of partially missing data. Also, as investigators/subjects are prompted to enter data for each assessment for the visit, the possibility of a full assessment being missing is also negated.

Scoring of assessments where validated algorithms are not required will be derived in SAS datasets.

Scoring of assessments where validated scoring tools are required, licenses for these tools will be purchased and used for scoring prior to incorporating into the SAS datasets.

8.2.1 Investigator-Administered Assessments

Assessments will be performed by a qualified physician or dermatologist or trained designee who is experienced in the assessment of psoriasis patients. To limit variability, every effort will be made so that the same individual conducts the assessment at all subsequent visits.

8.2.1.1 static Physician's Global assessment (sPGA)

The sPGA is a 5-point scale of an average assessment of all psoriatic lesions based on erythema, scale, and induration. The sPGA measure determines psoriasis severity at a single point in time (without taking into account the baseline disease condition) as clear (0), almost clear (1), mild (2), moderate (3), or severe (4). A higher score equates to higher severity of disease.

The individual scores at each visit for erythema (E), induration (I) and scaling (S) will be captured via the eCOA system. Scores will range from 0 to 4. A total score will also be computed based on the average of the 3 characteristic scores.

$$Total\ average\ score = \frac{E + I + S}{3}$$

The total average score will be calculated in the eCOA system. The average score will be rounded to the nearest whole number. For example, if the total average score is ≤1.49 the score will be rounded to 1. If the score is ≥1.5 the score will be rounded to 2. The primary endpoint is derived from the total average score.

sPGA 0 is derived as the binary indicator for sPGA from the calculation above equal to 0 or not;

sPGA 0/1 is derived as the binary indicator for sPGA from the calculation above is less than 2 or not;

[redacted]

All individual scores and total average score assessed at each week throughout the study will be transferred to [redacted] for analysis. The endpoint derivations will be performed in the analysis datasets.

8.2.1.2 Psoriasis Area and Severity Index (PASI)

The PASI is a measure of the average redness, thickness, and scaliness of psoriatic skin lesions (each graded on a 0–4 scale; 0 = none to 4 = very severe), weighted by the area of involvement

(head, arms, trunk to groin, and legs to top of buttocks). The PASI produces a numeric score that can range from 0 to 72, with higher PASI scores denoting more severe disease activity. The PASI includes multiple subscores and a final total score that will be provided by the eCOA system. Individual plaque characteristic rating scores are provided for each body region as well as the weighted score. Additionally, the degree of involvement of each body region is assessed and that score is multiplied by the weighted plaque characteristic score for a final score for each body region. The total PASI score is a sum of the 4 body regions: Head, Upper Extremities, Trunk and Lower Extremities.

The PASI Total score will be used to assess response to treatment. The percent change from baseline will be calculated at each visit. The PASI 75 endpoint is the proportion of subjects who experience at least a 75% improvement in PASI score as compared with the baseline value.

1 = $If\ \left(\frac{Baseline\ PASI - Visit\ PASI}{Baseline\ PASI}\right) x100 \geq 75\ then\ subject\ is\ a\ PASI\ 75\ responder$

0 = otherwise

The PASI 50, PASI 90, and PASI 100 are defined similarly. The endpoint derivations will be performed in the analysis datasets.

8.2.1.3 Body Surface Area (BSA)

Measurement of psoriasis BSA involvement is estimated using the handprint method with the size of a subject's handprint (including fingers and thumb) representing 1% of BSA involved. The total BSA = 100% with breakdown by body region as follows:

- Head and neck = 10% (10 handprints),
- Upper extremities = 20% (20 handprints),
- Trunk including axillae and groin = 30% (30 handprints),
- Lower extremities including buttocks = 40% (40 handprints).

The Total BSA is the sum of each body region and is assessed at each visit and recorded in the eCOA system.

The product of BSA and sPGA will be calculated. At baseline, baseline BSA will be multiplied by baseline sPGA score. The derivation will be performed at each subsequent visit.

8.2.1.4 scalp specific Physician's Global Assessment (ss-PGA)

The scalp specific assessment will only be performed in subjects with scalp involvement. If there is evidence of scalp involvement, scalp lesions are evaluated in terms of clinical signs of redness, thickness, and scaliness and scored on the following 5-point ss-PGA scale:

0 = absence of disease, 1 = very mild disease, 2 = mild disease, 3 = moderate disease, 4 = severe disease.

The ss-PGA is assessed at each visit throughout the study in subjects that have evidence of scalp psoriasis at baseline. The score will be collected in the eCOA system.

