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# Clinical Protocol IM011084

A Randomized, Placebo-Controlled, Double-blind, Multicenter Study to Assess the Efficacy and Safety of Multiple Doses of BMS-986165 in Subjects with Active Psoriatic Arthritis (PsA)

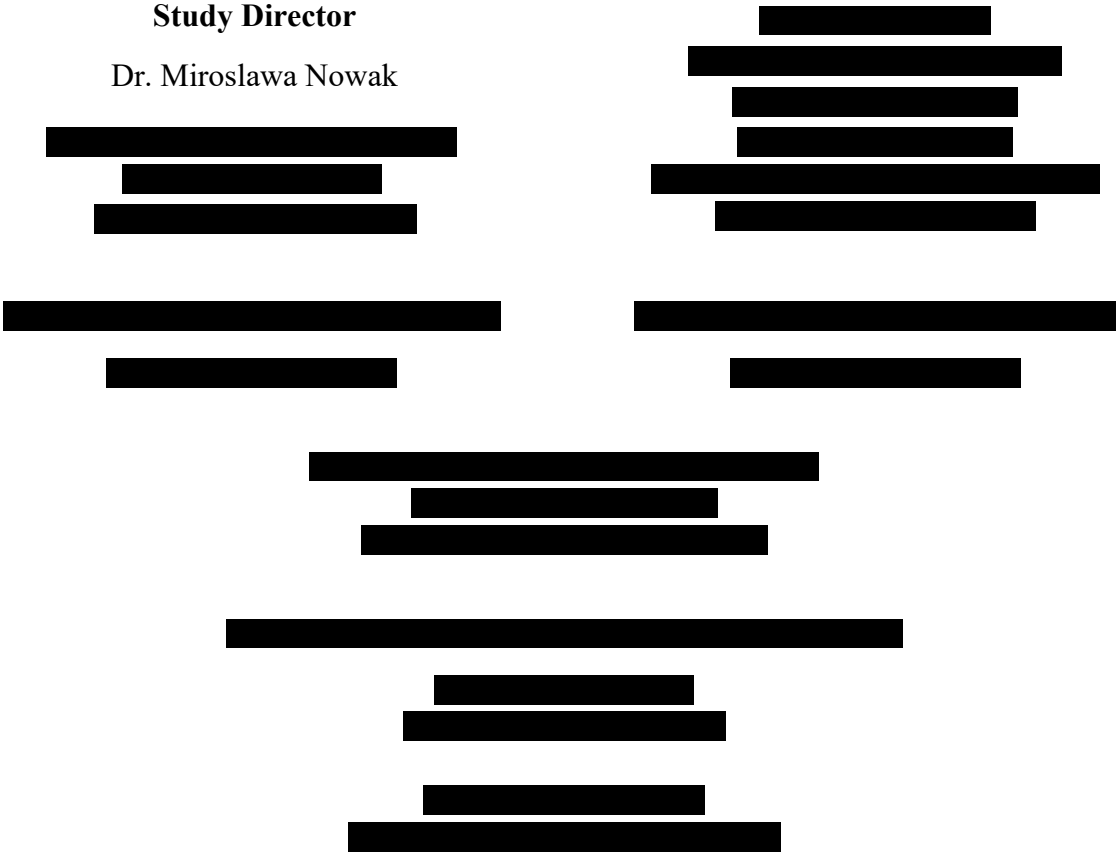
**Short Title:** Efficacy and Safety of BMS-986165 Compared with Placebo in Subjects with Active Psoriatic Arthritis (PsA)

**Revised Protocol Number 05**

Based on the Global Protocol IM011084, version 1.0, dated 06 December 2018

**Study Director**

Dr. Miroslawa Nowak





Approved v2.0

## DOCUMENT HISTORY

| Document | Date of Issue | Approver(s) | Summary of Change |
|---|---|---|---|
| Original Protocol | 03-December-2018 | [redacted] | Not applicable |
| Amendment 1<br>(Czech Republic, Hungary, Italy, and Russia) | 02 April 2019 | [redacted] | This country-specific amendment applies to all subjects enrolled in the Czech Republic, Hungary, Italy, and Russia. This amendment is to limit the PROMIS questionnaire to the standard short form 13a. The additional 5 questions that are included in the global protocol v1.0 Appendix 13 were removed because they are not translated into the languages of these 4 countries. |
| Amendment 2<br>(Poland) | 14 May 2019 | [redacted] | This country-specific amendment applies to all subjects enrolled in Poland. This amendment is to limit the PROMIS questionnaire to the standard short form 13a. The additional 5 questions that are included in the global protocol v1.0 Appendix 13 were removed because they are not translated into the local language. |

