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A MULTI-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL GROUP PHASE 2 STUDY TO EVALUATE THE CLINICAL EFFICACY AND SAFETY OF BMS-986165 IN SUBJECTS WITH MODERATE TO SEVERE PSORIASIS

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STATISTICAL ANALYSIS PLAN
FOR CLINICAL STUDY REPORT

A MULTI-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL GROUP PHASE 2 STUDY TO EVALUATE THE CLINICAL EFFICACY AND SAFETY OF BMS-986165 IN SUBJECTS WITH MODERATE TO SEVERE PSORIASIS

PROTOCOL IM011011

VERSION # 2.0

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2 STUDY DESCRIPTION

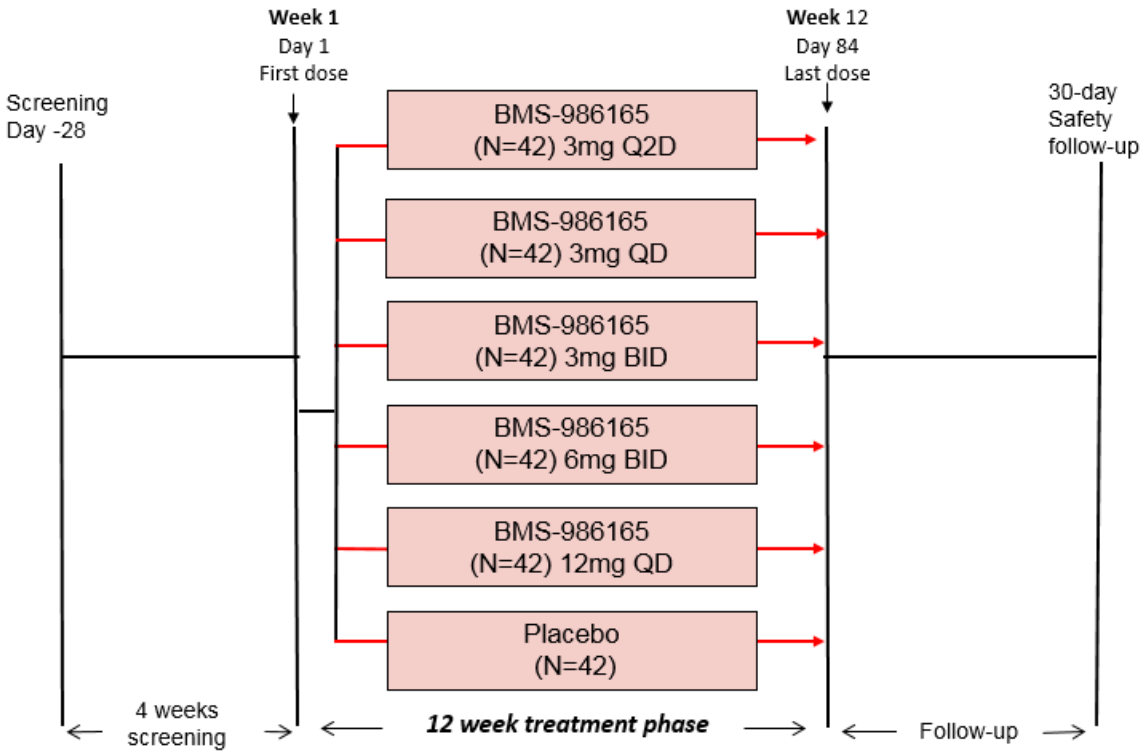
2.1 Study Design

This is a 12 week, multi-center, randomized double-blind, placebo-controlled, parallel-group multiple oral dose study in subjects with moderate to severe psoriasis. Subjects will be randomly assigned to one of six treatment groups, i.e., to receive BMS-986165 (3mg every other day (Q2D); 3mg every day (QD); 3mg twice daily (BID); 6mg BID; 12mg QD) or placebo. Subjects will undergo screening evaluations to determine eligibility within 28 days prior to administration of study medication.

This is an outpatient study. Subjects will receive BMS-986165 or placebo capsules to be taken at home.

The study design schematic is presented in Figure 1.

Figure 1: Study Design Schematic



Q2D=every other day, QD=every day, BID=twice daily

The approximate duration of the study is 20 weeks (143 days). This includes a 4-week screening period (28 days), a 12-week treatment period (85 days), and a 4-week follow-up period (30 days).

The start of the trial is defined as the date of the first Screening Visit (date of signing the informed consent) for the first subject screened. The end of trial is defined as the last visit or scheduled procedure shown in the Time & Events schedule (Table 5.1-1 and Table 5.1-2 of the study protocol) for the last subject. Study completion is defined as the final date on which data for the primary endpoint was or is expected to be collected, if this is not the same.

2.2 Treatment Assignment

After completion of all screening evaluations, on Day 1, all eligible subjects will be randomly assigned to 1 of 6 treatment arms (BMS-986165, 3mg Q2D; BMS-986165, 3mg QD; BMS-986165, 3 mg BID; BMS-986165, 6mg BID; BMS-986165, 12mg QD; and Placebo) in an equal ratio.

Enrolled subjects meeting inclusion and exclusion criteria will be eligible to be randomized. Randomization numbers will be assigned prior to dosing. During the screening visit, the investigative site will call into the enrollment option of the Interactive Web Response System (IWRS) designated by BMS for assignment of a 5-digit subject number that will be unique across all sites. Enrolled subjects, including those not dosed, will be assigned sequential subject numbers starting with 00001, (e.g., 00001, 00002, 00003....00010). The patient identification number (PID)

will ultimately be comprised of the site number and subject number. Once it is determined that the subject meets the eligibility criteria following the screening visit, the investigative site will call the IWRS to randomize the subject. Randomization will be stratified by the use of previous treatment with a biologic (yes/no) and region (Japan vs rest of world).