[redacted]

[redacted]

8.2.1.6 Physician's Global Assessment-Fingernails (PGA-F)

In this assessment, fingernail psoriasis is evaluated. The PGA-F will be performed at baseline. If a subject shows evidence of psoriatic fingernail involvement, the assessment will be performed at each subsequent visit to assess severity and improvement over time. Only subjects with PGA-F at baseline will be assessed throughout the study. The overall condition of the fingernails is rated on a 5-point scale:

0 = clear, 1 = minimal, 2 = mild, 3 = moderate, and 4 = severe

The rating score will be collected in the eCOA system.

[redacted]

8.2.1.8 Palmoplantar PGA (pp-PGA)

This measure will be used for subjects with palmoplantar (finger and toe surfaces) involvement at baseline. Only subjects with baseline palmoplantar involvement will continue to have these

assessments at each subsequent visit throughout the study. The pp-PGA uses a 5-point (0-4) overall severity scale:

0 = clear; 1 = almost clear; 2 = mild; 3 = moderate; and 4 = severe.

Scores are collected at each visit and entered in the eCOA system.

[redacted]

8.2.2 Subject-Reported Assessments

8.2.2.1 Psoriasis Symptoms and Signs Diary (PSSD)

The PSSD is an 11-item subject-reported instrument that assesses severity of symptoms and subject-observed signs commonly associated in plaque psoriasis. It has been shown to be reliable and valid in measuring symptoms and signs of subjects with moderate-to-severe plaque psoriasis in the clinic and has strong psychometric properties in assessing treatment effects in clinical trials. The PSSD assesses severity of 5 symptoms (itch, pain, stinging, burning, skin tightness) and 6 subject-observed signs (skin dryness, cracking, scaling, shedding or flaking, redness, bleeding) using 0–10 numerical ratings. The severity of each item is rated on an 11-point numeric rating scale ranging from 0 (absent) to 10 (worst imaginable).

The following questions in the instrument are included in the symptom score: Q1, Q4, Q9, Q10, Q11

The following questions in the instrument are included in the sign score: Q2, Q3, Q5, Q6, Q7, Q8

Two versions of the PSSD were developed, one with a 24-hour recall period (PSSD-24h) and one with a 7-day recall period. The PSSD-24h will be administered daily in this trial to avoid recall bias

with a longer recall period. Individual scores to each question are collected daily in the PSSD. For visit PSSD scoring, the daily scores (with 24-h recall periods) over the prior 7 day will be used and the average score to each of the 11 questions will be used as the score at that visit. In case missing data arise during the 7 days prior to the visit, daily scores of at least 4 days out of the 7 can be used. If >3 scores are missing, the average score will be missing. Baseline PSSD score is calculated based on the daily diary collected data during the screening period. Baseline for each PSSD question will be calculated as the average value over the 7 days prior to the randomization visit. In the event of missing values in the 7 days prior to the randomization visit, daily scores from at least 4 days out of the 7 days can be used to calculate the average score. If > 3 daily scores in the last 7 days are missing for a particular question, then the baseline value for that question will be missing. If any questions are missing baseline after using the described rule, then the baseline value for the subscore using that question and the baseline value for the total score will be missing.

A symptom score will be derived by averaging the 5 questions included in the symptom score and multiplying by 10. To obtain a symptom score on a given day, responses to at least 2 of the 5 questions must be available. If 3 or more questions are missing, the symptom score is considered missing.

A sign score will be derived by averaging the 6 questions included in the sign score and multiplying by 10. Responses to at least 3 of the 6 questions must be available in order to obtain a sign score for a given day. If more than 3 questions are missing, the sign score is considered missing.

Both scores range from 0-100, where 0 representing the least severe symptom/sign and 100 the most severe. A total PSSD score with range 0-100 will be derived from taking the average of the symptom and sign scores.

8.2.2.2 Dermatology Life Quality Index (DLQI)

The DLQI is a subject-reported quality of life index which consists of 10 questions concerning symptoms and feelings, daily activities, leisure, work, school, personal relationships, and treatment during the last week. Each question is scored on a scale of 0 to 3 where 0="not at all", 1="a little", 2="a lot", or 3="very much". The scores are summed, giving a range from 0 (no impairment of life quality) to 30 (maximum impairment). Question 7 includes 2 questions, if the subject answers ‘Yes’ to Q7, the score given is a 3. If the subject answers ‘No’ to Q7, they are asked the second question where a score of 0=’not at all’, 1=’a little’, or 2=’a lot’ is given. Certain questions include an option for not relevant. When scoring, any questions deemed ‘not relevant’ will take on a value of 0.