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| Revised Protocol 3<br>(United Kingdom) | 11 July 2019 | [redacted] | This country-specific amendment applies to all subjects enrolled in the United Kingdom. The purpose and management of Part B of the study have been clarified with regard to [redacted], study objectives, and use of ustekinumab. Several exclusion criteria and, where applicable, the corresponding item in Section 6.7.1 (Prohibited and/or Restricted Treatments) have been revised. Language in APPENDIX 4 (Women of Childbearing Potential Definitions and Methods of Contraception) and Section 7 (Discontinuation Criteria) has been clarified. |
| Revised Protocol 4<br>(Germany) | 08 August 2019 | [redacted] | This country-specific amendment applies to all subjects enrolled in Germany. Changes incorporated into this protocol include:<br>1) Exclusion Criterion 7a has been revised to exclude prisoners or subjects who are involuntarily incarcerated from trial participation.<br>2) Section 7.1.1 (Post Study Treatment Follow-up) has been revised to state that participants who discontinue study treatment will be followed through the 30-day safety follow-up visit or longer, as required, and in line with Section 8.2.4.<br>3) Section 8.2.2 and Appendix 3 have been |

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| | | | revised to state that SAEs need to be reported 'immediately' to Sponsor or designee but no later than 24 hours, after awareness of the event<br><br>4) Section 8.2.6 (Pregnancy) has been revised to state that study drug treatment must be discontinued immediately in case of pregnancy and language regarding any consideration regarding re-instating treatment has been removed. |
| Revised Protocol 5<br><br>(Global) | TBD | [redacted] | [redacted]<br><br>conditions for the exclusion of TNFi-experienced subjects have been clarified.<br><br>3) Part B, allowed rescue meds and conditions for discontinuation have been clarified<br><br>4) Time frames for assessments of endpoints have been clarified.<br><br>5) Use of the FACIT-Fatigue and PROMIS-Fatigue questionnaires for assessing fatigue has been clarified.<br><br>6) Inclusion criteria have been modified to allow the use of Class V or higher topical corticosteroids<br><br>7) Text has been added to confirm that unblinded site monitors will be involved in drug accountability in Part B |

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| | | | 8) Text has been added to clarify that only prior and prescribed meds are allowed during study and are recorded in the CRF<br><br>9) Specification that the WLQ short form is being used in the study<br><br>[redacted]<br><br>11) Systemic exposure to BMS-986165 defined as 3 days after the end of study treatment, plus 30 days.<br><br>12) Added reference to Appendix 4 for contraception instructions<br><br>13) Clarified time periods pre- and post-study when subjects are allowed live vaccinations<br><br>14) Redefined exclusion criteria re: prohibition of prior psoriasis meds<br><br>This global amendment supersedes and replaces the country-specific Amendment 1 in the Czech Republic, Hungary, Italy, and Russia and the country-specific Amendment 2 in Poland. |

## SUMMARY OF CHANGES

[redacted]