Specific instructions (including an enrollment/randomization worksheet) for the central enrollment and randomization procedure using an IWRS will be provided to the site.

2.3 Blinding and Unblinding

This is a double-blinded study. The subjects and all site personnel, including the investigator, the site monitor, and the study team, will be blinded. The study will be kept in the blinded nature until the last patient last visit, after which the database undergoes a final lock and unblinding for the final analysis.

Blinding of treatment assignment is critical to the integrity of this clinical study. However, in the event of a medical emergency or pregnancy in an individual subject in which knowledge of the investigational product is critical to the subject's management, the blind for that subject may be broken by the investigator. The subject's safety takes priority over any other considerations in determining if a treatment assignment should be unblinded.

Before breaking the blind of an individual subject's treatment, the investigator should determine that the unblinded information is necessary, (i.e., that it will alter the subject's immediate management). In many cases, particularly when the emergency is clearly not related to the investigational product, the problem may be properly managed by assuming that the subject is receiving active product. It is highly desirable that the decision to unblind treatment assignment be discussed with the medical monitor, but the investigator always has ultimate authority for the decision to unblind. The principal investigator should only call in for emergency unblinding AFTER the decision to discontinue the subject has been made.

In cases of accidental unblinding, contact the medical monitor and ensure every attempt is made to preserve the blind.

Any request to unblind a subject for non-emergency purposes should be discussed with the medical monitor.

In case of an emergency, the investigator(s) has unrestricted access to randomization information via the IWRS and is capable of breaking the blind through the IWRS system without prior approval from sponsor. Following the unblinding the Investigator shall notify the medical monitor and/or study director.

For analyses for the Independent Data Monitoring Committee (IDMC), a separate unblinded study team, comprising an unblinded biostatistician(s) and unblinded programmer(s), will be performing the required analyses.

2.4 Protocol Amendments

Not applicable.

2.5 Data Monitoring and Other External Committees

An Independent Data Monitoring Committee (IDMC) will be established to monitor data on an ongoing basis to ensure the continuing safety of subjects enrolled in this study, to ensure the integrity of the blinded nature of the study. An IDMC charter will be developed which will specify the roles and responsibilities of the members and interim decision rules. The Sponsor Steering Committee will receive and act on the recommendations from the IDMC. A firewall will be established to ensure the maintenance of the study blind for the Sponsor, the investigational site staff, and study subjects and their study partners.

Data summaries and listings will be provided to the IDMC to facilitate their safety assessment at the regularly scheduled times and on an ad hoc basis if needed. The safety review includes serious adverse events and events of special interest, focusing on early signal detection. Further details on the frequency, content and methods of data reports to the IDMC are outlined in the IDMC charter and IDMC Statistical Analysis Plan (SAP).

3 OBJECTIVES

3.1 Primary

- To compare the proportion of subjects with moderate to severe psoriasis experiencing a 75% improvement as measured by a reduction in PASI score (PASI-75) after 12 weeks of treatment between doses of BMS-986165 and placebo
- To assess the safety and tolerability of multiple oral doses of BMS-986165 in subjects with moderate to severe psoriasis

3.2 Secondary

- To assess that the proportion of subjects experiencing a 75% reduction in PASI score in the most efficacious treatment group
- To compare the proportions of subjects experiencing a 75% reduction in PASI score between treatment groups
- To assess a positive trend between treatment groups of BMS-986165 and proportion of subjects experiencing a 75% reduction in PASI score after 12 weeks of treatment
- To assess clinical efficacy of BMS-986165 as measured by improvement in skin disease area and severity indices PASI-50, -75, -90 and -100 over time in subjects with moderate to severe psoriasis
- To assess a significantly higher proportion of subjects achieving Static Physician's Global Assessment (sPGA) score of "0" ("cleared") or "1" ("minimal") after 12 weeks of treatment with BMS-986165 than after 12 weeks of treatment with placebo
- To assess improvement by BMS-986165 in Dermatology Life Quality Index (DLQI)
- To assess the trough concentrations of BMS-986165 in subjects with moderate to severe psoriasis

[redacted]

4 ENDPOINTS

4.1 Primary Efficacy Endpoint

The primary endpoint is the response rate in PASI-75: the proportion of subjects with moderate to severe psoriasis experiencing a 75% improvement (reduction from baseline) in PASI score at Day 85.

4.2 Secondary Endpoints

The following secondary endpoints will be evaluated in this trial:

- Proportion of subjects at Day 85 with PASI-50, PASI-75, PASI-90, PASI-100
- Change from baseline in DLQI scores at Day 85
- Change from baseline in body surface area (BSA) at Day 85
- Proportion of subjects at Day 85 with sPGA score of 0 or 1
- Pharmacokinetics (PK) parameter: Ctrough

4.3 Primary Safety Endpoint

- The safety and tolerability of BMS-986195 will be assessed by the incidence, potential significance, and clinical importance of adverse events measured during multiple doses of BMS- 986195 and up to 30 days after the last dose, as determined by medical review of adverse event reports, vital sign measurements, electrocardiograms (ECGs), and results of physical examination and laboratory tests.

5 SAMPLE SIZE AND POWER

The sample size calculation is driven by several considerations.