. Interpretation of DLQI scores is as follows:

1. 0-1 = no effect at all on patient’s life
2. 2-5 = small effect on patient’s life
3. 6-10 = moderate effect on patient’s life
4. 11-20 = very large effect on patient’s life
5. 21-30 = extremely large effect on patient’s life

Individual scores for each question will be provided by the eCOA system. The DLQI score will be derived in the analysis datasets.

[redacted]

[redacted]

Approved v2.0 [redacted]

8.2.2.8 Psoriatic Arthritis Screening and Evaluation (PASE) Questionnaire

The PASE questionnaire will be administered at Screening in subjects with peripheral joint complaints. The PASE questionnaire is a self-administered tool that is used to screen for psoriatic arthritis among subjects who have psoriasis. The PASE questionnaire consists of 15 questions subdivided into 7 questions focusing on symptoms of psoriatic arthritis, and 8 questions focusing on the impact of psoriatic arthritis on function. Each question is scored on a 1 to 5 scale, with a maximum symptom sub-scale score of 35, a maximum function sub-scale score of 40 giving a total maximum score of 75. A score of 47 or above has been shown to distinguish between psoriatic arthritis and non-psoriatic arthritis. This questionnaire is only intended to be a screening tool for psoriatic arthritis and does not replace a comprehensive musculoskeletal exam performed by a rheumatologist. This information will not be summarized.

Individual score to each of the 15 questions will be collected in the eCOA system. The sub-scale scores and total score will be derived in the analysis datasets.

8.2.2.9 Eight-Item Patient Health Questionnaire (PHQ-8)

The PHQ-8 is established as a valid diagnostic and severity measure for depressive disorders in large clinical studies. Each of the 8 questions is based on a 2-week recall and scored on a scale of 0 to 3 by a tick box as: 0=Not at All, 1=Several Days, 2=More than Half the Days, and 3=Nearly Every Day. A PHQ-8 score is derived by summing the scores for the 8 questions. The total PHQ-8 score ranges from 0-24. Scoring interpretation is as follows:

- 0-4 = no significant depressive symptoms
- 5-9 = mild depressive symptoms
- 10-14 = moderate depressive symptoms
- 15-19 = moderately severe depressive symptoms
- 20-24 = severe depressive symptoms

Response to each individual question is collected in the eCOA system. The total score will be derived in the analysis datasets.

8.2.2.10 electronic Columbia-Suicide Severity Rating Scale (eC-SSRS)

The electronic Columbia-Suicide Severity Rating Scale (eC-SSRS) is a computer-automated, patient-reported version of the C-SSRS instrument that defines 11 categories of suicidal ideation and behavior (SIB) events. Categories and definitions are provided in Appendix 23 of the protocol. The categories are as follows:

- Suicidal ideation
    1. Wish to be dead

2. Non-specific active suicidal thoughts
3. Active suicidal ideation with any methods without intent to act
4. Active suicidal ideation with some intent to act, without specific plan
5. Active suicidal ideation with specific plan and intent

- Suicidal behavior
  1. Preparatory acts or behavior
  2. Aborted attempt
  3. Interrupted attempt
  4. Actual attempt (Non-fatal)
  5. Completed suicide
- Self-injurious behavior, no suicidal intent

8.3 Missing, Unknown, or Partial Dates

Start Date		Stop Date: Complete: *yyyymmdd* <1st dose	Complete: *yyyymmdd* ≥1st dose	Partial: *yyyymm* <1st dose *yyyymm*	Partial: *yyyymm* ≥1st dose *yyyymm*	Partial: *yyyy* <1st dose *yyyy*	Partial: *yyyy* ≥1st dose *yyyy*	Missing /Ongoing
Partial: *yyyymm*	= 1st dose *yyyymm*	2	1	n/a	1	n/a	1	1
	≠ 1st dose *yyyymm*		2	2	2	2	2	2
Partial: *yyyy*	= 1st dose *yyyy*	3	1	3	1	n/a	1	1
	≠ 1st dose *yyyy*		3		3	3	3	3
Missing		4	1	4	1	4	1	1

1 = Impute as the date of first dose
2 = Impute as the first of the month
3 = Impute as January 1 of the year
4 = Impute as January 1 of the stop year
Note: If the start date imputation leads to a start date that is after the stop date, then there is a data error and the start date is not imputed.