<table>
<tr><th>Protocol Section</th><th>Revised Protocol Text</th><th>Rationale for Change</th></tr>
<tr><td>Document History</td><td>Amendment 1: (Czech Republic, Hungary, Italy, and Russia)<br>Amendment 2: (Poland)<br>Amendment 3: (United Kingdom)<br>Amendment 4: (Germany)</td><td>[redacted]</td></tr>
<tr><td>Section 1.3, Schedule of Assessments, Table 2 and Table 3, Clinical Efficacy/Health Outcomes</td><td><u>Clinical Efficacy/Health Outcomes:</u><br>Fatigue (PROMIS Fatigue or FACIT-Fatigue)<br><u>Column Note:</u><br>See Section 8.1.15</td><td>[redacted]</td></tr>
<tr><td>Section 1.3 Schedule of Assessments, Table 3</td><td>Table 3: → Procedural Outline IM011084: Part B – Optional (Week 16 to We
<table>
<tr><th>Procedure</th><th>Week 16 D113 (±3 d) V8</th><th>Week 20 D141 (±3 d) V9</th><th>Week 24 D169 (±3 d) V10</th><th>Week 28 D197 (±3 d) V11</th><th>Week 32 D225 (±3 d) V12</th><th>Week 36 D253 (±3 d) V13</th><th>Week 40 D281 (±3 d) V14</th></tr>
<tr><td>Clinical Efficacy/Health Outcomes</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>ACR: Tender/Painful Joint Count (68)</td><td></td><td>X</td><td>X</td><td>X</td><td>X</td><td></td><td>X</td></tr>
<tr><td>ACR: Swollen Joint Count (66)</td><td></td><td>X</td><td>X</td><td>X</td><td>X</td><td></td><td>X</td></tr>
<tr><td>ACR: Patient Assessment of Pain</td><td></td><td>X</td><td>X</td><td>X</td><td>X</td><td></td><td>X</td></tr>
<tr><td>ACR: Physician Global Assessment of psoriatic arthritis</td><td></td><td>X</td><td>X</td><td>X</td><td>X</td><td></td><td>X</td></tr>
<tr><td>ACR: Subject Global Assessment of Disease Activity</td><td></td><td>X</td><td>X</td><td>X</td><td>X</td><td></td><td>X</td></tr>
<tr><td>ACR: hs-CRP</td><td></td><td>X</td><td>X</td><td>X</td><td>X</td><td></td><td>X</td></tr>
<tr><td>ACR: HAQ-DI</td><td></td><td>X</td><td>X</td><td>X</td><td>X</td><td></td><td>X</td></tr>
<tr><td>Dactylitis (Count, LDI)</td><td></td><td>X</td><td>X</td><td>X</td><td>X</td><td></td><td>X</td></tr>
<tr><td>Enthesitis (LEI, SPARCC)</td><td></td><td>X</td><td>X</td><td>X</td><td>X</td><td></td><td>X</td></tr>
<tr><td>Nail Changes (PGA-F)[a]</td><td></td><td>X</td><td>X</td><td>X</td><td>X</td><td></td><td>X</td></tr>
<tr><td>PASI[b]</td><td></td><td>X</td><td>X</td><td>X</td><td>X</td><td></td><td>X</td></tr>
<tr><td>PASDAS</td><td></td><td>X</td><td>X</td><td>X</td><td>X</td><td></td><td>X</td></tr>
<tr><td>DAS 28 CRP</td><td></td><td>X</td><td>X</td><td></td><td>X</td><td></td><td>X</td></tr>
</table></td><td>[redacted]</td></tr>
<tr><td>Section 3 Objectives and Endpoints</td><td><u>Efficacy:</u><br>• <u>PROMIS-Fatigue where available or FACIT-Fatigue where PROMIS is not available</u><br>[redacted]</td><td>[redacted]</td></tr>
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| Protocol Section | Revised Protocol Text | Rationale for Change |
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| | [redacted] | [redacted] |
| Section 4.1 Overall Design, Part B | All ~~Part A placebo subjects will~~**who** receive ~~ustekinumab~~**placebo** in Part ~~B; Part A~~ **A will receive ustekinumab in Part B according to approved labeling for PsA; subjects who receive** BMS- 986165 ~~subjects who~~ **in Part A and** achieve MDA will continue treatment with BMS-986165 at the same dose in Part B, and ~~Part A~~**subjects who receive** BMS-986165 ~~subjects who~~ **in Part A and** fail to achieve MDA will receive ustekinumab in Part B. | [redacted] |
| Section 4.1 Overall Design, Part B<br>Section 6.7.2 Rescue Medications<br>Section 7.2 Discontinuation from Study | Subjects who need ~~additional~~ rescue therapy ~~with glucocorticosteroids~~**or additional therapy for PsA and/or flares** after the Week 28 timepoint of Part B will be discontinued from the study. | [redacted] |
| Sec 4.1.1 Data Monitoring Committee and Other External Committees | ***4.1.1** Data Monitoring Committee and Other External Committees*<br>***4.1.1.1 Data Monitoring Committee***<br>***4.1.1.2 Infection Adjudication Committee***<br>**An independent Infection Adjudication Committee, composed of individuals with relevant expertise, will review and adjudicate infection AEs, such as opportunistic infections, influenza, herpes zoster, and TB, reported in the study. Additional information about these infections may be collected on the case report form (CRF) in order to characterize and understand them. The Adjudication Committee members will** | [redacted] |