The first consideration is to compare the response rate in PASI-75, the proportion of subjects with moderate to severe psoriasis experiencing a 75% improvement in PASI score after 12 weeks, between BMS-986165 and placebo arms. With a one-sided, two-sample Fisher's exact test at significant level 0.05, a sample size of 42 per arm will provide at least 99% power to detect 50% increase in the PASI-75 response rate in an active arm (i.e., 60% response rate) compared to the placebo assuming the response rate is 10% in the placebo arm.

The second consideration is to assess the response rate in PASI-75 in active dose arms. Data from 42 treated subjects per arm will produce a two-sided 95% confidence interval (CI) with a margin of error at most 15.1% (half width) using normal approximation.

The third consideration is to compare the response rates in PASI-75 in two active arms. With a one-sided, two-sample Fisher's exact test at significant level 0.05, 42 subjects per arm will provide at least 82% power to detect at least 30% difference in the response rate in PASI-75 between any two active dose arms.

The proposed sample size is mainly driven by the third consideration. In addition, administration of BMS-986165 to 42 subjects in each active treatment group provides 34%, 88%, and 99% probability of observing at least one occurrence of any adverse event that would occur with 1%, 5%, or 10% incidence rate respectively.

6 STUDY PERIODS, TREATMENT REGIMENS AND POPULATIONS FOR ANALYSES

6.1 Study Periods

The following periods are defined in this SAP for the purpose of analyses and reporting.

Screening period: Covers the time period which starts from the day of enrollment and lasts until the initiation of randomized double-blind treatment.

Treatment period: Starts at the time of the first dose of blinded treatment (BMS-986165 or placebo) and lasts until the date of the last dose of double-blinded treatment.

Follow-up period: Starts at the date of the last dose of blinded treatment and lasts 30 days post.

6.2 Treatment Regimens

Subjects will receive one of the following treatments for 12 weeks:

- BMS-986165 3mg Every Other Day (Q2D)
- BMS-986165 3mg Every Day (QD)
- BMS-986165 3mg Twice Daily (BID)
- BMS-986165 6mg BID
- BMS-986165 12mg QD
- Placebo

6.3 Populations for Analyses

The following subject populations will be considered in this trial:

- All Enrolled Subjects: All subjects who sign an informed consent.
- All Randomized Subjects: All subjects who are randomized to a treatment.
- All Randomized and Treated Subjects: All randomized subjects who receive at least one dose of the study medication. Subjects will be grouped according to the treatment to which they are randomized by IWRS at the start of the study.
- As-Treated Analysis Population: All subjects who have received at least one dose of study medication. Subjects will be grouped according to the treatment that they actually receive as opposed to the treatment to which they are randomized. Subjects will be grouped on an as-randomized basis unless the subject received the incorrect medication for the entire treatment period. In that case, the subject will be analyzed in the treatment group associated with the incorrect medication he/she receives.
- Efficacy Analysis Population: All Randomized and Treated Subjects.
- Biomarker Analysis Population: All subjects that receive any study medication and have at least 1 post-treatment biomarker measurement.
- Pharmacokinetic Population: All subjects who receive any study medication and have any available concentration-time data.
- Per-Protocol Population: All randomized subjects without relevant protocol deviations (Section 7.2.1). The primary efficacy analysis will be performed using this population if there are more than 10% of the study subjects with relevant protocol deviations.

7 STATISTICAL ANALYSES

7.1 General Methods

Categorical variables will be summarized using counts and percentages of subjects falling into each category by treatment group and visit. Percentages given in these tables will be rounded and,

therefore, may not always sum to 100%. Continuous variables will be summarized by treatment group using the mean, standard deviation, median, Q1, Q3, minimum and maximum values.

SAS® version 9.4 will be used for statistical analyses, tabulations and graphical presentations.

7.2 Study Conduct

7.2.1 Relevant Protocol Deviations

Relevant protocol deviations, which could have an impact on the primary efficacy endpoint, will be identified for all subjects who are randomized and receive study medication during the treatment period. Details of relevant protocol deviations are provided in Appendix 1.

All subjects with relevant protocol deviations will be identified prior to database lock and unblinding of treatment assignment. All relevant protocol deviations will be listed and summarized by treatment group based on All Randomized and Treated Subjects.

If there are more than 10% of the study subjects with relevant protocol deviations, a Per-Protocol analysis excluding these subjects will be performed for the primary efficacy endpoint.

7.3 Study Population

Unless otherwise specified, the study population data will be presented on All Randomized and Treated Subjects by treatment group, all active treatment groups combined, and all treated subjects combined.

7.3.1 Subject Disposition

The following summary tables will be provided:

- Pre-Randomized Subject Status: subjects enrolled, randomized, not randomized, reason for being not randomized.
- Treatment Phase Subject Status: subjects completing the treatment period, not completing the treatment period, reason for not completing the treatment period, not reported (if any).
- End of Study Subject Status: subjects completing the study, not completing the study, reason for not completing the study, not reported (if any).
- The following by-subject listings will be provided:
    - Pre-randomized subject status
    - Treatment phase subject status
    - End of study subject status

7.3.2 Demographic Characteristics

The following summary table will be provided by treatment group:

- Demographic Characteristics Summary: age, gender, race, ethnicity, region, country.

The following by-subject listing will be provided:

- Demographic Characteristics: region, country, treatment group, informed consent date, birth date, age, gender, ethnicity, race.

7.3.3 Physical Measurement Summary

The following summary table will be provided by treatment group:

- Physical Measurement Summary: height (cm), weight (kg), body mass index (kg/m^2).

The following by-subject listing will be provided:

- Physical Measurements: visit, date, study day, height (cm), weight (kg), BMI (kg/m^2).