Imputation rules for partial or missing stop dates:

1. Initial imputation
   a. For partial stop date “mmyyyy”, impute the last of the month.
   b. For partial stop date “yyyy”, impute December 31 of the year.
   c. For completely missing stop date, do not impute.

2. If the stop date imputation leads to a stop date that is after the death date, then impute the stop date as the death date.
3. If the stop date imputation leads to a stop date that is before the start date, then there is a data error and the stop date is not imputed.

Imputation rules for partial or missing death dates:

1. If death year and month are available but day is missing:

    a. If “mmyyyy” for last contact date = “mmyyyy” for death date, set death date to the day after the last contact date.

    b. If “mmyyyy” for last contact date < “mmyyyy” for death date, set death date to the first day of the death month.

    c. If “mmyyyy” for last contact date > “mmyyyy” for death date, data error and do not impute.

If both month and day are missing for death date or a death date is totally missing, set death date to the day after the last contact date.

8.4 Study Periods

Period 1 = Week 0 to Week 16 visit date

Period 2 = Week 16 visit date +1 to Week 52 visit date

Follow-up = 4 week follow-up period

8.5 Day Ranges for Analysis Visits

Below are the day ranges for the analysis visit definitions. If more than one visit occurs within an analysis visit, then the visit that is closest to the target date should be used for analysis.

Period Week	Target Day	Day Range
Baseline		Screening, 1
Period 1		
Week 1	8	2, 11
Week 2	15	12, 18
Week 4	29	19, 43
Week 8	57	44, 71
Week 12	85	72, 99
Week 16	113	100, Week 16 drug dispense date (if available) or use 127 if missing
Period 2		
Week 20	141	1st day after Week 16 drug dispense date, 155
Week 24	169	156, 183
Week 28	197	184, 211
Week 32	225	212, 239
Week 36	253	240, 267
Week 40	281	268, 295
Week 44	309	296, 323
Week 48	337	324, 351
Week 52	365	352, last visit date prior to Safety Follow-up

Period Week	Target Day	Day Range
Safety Follow-up	393	Safety Follow-up visit*

* The Safety Follow-up visit is identified from the SDTM visit label, and no windowing is applied for the creation of this analysis visit. Subjects who continue into the extension study are not expected to complete a safety follow-up.

9.0 References

- Campbell G, Pennello G, Yue L. Missing data in the regulation of medical devices. Journal of Biopharmaceutical Statistics 2011;21:180-195.
- Yan X, Lee S, Li N. Missing data handling methods in medical device clinical trials. Journal of Biopharmaceutical Statistics 2009;19:1085-1098.
- Kenward MG, Roger J. Small sample inference for fixed effects from restricted maximum likelihood. Biometrics 1997;53(3):983-997.
- Rubin, DB (1987). Multiple Imputation for Nonresponse in Surveys. New York, J. Wiley & Sons.

10.0 Document History

Version Number	Version Date	Summary of Changes
1.0 - Original Document	06-Apr-2021	Not applicable
2.0 – Amendment 01	22-Jul-2021	Revisions provided below.

Revisions for Amendment 01: Key additions and revisions in this amendment are specified below. Minor clarifications or typographical and formatting changes were made but are not repeated here. Additions are noted by bold text. Removals are noted by strikethrough.

SAP Section	Revised Text	Rationale for Change
[redacted]		

Approved v2.0 [redacted]

[redacted]

6.1.4	Subgroup analyses will be performed on the coprimary endpoints using the FAS. The primary imputation method will be applied for these analyses. The CMH test using the stratification factors from IRT will be the analysis method used. The following subgroups will be considered: • ~~Region (Greater China, Non-Greater China)~~ • Country (Mainland China, Taiwan, South Korea) • Sex (male, female) • Age group (<65 y, ≥65 y) • Body weight (<90 kg, ≥90 kg) • Prior biologic use (yes, no) – from case report form • Prior systemic treatment of psoriasis (Yes/No) • Prior phototherapy (Yes/No) • sPGA (3, 4) • PASI score (≤20, >20) • BSA involvement (10-20, >20)	Key analyses will be repeated for Greater China under country specific analysis.