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| | **be blinded to the treatment assignment of subjects. The structure, responsibilities, and procedures of the Adjudication Committee will be outlined in a charter. The Adjudication Committee is distinct from the DMC and Adjudication Committee members will not be investigators on the study.**<br>***4.1.1.3 Cardiovascular (CV) Adjudication Committee***<br>**An independent cardiovascular (CV) Adjudication Committee, composed of individuals with relevant expertise, will review and adjudicate CV and cerebrovascular AEs such as, but not limited to, Major Adverse Cardiovascular Events (MACE) that include death, nonfatal myocardial infarction, nonfatal stroke; revascularization procedures; heart failure; dysrhythmias; heart blocks; and thrombotic events reported in the study. Additional information about CV and cerebrovascular AEs may be collected on the CRF in order to characterize and understand them. The Adjudication Committee members will be blinded to the treatment assignment of subjects. The structure, responsibilities, and procedures of the Adjudication Committee will be outlined in a charter. The Adjudication Committee is distinct from the DMC and Adjudication Committee members will not be investigators on the study** | |
| Section 5.1 Inclusion Criteria, 2(b) | b) **Note: If a prospective subject was previously exposed to a second TNFi and discontinued for reasons other than intolerance or lack of response (eg, used < 3 months), the Medical Monitor should be contacted to discuss whether the subject should be enrolled.** | [redacted] |
| Section 5.1 Inclusion Criteria 2j<br>Section 6.7.1 Prohibited and/or restricted treatments, 9 | Note: Only low potency (Class V or ~~VI~~**higher**) topical corticosteroids are permitted and restricted to use solely on the palms, soles, face, and intertriginous areas | [redacted] |
| Section 5.1 Inclusion Criteria, 2k | [redacted] | [redacted] |
| Section 5.1 Inclusion Criteria, 3d and 3e | 3 d) Women of childbearing potential (WOCBP) must agree to follow instructions for method(s) of contraception (APPENDIX 4) for the duration of treatment with study drugs **and until the end of relevant systemic exposure** plus 5 half-lives of study drug plus 30 | [redacted] |

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| | days (duration of ovulatory cycle) post-treatment completion. Therefore, in Part A, WOCBP must agree to follow instructions for methods of contraception for 33 days post~~-~~ ~~treatment~~**treatment** completion**,** ~~while~~ **and** in Part B, WOCBP must agree to follow instructions for methods of contraception for 190 days ~~post-treatment~~**after** completion **of treatment.**<br><br>i) Note:<br><br>(1) ~~Longer duration~~**Local laws and regulations may require use of alternative and/or additional contraception methods; additionally, alternative and/or additional contraceptive** may be required **eg,** based on ~~local guidelines or if~~**background DMARDS** the subject ~~is~~**may be** taking ~~background DMARDs~~, such ~~as MTX or~~ **methotrexate**, leflunomide**, etc.**<br><br>3 e) Males who are sexually active with WOCBP must **also** agree to follow instructions for method(s) of contraception (APPENDIX 4) for the duration of ~~treatment with study treatment plus 5 half-lives of~~ **drugs and until** the ~~study treatment plus 90 days (duration of sperm turnover) post-treatment completion~~ **end of relevant systemic exposure.** Therefore, in Part A, ~~males who are sexually active with WOCBP~~male subjects must agree to follow instructions for methods of contraception for 93 days ~~post-treatment completion, while~~**(5 half-lives of study treatment plus duration of sperm turnover) after end of treatment, and** in Part B ~~males must agree to follow instructions for methods of contraception ,~~ for 250 days post-**after end** of treatment completion.<br><br>i) Note:<br><br>(1) ~~Longer duration~~**Local laws and regulations** may ~~be required~~**require use of alternative and/or additional contraception methods; eg,** based on ~~local guidelines or if~~**background DMARDS** the subject ~~is~~**may** be taking ~~background DMARDs,~~ such as ~~MTX or~~**methotrexate,** leflunomide**, etc.** | [redacted] |
| Section 5.2 Exclusion Criteria, 2d | 2 d) Received live vaccine(s) within 60 days prior to Day 1, or plans to receive a live vaccine during the study, or within 60 days after completing ~~study~~**Part A, or within 15 weeks of receiving the last dose of Part B** treatment | [redacted] |
| Section 5.2 Exclusion Criteria, 4a iii | iii) History of use of agents that modulate lymphocyte trafficking (eg, natalizumab, efalizumab), or agents that modulate B cells or T cells (eg, **alemtuzumab**, abatacept, alefacept, or visilizumab) | [redacted] |