7.3.4 Medical History

The following summary table will be provided by treatment group:

- Medical History: history system.

The following by-subject listing will be provided:

- Medical History: history system, history details.

7.3.5 Prior and Concomitant Therapy

Prior medication is defined as any medication that is stopped prior to the first dose of study treatment; and concomitant medication is defined as any medication that is on-going at the time of the first dose or started after the first dose of study treatment. Medications will be coded using the WHO DRUG Dictionary Coding Guidelines (WHODrug Enhanced).

The following summary tables will be provided by treatment group:

- Concomitant Medication Summary: total subjects using medication, subjects by anatomic class/therapeutic class/generic name.
- Prior Medication Summary: total subjects using medication, subjects by anatomic class/therapeutic class/generic name.

The following by-subject listing will be provided:

- Prior and Concomitant Medications: start date, stop date, study day, anatomic class/therapeutic class/generic name/reported medication, total daily use, prior or concomitant.

7.4 Extent of Exposure

The exposure data will be presented on the As-Treated Analysis Population by treatment group.

7.4.1 Administration of Study Therapy

Table 7.4-1 provides the definition of parameters for administration of study therapy.

Table 7.4-1: Administration of Study Therapy: Definition of Parameters

	BMS-986165
Dosing schedule per protocol	***3mg Q2D, 3mg QD, 3mg BID, 6mg BID, and 12mg QD***
Total Dose	*Total dose (mg) is sum of all doses administered during the study*
Duration of treatment	*Last dose date - Start dose date +1*

The following parameters will be summarized (descriptive statistics):

- Number of doses received
- Total dose
- Duration of treatment

The following by-subject listing will be provided:

- Study Drug Administration: visit, date/day of dose, blister card number (flag if drug assigned but not taken), number of capsules per day.

7.4.2 Treatment Compliance

The CRF for this study will capture information on doses of the study medication. All subjects who skip any study drug dose will be listed. The number of subjects with missed doses (excluding missed doses due to premature discontinuation from the study) by number of missed doses will be summarized by treatment groups.

7.5 Efficacy

Unless otherwise specified, the efficacy data will be presented using the Efficacy Analysis population.

7.5.1 Primary Efficacy Analysis

The algorithm for PASI scoring is provided in Section 8.1.1. The percentage change from baseline in PASI will be calculated using the following formula:

[(PASI Score at Day 85 – Baseline)/Baseline]*100

For a subject, PASI-75 is 1 if the percentage change from baseline is less than or equal to -75%, i.e., the subject has greater than or equal to 75% improvement in PASI score comparing to baseline. Otherwise, PASI-75 is 0. Missing value for PASI-75 will be imputed and the imputation method is described in Section 8.3.1.

The following analyses will be provided:

- To compare the response rates between each treatment group and placebo, the PASI-75 at Day 85 will be analyzed by two-sample Fisher's exact test or Chi-square test based on the observed counts. The odds ratio (odds in treatment group/odds in placebo) and the

difference in the response rates and their corresponding two-sided 95% confidence intervals (CIs) will be provided.

There will be no adjustment for multiplicity. All comparisons will be performed in a pre-specified hierarchical procedure starting from the highest dose arm to the lowest dose arm. If a comparison is not significant at level 0.05, all p-values in subsequent comparisons will be considered nominal.

- For the primary efficacy endpoint, the proportion of subjects with moderate to severe psoriasis experiencing a 75% improvement in PASI score at Day 85 (PASI-75), the count and percentage of subjects with PASI-75, along with the 95% asymptotic and Clopper-Pearson exact two-sided CIs, will be provided in each treatment group.
- A logistic regression model analysis will be performed to evaluate the impact of treatments on PASI-75 at Day 85, with treatment group, age, gender, weight, BMI, baseline PASI score, use of previous biologic treatment, study region, and use of previous biologic treatment-by-study region interaction as covariates, if applicable.
- A bar chart of PASI-75 response rate at Day 85 by treatment group will be provided.

7.5.2 Secondary Efficacy Analyses

7.5.2.1 PASI-75

The following analyses will be provided for PASI-75:

- The Cochran-Armitage trend test will be performed to assess a positive trend between treatment groups of BMS-986165 and proportion of subjects experiencing a 75% reduction in PASI score at Day 85.
- A repeated measures logistic regression model analysis will be performed using a generalized estimating equations (GEE) model. The model will be fitted with treatment, visit, and treatment-by-visit interaction as the fixed effects and measurements within each subject as the repeated measurements. The use of previous biologic treatment, study region, and use of previous biologic treatment-by-study region interaction will be added into the model as covariates.
- A longitudinal line plot of the response rate in PASI-75 grouped by treatment will be provided.

7.5.2.2 PASI Score

The following analyses will be provided for PASI score:

- PASI score will be presented using the descriptive statistics (n, mean, median, min, max, standard deviation, Q1, Q3) at Day 1 (baseline), Day 8, Day 15, Day 29, Day 57, Day 85, and Day 115 for each group. Point estimates at each visit and two-sided 95% CIs for mean change from baseline within each treatment group will be provided.
- A longitudinal line plot of mean change (with standard error) in PASI score from baseline grouped by treatment will be provided.
- A mixed effect model analysis with repeated measures will be performed to evaluate the impact of treatments on PASI score over time. The mixed effect model will be fitted with

treatment, visit, and treatment-by-visit interaction as the fixed effects and change from baseline measurements within each subject as the repeated measurements. The baseline value, use of previous biologic treatment, study region, and use of previous biologic treatment-by-study region interaction will be added into the model as covariates. Based on the mixed effect model, the estimate and 95% confidence interval will be calculated for the difference between each active treatment and the placebo at each specified visit.