	• Duration of disease (< 10 y, ≥ 10 y)Age at disease onset (<18, 18-39, ≥40)	
6.1.5.1	Binary Repeated Measures Analysis Additionally, longitudinal analyses over time (through Week 16) of binary repeated measures data will be performed for the primary ~~and key secondary~~ endpoints. Generalized estimation equation methodology will be used to perform the longitudinal analysis. Treatment group, stratification factors from IRT, visit, and treatment-by-visit interaction will be included in the model as fixed effects. Treatment differences in proportions for Week 16 and the 95% CI for the treatment difference will be provided. No imputation methods will be used for this analysis. Any p-values that are provided will be considered nominal.	GEE models provided minimal value in other protocols and will applied only to primary endpoints.
6.1.5.2	~~Mixed Model Repeated Measures (MMRM)~~ ~~Additionally, for key secondary continuous change from baseline endpoints assessed over time (through Week 16), an MMRM analysis will be used. Treatment group, stratification factors from IRT, visit, and treatment-by-visit interaction will be included in the model as fixed effects. Baseline value of the specified endpoint will be added to the model as a covariate, if applicable. An unstructured covariance structure will be used for modeling the data over time. Kenward and Roger's (1997) approach will be used to approximate the denominator degrees of freedom. The adjusted LS means and treatment differences based on LS means will be provided along with the corresponding 95% CIs for comparisons between BMS-986165 and placebo. Data is assumed to be missing at random. No imputation methods will be used for this analysis. Any p-values that are provided will be considered nominal.~~	This section is removed since key secondary endpoints do not include any continuous parameters.
6.2.3	Laboratory parameters will be summarized using the International System (SI) of Units ~~and US conventional units~~.	Only SI units will be presented since study

	Data will be summarized by time point, as applicable. The following summaries will be provided for each parameter:
	• Absolute, change from baseline values for continuous parameters
	• Number and percentage of subjects for the following:
	  ○ Maximum postbaseline CTCAE grade for each applicable laboratory parameter
	  ○ Shifts from baseline based on maximum postbaseline CTCAE grade
	• Drug-induced Liver Injury (DILI) and Hy's Law summaries
		is conducted in Mainland China, Taiwan, and South Korea.

6.3.2	Demographic and baseline characteristics will be summarized by treatment group for the FAS. Demographic characteristics include the following: • Sex • Race • Ethnicity • Age (in years, at time of signing informed consent) and age category (<65 vs ≥65) • Weight (in kg, at baseline) and weight category (<90 kg vs ≥90 kg) • Body mass index (BMI in kg/m^2, at baseline) • ~~Region (Greater China, Non-Greater China)~~ • Country (Mainland China, Taiwan, South Korea)	Key analyses will be repeated for Greater China under country specific analysis.

	• Prior biologic use for psoriasis, psoriatic arthritis and other inflammatory diseases only (yes, no) • Reason for discontinuation of prior biologic use • Prior systemic treatment use (yes/no) • Prior phototherapy use (yes/no) • Stratification factors obtained from IRT: country (mainland China, non-Mainland China) and prior biologic use • Stratification factors obtained from database: country (mainland China, non-Mainland China) and prior biologic use • sPGA (3, 4) • PASI score (≤20, >20) • BSA involvement (10-20, >20) • Duration of disease (< 10 y, ≥ 10 y) • Age at disease onset (<18, 18-39, ≥40) • Additional demographics or baseline data may be added to summary tables.	
6.6	Country or region specific analyses may take place to support regional health authorities submissions. In general these would consist of repeating a subset of the analyses described in this SAP for subjects from a specific country, which would potentially be used for evaluation of consistency between the country and the overall population.	Regulatory requirement for certification of sites within Taiwan.

	Unless otherwise noted, the same analysis methods will be used as for the global population. Also, unless otherwise noted, no formal hypothesis testing will be performed and descriptive summary statistics and estimates will be provided for evaluation of consistency of the population. No adjustment for multiplicity will be made. Stratification factors may or may not be used in analyses as appropriate, taking into account the size of the population. Country specific analysis will be performed for the Greater China subgroup. This population contains subjects that are Chinese by race and enrolled at sites within mainland China and **National Medical Products Administration certified sites within**Taiwan.	