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| Section 5.2 Exclusion Criteria, 4c and 5g | 4 c) Any major surgery within 4 weeks prior to Day 1, or any planned surgery ~~for the first 52 weeks of~~ **during** the study<br><br>5 g) Total, unconjugated and/or conjugated bilirubin > 1.5 × **upper limit of normal (**ULN) at screening ~~except for any subject with a diagnosis of Gilbert's syndrome~~ | [redacted] |
| Section 6.1.1 Dose Schedule, Part A | Any missed ~~doses~~**dose should be taken within the next 6 hours. If the subject is unable to take this dose within this time period, the subject should skip this dose. Any missed dose** should be returned at the next study visit | [redacted] |
| Section 6.3.1 Maintaining the Blind | Investigative site staff, the Sponsor, and subject will remain blinded to treatment assignment with the exception of an unblinded pharmacist (or appropriate drug preparation person), an unblinded study drug administrator (Part B), and an unblinded site monitor who will ~~only~~ be involved **only** with drug accountability **in Part B.**<br><br>The syringe used for administration of ustekinumab or placebo must be identical~~. However;~~ the color and viscosity of the solutions may be different. Even though the subject will not be able to distinguish the difference, study personnel who ~~administers both preparations may be able to perceive the difference. Even though the subject will not be able to distinguish the difference, study personnel who~~ administer both preparations may be able to perceive the difference. | [redacted] |
| Section 6.7.1 Prohibited and/or Restricted Treatments, (2), (3), (11), and (12), plus text at end of section | 2) Use of any medications/therapy that would aggravate psoriasis. These include agents such as lithium, antimalarials, propranolol, indomethacin, and quinidine, **unless allowed (see Section 5.1) or** it is considered necessary for the subject's welfare and/or treatment of an AE/SAE.<br><br>3) Use of opioid analgesics**, if the average daily dose is > 30 mg/day (Section 5.2)**, unless it is considered necessary for the subject's welfare and/or treatment of an AE/SAE<br><br>**11) Live vaccination during the study or within 60 days after completing Part A, or within 15 weeks of receiving the last dose of Part B study treatment (Section 5.2)**<br><br>**12) Immune suppressing immunomodulatory agents tacrolimus, sirolimus, mycophenolate mofetil, JAK inhibitors, and immunosuppressant biologic agents including TNF antagonists, natalizumab, vedolizumab, and abatacept**<br><br>No **additional** concomitant medications (prescription, over-the-counter, or herbal **medications not being taken at Day 1)** are to be administered during the study unless prescribed for treatment of specific clinical events. | [redacted] |

| Protocol Section | Revised Protocol Text | Rationale for Change |
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| Section 7.1 Discontinuation from Study Treatment | • **Clinically significant worsening of disease, while taking study treatment, that requires the use of medications listed as prohibited in the protocol** | [redacted] |
| Section 7.1.1 Post-Treatment Study Follow-Up | Subjects who discontinue study treatment will ~~not~~ be followed ~~beyond~~**through** the scheduled 30-day safety follow-up ~~visit~~**period or longer, as required, and in line with Section 8.2.4.** | [redacted] |
| Section 7.2 Discontinuation from the Study | • During Part B of the study (Week 16 to Week 52), and after ~~at least 8~~**12** weeks of treatment (**at** Week 28 **only**), for subjects who do not achieve MDA, the study design provides for rescue therapy for relief of joint symptoms with NSAIDs, intra-articular injections of steroids, systemic glucocorticoids or DMARDs. ~~Subjects~~**After Week 28, subjects** who need ~~additional glucocorticosteroid~~ rescue therapy **or additional therapy for PsA and/or flares** will be discontinued from the study. | [redacted] |
| Section 8.1.1 Rater Qualification | ~~Every effort must be made to ensure the same assessor will complete the clinical efficacy/health outcome assessments for each subject at all visits at approximately the same time throughout the study, according to the Schedule of Activities (Section 1.3). Visits should be scheduled with the availability of the evaluator(s) taken into account. If the assessor is unable to complete the evaluation, then another qualified individual can take the place of the initial evaluator, but the substitute evaluator should have examined and reviewed the subject with the initial evaluator in order to assure overlapping experience (consistency between subject evaluations). Documentation of who performed the evaluation is to be recorded in source notes.~~<br><br>~~To be an eligible Joint Assessor, individuals must receive the standardized joint count training provided by BMS or be trained by an individual who did receive the standardized training (documentation filed in the Investigator File and the BMS Study File). Such individuals should have appropriate medical credentials and/or should be individuals with appropriate scientific/medical background who are experienced in performing joint assessments. If the individual does not have medical credentials, documentation of their experience (preferably on a curriculum vitae) must be provided to the BMS site manager, and their eligibility as joint assessor must be confirmed by the BMS medical monitor before the individual's participation in the study as joint assessor.~~ | [redacted] |
| Section 8.1.4, PASI | All PASI assessments should be performed by a trained ~~physician (dermatologist)~~**assessor** ~~or appropriately trained investigator who is~~ experienced in the assessment of psoriasis patients. | [redacted] |