The following by-subject listing will be provided:

- PASI: date of assessment, visit, body location, area of involvement score, induration (thickness) score, erythema (redness) score, scaling (desquamation) score, derived PASI score, change from baseline, percentage change from baseline, PASI-50, PASI-75, PASI-90, and PASI-100.

7.5.2.3 PASI-50, PASI-90, and PASI-100

Similar analyses as in primary efficacy analyses will be performed for PASI-50, PASI-90, and PASI-100.

- The proportion of subjects with moderate to severe psoriasis experiencing a 50%, 95%, and 100% improvement in PASI score at Day 85, along with the 95% asymptotic and Clopper-Pearson exact two-sided CIs will be provided in each group, respectively.
- To compare the response rates between each treatment group and placebo, the PASI-50, PASI-90, and PASI-100 will be analyzed by two-sample Fisher's exact test or Chi-square test based on the observed counts. The odds ratio (odds in treatment group/odds in placebo) and the difference in the response rates and their corresponding two-sided 95% CIs will be provided.
- A logistic regression model analysis will be performed to evaluate the impact of treatments on PASI-50, PASI-90, or PASI-100 at Day 85, with treatment group, age, gender, weight, BMI, baseline PASI score, use of previous biologic treatment, study region and use of previous biologic treatment-by-study region interaction as covariates.
- A repeated measures logistic regression model analysis will be performed using a GEE model. The model will be fitted with treatment, visit, and treatment-by-visit interaction as the fixed effects and measurements within each subject as the repeated measurements. The use of previous biologic treatment, study region, and use of previous biologic treatment-by-study region interaction will be added into the model as covariates.

7.5.2.4 sPGA

The algorithm for sPGA scoring is provided in Section 8.1.2.

The following analyses will be provided:

- The sPGA score of 0/1 (0/cleared, 1/minimal) versus > 1 will be presented using descriptive statistics (count and percentage) at Day 1, Day 8, Day 15, Day 29, Day 57, Day 85, and Day 115 for each group.
- To compare the response rates between each treatment group and placebo, the sPGA distribution of 0/1 vs. >1 at Day 85 will be analyzed by a two-sample Fisher's exact test or a Chi-square test. The odds ratio and the difference in the response rates and their corresponding two-sided 95% CIs will be provided.

- A logistic regression model analysis will be performed to evaluate the impact of treatments on sPGA (0/1 vs. >1) at Day 85, with treatment group, age, gender, weight, BMI, baseline PASI score, use of previous biologic treatment, study region, and use of previous biologic treatment-by-study region interaction as covariates.

The following by-subject listing will be provided:

- sPGA: date of completion, visit, language code, BMS scale identifier, scale question identifier, sub-scale score (I/E/S), and sPGA score.

7.5.2.5 DLQI

The following analyses will be provided:

- The DLQI score will be presented using the descriptive statistics (n, mean, median, min, max, standard deviation, Q1, Q3) for each group at Day 1 (baseline), Day 29, Day 57, Day 85, and Day 115. Point estimates for each visit and two-sided 95% CIs for mean change from baseline within each treatment group will be provided.
- A mixed effect model analysis with repeated measures will be performed to evaluate the impact of treatments on DLQI score over time. The model will be fit with treatment, visit, and treatment-by-visit interaction as the fixed effects and measurements (changes from baseline) within each subject as the repeated measurements. The baseline value, use of previous biologic treatment, study region, and use of previous biologic treatment-by-study region interaction will be added into the model as covariates. Based on the mixed effect model, the estimate and 95% confidence interval will be calculated for the difference between each active treatment and the placebo at each specified visit.

The following by-subject listing will be provided:

- DLQI: date of completion, visit, language code, BMS scale identifier, question 1-10, score total, and change from baseline.

7.5.2.6 BSA

The following analyses will be provided:

- BSA will be presented using the descriptive statistics (n, mean, median, min, max, standard deviation, Q1, Q3) for each group at Day 1, Day 8, Day 15, Day 29, Day 57, Day 85 and Day 115 for each group. Point estimates for each visit and two-sided 95% CIs for mean change from baseline within each treatment group will be provided.
- A mixed effect model analysis with repeated measures will be performed to evaluate the impact of treatments on BSA over time. The model will be fitted with treatment, visit, and treatment-by-visit interaction as the fixed effects and measurements (changes from baseline) within each subject as the repeated measurements. The baseline value, use of previous biologic treatment, study region, and use of previous biologic treatment-by-study region interaction will be added into the model as covariates. Based on the mixed effect model, the estimate and 95% confidence interval will be calculated for the difference between each active treatment and the placebo at each specified visit.

The following by-subject listing will be provided:

- BSA: date of assessment, visit, BSA result (%), and change from baseline.

[redacted]

7.5.4 Subgroup Analyses

To investigate the impact of study region (Japan vs rest of world) and the use of previous biologic treatment on the primary efficacy endpoint, subgroup analyses will be performed. The Cochran–Mantel–Haenszel Chi-square test on the response rates in PASI-75 at Day 85 will be conducted and the odds ratio (odd in a treatment group/odd in placebo) in the response rates and its corresponding two-sided 95% CI will be provided.

7.5.5 Sensitivity Analyses

If more than 10% of total subjects in the efficacy analysis population discontinued due to any reasons other than lack of efficacy, AE or unknown reason, a sensitivity analysis may be performed for the primary efficacy endpoint.