Appendix 1 Planned Analyses for Primary and Key Secondary Endpoints

List of Planned Analyses: Comparisons of BMS-986165 6 mg QD vs. Placebo			
Measure of Interest	**Population**	**Analysis at Week 16**	[redacted]
sPGA 0/1 – coprimary PASI 75 – coprimary	FAS	NRI+CMH - primary	
sPGA 0/1 – coprimary PASI 75 – coprimary	FAS	LOCF+CMH – sensitivity LOCF/NRI+CMH – sensitivity LOCF/NRI+CMH w/ COVID subjects – sensitivity Tipping Point+Chi-square – sensitivity Multiple Imputation + CMH - sensitivity	
sPGA 0/1 – coprimary PASI 75 – coprimary	FAS	NRI+CMH – subgroups	
PASI 90 – key secondary	FAS	NRI+CMH	
sPGA 0 – key secondary	FAS	NRI+CMH	
PASI 100 – key secondary	FAS	NRI+CMH	
ss-PGA 0/1 among subjects with a baseline ss-PGA ≥3 – key secondary	FAS	NRI+CMH	
PSSD symptom score of 0 among subjects with baseline PSSD symptoms score ≥1 – key secondary	FAS	NRI+CMH	

List of Planned Analyses: Comparisons of BMS-986165 6 mg QD vs. Placebo			
Measure of Interest	**Population**	**Analysis at Week 16**	[redacted]
DLQI 0/1 among subjects with baseline DLQI score ≥2 – key secondary	FAS	NRI+CMH	
PGA-F 0/1 among subjects with a baseline PGA-F ≥ 3 – key secondary	FAS	NRI+CMH	

Appendix 2 Summary of Efficacy Assessments

Assessment	Outcome Measure	Endpoint	Comparison	Analyses
sPGA (Sec 8.2.1.1)	sPGA 0/1 with at least 2 point improvement from baseline	W16	BMS vs. PBO	CMH, sensitivity analyses including tipping point analysis, multiple imputation (Sec 6.1.1.1-3)
		[redacted]		
		Baseline->W16 over time	BMS vs. PBO	Binary GEE and CMH by Week (Sec 6.1.5.1)
	sPGA 0	W16	BMS vs. PBO	CMH (Sec 6.1.2.1)
		Baseline->W16 over time	BMS vs. PBO	CMH by Week (Sec 6.1.5.1)
	[redacted]			
PASI (Sec 8.2.1.2)	PASI 75	W16	BMS vs. PBO	CMH, sensitivity analyses including tipping point analysis, multiple imputation (Sec 6.1.1.1-3)
		[redacted]		
		Baseline->Week 16 over time	BMS vs. PBO	Binary GEE and CMH by Week (Sec 6.1.5.1)
	[redacted]			
	PASI 90	W16	BMS vs. PBO	CMH (Sec 6.1.2.1)
		Baseline->W16 over time	BMS vs. PBO	CMH by Week (Sec 6.1.5.1)
	PASI 100	W16	BMS vs. PBO	CMH (Sec 6.1.2.1)
		Baseline->W16 over time	BMS vs. PBO	CMH by Week (Sec 6.1.5.1)
[redacted]				
ss-PGA (Sec 8.2.1.4)	ss-PGA 0/1 among subjects with a baseline ss-PGA ≥3	W16	BMS vs. PBO	CMH (Sec 6.1.2.1)
		Baseline->W16 over time	BMS vs. PBO	CMH by Week (Sec 6.1.5.1)

[redacted]

PGA-F (Sec 8.2.1.6)	PGA-F 0/1 among subjects with a baseline PGA-F score ≥3	W16	BMS vs. PBO	CMH (Sec 6.1.2.1)
		Baseline->W16 over time	BMS vs. PBO	CMH by Week (Sec 6.1.5.1)
[redacted]				
pp-PGA (Sec 8.2.1.8)	pp-PGA 0/1 among subjects with a baseline pp-PGA ≥3	W16	BMS vs. PBO	CMH (Sec 6.1.2.1)
		Baseline->W16 over time	BMS vs. PBO	CMH by Week (Sec 6.1.5.1)
[redacted]				
PSSD / Symptom Score (Sec 8.2.2.1)	PSSD/Symptom 0 among subjects with baseline PSSD/symptom score ≥1	W16	BMS vs. PBO	CMH (Sec 6.1.2.1)
		Baseline->W16 over time	BMS vs. PBO	CMH by Week (Sec 6.1.5.1)
	[redacted]			

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[redacted]

DLQI (Sec 8.2.2.2)	DLQI 0/1 among subjects with a baseline DLQI score ≥2	W16	BMS vs. PBO	CMH (Sec 6.1.2.1)
		Baseline->W16 over time	BMS vs. PBO	CMH by Week (Sec 6.1.5.1)

[redacted]

[redacted]

PASE (Sec 8.2.2.8)	PASE	Screening only		No Analysis