| Protocol Section | Revised Protocol Text | Rationale for Change |
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| | | [redacted] |
| Section 8.1.8, PGA-F | The PGA-F should be performed by an ~~dermatologist or~~ appropriately trained **assessor** ~~investigator who is~~experienced in the assessment of psoriasis patients. | [redacted] |
| Section 8.1.15 Patient-Reported Outcome Measures Information System-Fatigue (PROMIS-FATIGUE) and Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-Fatigue) | Section 8.1.15 Title:<br>Patient Reported Outcome Measures Information System-Fatigue (PROMIS-FATIGUE) **and Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-Fatigue)**<br>Section Text:<br>The Patient Reported Outcome Measures Information System Fatigue (PROMIS-Fatigue) **and Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-Fatigue)** instruments evaluate a range of self-reported symptoms over the past week, from mild subjective feelings of tiredness to an overwhelming, debilitating and sustained sense of exhaustion that likely decreases one's ability to execute daily activities. … Fatigue is divided into the experience of fatigue (frequency, duration, and intensity) and the impact of fatigue on physical, mental; and social activities. **The first 13 questions of the PROMIS-Fatigue questionnaire comprise the FACIT-Fatigue questionnaire.**<br>**The PROMIS-Fatigue questionnaire is not yet available in all languages and will be administered at sites where it is available in the local language. In countries where the PROMIS-Fatigue questionnaire is not available in the local language, sites will administer the FACIT-Fatigue questionnaire to start the protocol. Once the PROMIS-Fatigue questionnaire is available in the local language, and with approval from the ethics committee, any newly enrolled subjects will complete the PROMIS-Fatigue questionnaire. Subjects who were administered the FACIT-Fatigue at Day 1 will continue to be administered the FACIT-Fatigue throughout the study.** The PROMIS-Fatigue Short Form 13a **(FACIT-Fatigue)**, along with 5 supplemental fatigue items from the PROMIS item bank, are provided in APPENDIX 13. | [redacted] |
| Section 8.1.16 Work Limitation Questionnaire (WLQ) | **The WLQ Short Form will be used in this study.** | [redacted] |

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| Section 8.4.5, Chemistry | ~~Fasting glucose~~**Glucose (fasting at some visits)** | [redacted] |
| Section 8.5 [redacted] | [redacted] | [redacted] |
| Section 8.5.1 Sampling Schedule | [redacted] | [redacted] |

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| | [redacted] | |
| Section 8.5.2 Sampling Window | [redacted] | [redacted] |
| Section 9.1 Sample Size Determination | A total sample size of 60 subjects per arm randomized in a blinded fashion at a 1:1:1 ratio to BMS-986165 6 mg QD arm, BMS-986165 12 mg QD arm, and placebo will provide 87.5% power in a mixed population to detect a significant dose-response trend compared to placebo for the primary endpoint of ACR 20 response at Week 16 using a trend test with ~~α=0.05 (1-sided). Alternatively, if the test is conducted at a 2-sided 0.05 level of significance, the planned sample size will provide approximately 79.5% power to detect the above difference.~~ **α= 0.05 (1-sided) or with α = 0.10 (2-sided).** | [redacted] |

| Protocol Section | Revised Protocol Text | Rationale for Change |
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| [redacted] | [redacted] | [redacted] |
| Section 9.4.1.1 Primary Endpoint Analyses | The primary efficacy analysis model for binary endpoints (responder/non-responder) will use a logistic regression model to assess whether there is a dose-response trend between ACR 20 response and dose level. The model will include dose level (0, 6, 12) as a continuous variable, and the following covariates: ~~geographic region,~~ TNFi use (experienced/naïve)~~, DMARD use (yes/no), glucocorticosteroid use (yes/no),)~~ and body weight (≥ 90 kg and < 90 kg) in the model. ~~If the model does not converge, then pre-specified covariates will be removed from the model.~~ The odds ratio ~~of the dose parameter~~ and the corresponding 2-sided 95% confidence interval (CI) will be provided. | [redacted] |
| Section 9.4.1.2.2 [redacted] | [redacted] | [redacted] |
| Section 9.4.1.3 Secondary Endpoint Analyses | The ~~following~~secondary continuous endpoints will be assessed at Week 16 using dose-response linear regression analysis. The change from baseline in ~~HAQ-DI~~ score will be calculated at Week 16 and analyzed using an analysis of covariance (ANCOVA). Dose level (0, 6, 12) will be assessed in the model as a continuous variable and the following covariates as fixed effects: ~~geographic region,~~ TNFi use (experienced/naïve)~~, DMARD use (yes/no), glucocorticosteroid use (yes/no),)~~ and body weight (< 90 kg and ≥ 90 kg). The baseline ~~HAQ-DI~~ value will be added into the model as a covariate. Treatment differences based on least-squares (LS) means and the corresponding 2-sided 95% CIs will be provided **for the dose-response parameter.**<br><br>~~The change from baseline in SF-36 PCS score at Week 16 will use a similar analysis method as was used for the change from baseline in HAQ-DI score.~~ | [redacted] |
| Section 9.4.1.4 Adjustment for Multiplicity of Primary and Key Secondary Endpoints | … Testing of secondary endpoints will occur sequentially and may only proceed to the next secondary endpoint if the null hypothesis is rejected at alpha = ~~0.05~~ **(0.10 (2**-sided) for the prior endpoint showing a positive dose-response in that endpoint. If an endpoint fails at any step, then all subsequent p-values will be considered nominal.<br><br>Secondary Family – ~~secondary~~Secondary endpoints will be tested for a positive dose-response trend ~~at a 1-sided alpha = 0.05. Testing order of secondary endpoints will be tested~~ in the following order: ~~if the primary endpoint is significant at 1-sided alpha = 0.05 for a dose-response relationship:~~<br><br>a. Change from baseline in HAQ-DI score at Week 16 | [redacted] |