7.5.6 Per-Protocol Analyses

If at least 10% of total subjects in efficacy analysis population demonstrate relevant protocol deviations, a per-protocol analysis may be performed. A Per-protocol (PP) analysis population will exclude all subjects with at least one relevant protocol deviation (defined in Appendix 1) from the efficacy analysis population. A per-protocol analysis will be carried out for the primary efficacy

endpoint based on the PP analysis population. The grouping scheme will be the same as in the primary efficacy analysis.

7.6 Safety

Unless otherwise specified, the safety data will be presented using the As-Treated Analysis Population by treatment group, BMS combined treatment group, and all treated subjects combined.

All AEs will be coded using version 19.1 of the Medical Dictionary for Regulatory activities (MedDRA) to a standard system-organ class (SOC) and preferred term (PT).

AEs are classified as treatment emergent (TEAEs) if they begin after the administration of study drug and within 30 days after the last dose.

7.6.1 Deaths

A by-subject listing of deaths will be provided for the All Enrolled Subjects population.

7.6.2 Serious Adverse Events

The following summary tables (counts and percentages) will be provided:

- Serious TEAEs summary by SOC/PT
- Serious drug-related TEAEs by SOC/PT

A by-subject SAE listing will be provided.

7.6.3 Adverse Events Leading to Discontinuation of Study Therapy

The following summary tables (counts and percentages) will be provided:

- AEs leading to discontinuation by SOC/PT

A by-subject listing of AEs leading to discontinuation of study therapy will be provided.

7.6.4 Adverse Events Leading to Dose Modification

The following summary tables (counts and percentages) will be provided:

- Summary of AEs leading to reduction and/or interruption by SOC/PT

A by-subject listing of AEs leading to dose reduction and/or interruption will be provided.

7.6.5 Adverse Events

The following summary tables (counts and percentages) will be provided:

- TEAEs summary of by SOC/PT
- Study drug-related TEAEs by SOC/PT

A by-subject AE listing will be provided.

7.6.6 Clinical Laboratory Evaluations

The following summary tables will be provided:

- Laboratory Test Results Summary of Marked Laboratory Abnormalities: hematology, liver and kidney function, and chemistry panel.

The following by-subject listings will be provided:

- Marked Laboratory Abnormality Criteria.
- Laboratory Listing by Lab Test.

- Subjects meeting marked laboratory abnormality criteria.
- Subjects with aspartate transaminase (AST)/alanine transaminase (ALT)>3x upper limit of normal (ULN) and total bilirubin>2xULN on the same date.

7.6.7 Electrocardiogram

Summary statistics (n, mean, standard deviation, median, minimum, and maximum) will be presented for each ECG parameters and the corresponding changes from baseline by treatment and visit. The baseline value is defined as the last measurement before the first dose. ECG readings will be evaluated by the Investigator and abnormalities, if present, will be listed.

The frequency distribution of subjects' maximum recorded post-dose QTcF, PR, QRS and

ΔQTcF will be summarized by treatment group for the following ranges:

- QTcF: QTcF ≤ 450 msec, 450 msec < QTcF ≤ 480 msec, 480 msec < QTcF ≤ 500 msec, QTcF > 500 msec
- PR: PR ≤ 200 msec, PR > 200 msec
- QRS: QRS ≤ 120 msec, QRS > 120 msec
- ΔQTcF: ΔQTcF ≤ 30 msec, 30 msec < ΔQTcF ≤ 60 msec, ΔQTcF > 60 msec

Individual QTcF, PR, QRS or ΔQTcF values meeting the above criteria will be flagged in the data listing.

The following summary tables will be provided:

- Electrocardiogram Summary: Summary Statistics for ECG Values and changes from baseline
- Frequency Distribution of Maximum Post-Dose ECG Interval

The following by-subject listings will be provided:

- Electrocardiogram (ECG) Results: visit, date, study day, heart rate (bpm), interval (PR, QRS, QT, QTC), interpretation of findings.
- Investigator Identified Abnormal ECG Results: visit, date, study day, heart rate (bpm), interval (PR, QRS, QT, QTC), interpretation of findings
- Subjects with Heart Rates and Out-Of-Range ECG Intervals: visit, date, study day, time, heart rate (bpm), interval (PR, QRS, QT, QTcB, QTcF), change from baseline (HR, PR, QRS, QT, QTcB, QTcF).

7.6.8 Vital Signs and Physical Findings

Vital signs parameters (systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate and body temperature) will be listed. Summaries of vital sign parameters and respective changes from baseline will be provided at corresponding visits by treatment group. Subjects with vital signs outside of a pre-specified range will also be listed.

The following criteria will be used to determine vital sign results that are outside of a pre-specified range, where changes from baseline are based on matched postural positions and are calculated as parameter value - baseline parameter value:

Table 7.6.8-1: Vital Sign Parameter Cut-Off Values

Heart Rate(bpm)	Value > 100 and change from baseline > 30, or Value < 55 and change from baseline < -15
Systolic BP(mmHg)	Value > 140 and change from baseline > 20, or Value < 90 and change from baseline < -20
Diastolic BP(mmHg)	Value > 90 and change from baseline > 10, or Value < 55 and change from baseline < -10
Respiration(breaths/min)	Value > 16 or change from baseline > 10
Temperature (°C)	Value > 38.3°C or change from baseline > 1.6°C

The following summary tables will be provided:

- Vital Signs Summary: Summary Statistics for Vital Signs and Changes from Baseline

The following by-subject listings will be provided:

- Vital Signs by Subject: visit, date, study day, position, blood pressure (mmHg), heart rate (bpm), respiration rate (breaths/min), temperature (°C).
- Subjects with Out-Of-Range Vital Signs: visit, date, study day, position, blood pressure (mmHg) (systolic, diastolic), pulse rate (bpm), respiration rate (breaths/min), temperature (°C), criteria.
- Physical Examination with Abnormal Finding: examine criteria, abnormality.

7.6.9 Other Observations Related to Safety

The following by-subject listings will be provided:

- Medical Treatment Procedures: procedure, start and stop date, reason for procedure.
- Diagnostic Procedures: procedure, date of procedure, reason for procedure, findings.

7.7 Pharmacokinetic Results

The PK analysis will be performed for the Pharmacokinetic Population. Samples for PK assessment will be collected per the Pharmacokinetics Sampling Schedule as described in Table 5.5.1-1 of the study protocol. The summary statistics of BMS-986165 concentrations will be provided by treatment group and nominal visit.

The following summary table will be provided:

- Summary Statistics of Ctrough (mean, SD, geometric mean, % CV, median, min, and max).

The following by-subject listing will be provided:

- Concentration of BMS-986165, including treatment, study day, actual time of sampling, and nominal time. Actual time since previous dose and actual time since Day 1 will be calculated and included in the listing for samples other than Ctrough.

The following graph will be provided:

- Plot of Ctrough over time (Mean +/-SD) by treatment arm.
- Plot of individual Ctrough over time.

[redacted]

8 CONVENTIONS

8.1 Calculations of Key Measures

8.1.1 Evaluation of PASI

The PASI is a grading system used for the evaluation of the severity of psoriatic lesions and their response to treatment. The PASI produces a numeric score that can range from 0 to 72. The severity of a subject's disease is calculated as described below:

In the PASI system, the body is divided into 4 regions: the head (h), trunk (t), upper extremities (ux) and lower extremities (lx), which account for 10%, 30%, 20%, and 40% respectively of the total body surface area (BSA). Each of these areas are evaluated for erythema, induration and scaling, which are rated on a scale from 0 to 4.

The scoring system for the signs of disease (erythema, in duration and scaling) is below:

0 = none

1 = slight

2 = moderate

3 = severe

4 = very severe

The scoring system for estimating the area of involvement for psoriatic lesions is outlined below:

0 = no involvement

1 = 1% to 9% involvement

2 = 10% to 29% involvement

3 = 30% to 49% involvement

4 = 50% to 69% involvement

5 = 70% to 89% involvement

6 = 90% to 100% involvement

To aid in the area assessments, the following conventions are followed:

a. the neck is considered part of the head

b. the axilla and groin are considered part of the trunk

c. the buttocks are considered part of the lower extremities

The PASI formula is:

$PASI = 0.1(E_h + S_h + I_h)A_h + 0.3(E_t + S_t + I_t)A_t + 0.2(E_{ux} + S_{ux} + I_{ux})A_{ux} + 0.4(E_{lx} + S_{lx} + I_{lx})A_{lx}$

8.1.2 Evaluation of sPGA

The sPGA is used to determine the subject's psoriasis lesions overall at a given time point. Overall lesions will be graded for induration, erythema, and scaling based on the scales below. The sum of the 3 scales will be divided by 3 to obtain a final PGA score.

Induration (I) (averaged over all lesions; use the National Psoriasis Foundation Reference card for measurement)

0 = no evidence of plaque elevation

1 = minimal plaque elevation, = 0.25 mm

2 = mild plaque elevation, = 0.5 mm

3 = moderate plaque elevation, = 0.75 mm

4 = marked plaque elevation, = 1 mm

5 = severe plaque elevation, = 1.25 mm or more

Erythema (E) (averaged over all lesions)

0 = no evidence of erythema, hyperpigmentation may be present

1 = faint erythema

2 = light red coloration

3 = moderate red coloration

4 = bright red coloration

5 = dusky to deep red coloration

Scaling (S) (averaged over all lesions)

0 = no evidence of scaling

1 = minimal; occasional fine scale over less than 5% of the lesion

2 = mild; fine scale dominates

3 = moderate; coarse scale predominates

4 = marked; thick, nontenacious scale dominates

5 = severe; very thick tenacious scale predominates

Add I + E + S = / 3 = (Total Average)

Physician's Static Global Assessment based upon above Total Average

0 = Cleared, except for residual discoloration

1 = Minimal - majority of lesions have individual scores for I + E + S / 3 that averages 1

2 = Mild - majority of lesions have individual scores for I + E + S / 3 that averages 2

3 = Moderate - majority of lesions have individual scores for I + E + S / 3 that averages 3

4 = Marked - majority of lesions have individual scores for I + E + S / 3 that averages 4

5 = Severe - majority of lesions have individual scores for I + E + S / 3 that averages 5

Note: Scores should be rounded to the nearest whole number. If total ≤ 1.49, score = 1; if total ≥ 1.50, score = 2.

8.2 Baseline Measures

The baseline value is the last assessment taken prior to the first dose of study medication. In general, baseline value is the assessment taken on study Day 1 before the administration of study medication. If a measurement on Day 1 is missing, the last assessment taken at the screening period prior to the first dose of study medication will be used.

8.3 Missing Measurements

8.3.1 Imputation of Missing Data for Binary Variables

This imputation is applicable for all binary variables (PASI-50, PASI-75, PASI-90, PASI-100, sPGA score of 0/1).