| Protocol Section | Revised Protocol Text | Rationale for Change |
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| | b. PASI 75 response at Week 16<br><br>c. Change from baseline in SF-36 PCS score at Week 16<br><br>~~If the above dose response analyses provide a significant relationship, pairwise comparisons between each BMS-986165 dose group compared to placebo will follow. Testing for each BMS-986165 dose group will be set up in separate testing branches. The primary endpoint, ACR 20 at Week 16, will be tested for each BMS-986165 dose compared to placebo at an alpha = 0.025 (1 sided) using Bonferroni adjustment to the overall Type 1 error rate of 0.05 (1 sided). If the primary endpoint is significant for a particular BMS-986165 dose compared to placebo, then testing will proceed for the secondary endpoints for that BMS-986165 dose. A similar testing order as described above within each branch will be followed for each secondary endpoint.~~<br><br>There will be no multiplicity adjustment **for testing of** additional endpoints. Nominal p-values will be provided as descriptive statistics. | |
| [redacted] | [redacted] | [redacted] |
| Section 9.4.3.6 PROMIS-Fatigue and FACIT-Fatigue | **PROMIS-Fatigue score will be summarized by treatment and time point for subjects who were administered PROMIS-Fatigue. FACIT-Fatigue scores will be similarly presented as a pooled analysis, which will include FACIT-Fatigue scores combined with scores from the first 13 PROMIS-Fatigue questions.** | [redacted] |
| [redacted] | [redacted] | [redacted] |

| Protocol Section | Revised Protocol Text | Rationale for Change |
|---|---|---|
| | [redacted]. | |
| APPENDIX 4, Contraception Guidance for Female subjects of Childbearing Potential<br><br>Contraception Guidance for Male Subjects with Partner(s) of Childbearing Potential | CONTRACEPTION GUIDANCE FOR FEMALE SUBJECTS OF CHILD BEARING POTENTIAL<br><br>One of the highly effective methods of contraception listed below, in conjunction with the required restrictions in Inclusion Criterion Section 5.1 (3d) of the protocol, is required during study duration and until the end of relevant systemic exposure~~, defined as # Days/ Weeks Relevant Exposure days/weeks after the end of study treatment,~~ plus 30 days. **As such, in Part A WOCBP must agree to follow instructions for methods of contraception for 33 days post-treatment completion, and in Part B WOCBP must agree to follow instructions for methods of contraception for 190 days post-treatment completion.**<br><br>Local laws and regulations may require use of alternative and/or additional contraception methods. **Additionally, alternative and/or additional contraception methods may be required based on background DMARDS the subject may be taking (eg, methotrexate, leflunomide, etc.)**<br><br>CONTRACEPTION GUIDANCE FOR MALE PARTICIPANTSSUBJECTS WITH PARTNER(S) OF CHILD BEARING POTENTIAL.<br><br>• Male subjects with female partners of childbearing potential are eligible to participate if they agree to the following during the treatment and until the end of relevant systemic exposure.<br><br>• Male subjects are required to use a condom for study duration and ~~until the end of relevant systemic exposure defined as # Days/ Weeks Relevant Exposure~~**for 93** days~~/weeks after the end of~~ btreatment **completion** in ~~the male participant~~**Part A and 250 days post-treatment completion in Part B.**<br><br>• Female partners of males participating in the study to consider use of effective methods of contraception ~~until the end of relevant systemic exposure, defined as # Days/ Weeks Relevant Exposure~~**for 93 days~~/weeks~~ after the end of treatment in the male subject in Part A and 250 days** after the end of treatment in the male **subject in Part B.**<br><br>• Male subjects with a pregnant or breastfeeding partner must agree to remain abstinent from penile vaginal intercourse or use a male condom during each episode of penile penetration during the treatment ~~and until # Days/ Weeks Relevant Exposure~~**for 93 days~~/weeks~~** after the end of treatment **in Part A and 250 days after the end of treatment in Part B.**<br><br>• Refrain from donating sperm for the duration of the study treatment and for ~~# Days/ Weeks Relevant Exposure days/weeks~~**93** | [redacted] |

| Protocol Section | Revised Protocol Text | Rationale for Change |
|---|---|---|
| | **days after the end of treatment in Part A and 250 days after the end of treatment in Part B.** | |