If the response cannot be assessed due to missing data or a subject's early discontinuation, the following conventions will be implemented in a sequence:

- Any subject who prematurely discontinues the trial during the treatment period after receiving study medication will have data imputed as non-responder at all scheduled protocol visits subsequent to the point of discontinuation up to the end of the treatment period.
- If for some reason the binary variable still cannot be determined, including the case where baseline data is missing, then the value will be set to non-responder.

Efficacy data (PASI-50, PASI-75, PASI-90, PASI-100, sPGA score of 0/1) will be presented after imputation; and the number of the subjects with missing efficacy measures in each treatment group will be provided.

For listings, missing responses will be presented as missing.

8.3.2 Imputation of Missing Data for Continuous Variables

For analyses of change from baseline in efficacy measures, missing values will be dealt with via the longitudinal repeated measures analysis assuming MAR (missingness at random).

For all safety (including laboratory measurements) and PK measures, missing values will not be imputed.

8.4 Missing, Unknown or Partial Dates

The BMS safety guidelines for conventions relating to the handling of missing or partial dates and the determination of appropriate default values in such cases (in particular, for concomitant medication dose start-dates and end-dates and AE onset dates) will be utilized.

The following conventions may be used for imputing partial dates for analyses requiring dates:

For missing and partial adverse event onset dates, imputation will be performed using the Adverse Event Domain Requirements Specification1.

For missing and partial adverse event resolution dates, imputation will be performed as follows (these conventions may change):

- If only the day of the month is missing, the last day of the month will be used to replace the missing day.
- If the day and month are missing or a date is completely missing, it will be considered as missing.

Missing and partial non-study medication domain dates will be imputed using the derivation algorithm described in 4.3.3 of BMS Non-Study Medication Domain Requirements Specification2.

For other partial/missing dates, the following conventions may be used:

- If only the day of the month is missing, the 15th of the month will be used to replace the missing day.
- If both the day and the month are missing, “July 1” will be used to replace the missing information.

- If a date is completely missing, it will be considered as missing.

The following conversion factors will be used to convert days to months or years: 1 month = 30.4375 days and 1 year = 365.25 days.

All statistical analyses will be carried out using SAS (Statistical Analysis System software, SAS Institute, North Carolina, USA) unless otherwise noted.

8.5 Day Ranges for Analysis of Time Points

Subjects who do not always adhere strictly to the visit schedule timing in the protocol. Therefore, the designation of visits during the treatment period of the study will be based on the day of evaluation relative to the trial (day of first study medication = study Day 1) rather than the nominal visit recorded in the eCRF. Mutually exclusive relative day windows are defined below to provide derived visits that correspond to the post-baseline time points. If a visit falls outside of the pre-specified visit windows, then the data collected at that visit will not be assigned a derived visit but will remain in the derived data sets. Determination of baseline values is addressed in Section 8.2.

If a subject has more than 1 visit where a measurement is recorded within a window, the measurement closest to the target day will be used. In case of 2 visits being equidistant from the target, the earlier measurement will be used in analyses. For these safety indicators, the least favorable value (toward a positive response) in the window will be used.

Designation of visits for efficacy assessments during the treatment period is tabulated below.

Table 8.5-1: Day Ranges for Efficacy Assessments

Visit	Target Day	Days Range
Baseline/Day 1	**1**	**1**
Day 8	**8**	**2-11**
Day 15	**15**	**12-22**
Day 29	**29**	**23-43 ***
Day 57	**57**	**44-71**
Day 85	**85**	**72-100**

* DLQI is not assessed on Day 8 and Day 16. Days range for DLQI of Day 29 is 2-43.

9 CONTENT OF REPORTS

All analyses described in this SAP will be included in the Clinical Study Report except where otherwise noted. Other analyses may be performed upon the request of the study team. Refer to the Data Presentation Plan for mock-ups of all tables and listings.

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11 DOCUMENT HISTORY

Table 10-1: Document History

Version	Author	Summary of Changes
1.0	Mei Jiang	Original version
2.0	Mei Jiang	• Revised the definitions of some endpoints - Changed "after 12 week" to "at Day 85" - Revised wording for secondary endpoints in Section 4.2 • Further clarified the analysis: - Rearranged the analyses Sections - Added how to calculation PASI-75 from the PASI scores - Added sub-sections for subgroup analysis, sensitivity analysis, and per-protocol analysis under section 7.5 - Added "change from baseline" or "percentage change from baseline" for continuous efficacy endpoints and key endpoints (PASI-75, etc.) in the listing - Added a treatment compliance section under section 7.4 - Modified listing for study medication administration - Changed confidence level from 90% to 95% • Fixed several typos in the text • Fixed format for some bullets

APPENDIX 1 RELEVANT RROTOCOL DEVIATIONS

Eligibility Deviations:

- Subjects with a diagnosis of plaque psoriasis for < 6 months
- Body mass index (BMI) not within 18-40 kg/m^2 or total body weight ≤ 50 kg (110 lb.)
- Subject with psoriatic plaques cover < 10% of body surface area (BSA)
- Subject with PASI score < 12 or sPGA < 3

- Diagnosis of non-plaque psoriasis

Incorrect dosing:

- Subjects who receive treatment different than randomized group
- Subjects taking less than 80% or more than 120% of the planned medication during the entire treatment period
- Randomized subjects who do not take any blinded study medication for ≥ two consecutive weeks
- Restricted and Prohibited medications (refer to Protocol Section 3.4.1):
- Subjects receiving prohibited concomitant treatments while on study therapy. The prohibited and/or restricted treatments are described in Table 3.4.1-1 of the study protocol.