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[redacted]

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# 1 PROTOCOL SUMMARY

## 1.1 Synopsis

**Protocol Title:** A Randomized, Placebo-Controlled, Double-blind, Multicenter Study to Assess the Efficacy and Safety of Multiple Doses of BMS-986165 in Subjects with Active Psoriatic Arthritis (PsA)

**Short Title:** Efficacy and Safety of BMS-986165 Compared with Placebo in Subjects with Active Psoriatic Arthritis (PsA)

**Study Phase:** Phase 2

[redacted]

[redacted]

[redacted]

**Study Population:**

Men and women ≥18 years of age with PsA for ≥ 6 months, with at least 1 confirmed ≥ 2 cm lesion of plaque psoriasis, having active arthritis (a minimum of ≥ 3 swollen joints and ≥ 3 tender joints), and who are either biologic-naïve (approximately 70% of the study population) or who have failed or been intolerant to 1 TNF-inhibitor (TNFi-experienced, approximately 30% of the study population), will be eligible to participate in the study. In addition, subjects entering the study who have failed or have been intolerant to non-biologic DMARDs, NSAIDs and /or steroids will be allowed to continue their background medications during the study, the details of which are as specified in inclusion criteria.

It is imperative that subjects meet all eligibility criteria. All screening and randomization evaluations must be completed and reviewed to confirm that potential subjects meet all eligibility criteria. The investigator will maintain a screening log to record details of all subjects screened and to confirm eligibility or record reasons for screening failure, as applicable.

**Objectives and Endpoints:**

| Objective | Endpoint |
|---|---|
| **Efficacy** | |
| *Primary* | |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg once daily [QD]) at Week 16 in the treatment of subjects with active PsA | • ACR 20 response |
| *Secondary* | |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in daily functional activities | • Change from baseline in HAQ-DI score |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in reducing PsO severity | • PASI 75 response |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in Patient-Reported Outcomes (PROs) | • Change from baseline in the Physical Component Summary (PCS) score of the SF-36 Questionnaire |

| | |
|---|---|
| *Additional* | |
| • Assess the extent of the dose-response relationship of BMS-986165 treatment (6 or 12 mg QD) at Week 16 in active PsA | • ACR 50 response<br>• ACR 70 response |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in DAS 28 CRP | • DAS 28 CRP Low Disease Activity<br>• DAS 28 CRP Remission<br>• Change from baseline in DAS 28 CRP score |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in dactylitis | • Change from baseline in dactylitis count<br>• Change from baseline in LDI Basic<br>• Dactylitis resolution |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in enthesitis | • Change from baseline in enthesitis count by LEI and SPARCC index<br>• Enthesitis resolution by LEI and SPARCC |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in Physician's global assessment – fingernails (PGA-F) PsO | • PGA-F response of 0/1 |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in MDA | • MDA response |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in psoriatic arthritis activity | • PASDAS<br>• DAPSA<br>• Psoriatic Arthritis Response Criteria (PsARC) |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in ankylosing spondylitis activity | • Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in PROs | • SF-36 Score<br>  • Mental Component Summary (MCS)<br>• PsAID 12<br>• PROMIS-Fatigue where available or FACIT-Fatigue where PROMIS is not available<br>• Work Limitation Questionnaire (WLQ)<br>• Routine Assessment of Patient Index Data 3 |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in daily functional activities | • HAQ-DI 0.35 response |

| | |
|---|---|
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in reducing PsO severity | • PASI 90 response |
| **Safety** | |
| • To assess the safety and tolerability of BMS-986165 in subjects with active PsA | • Incidence of adverse events (AEs), SAEs, AEs leading to study discontinuation, and target AEs of interest (AEIs)<br>• Change in laboratory, electrocardiogram (ECG), physical examination, and vital sign parameters over time |
| [redacted] | |
| [redacted] | |
| [redacted] | [redacted] |
| [redacted] | |
| [redacted] | [redacted] |

[redacted]

**Overall Design:**

This is a 16-week (Part A) randomized, double-blind, placebo-controlled, multicenter study to evaluate the safety and efficacy of multiple doses of BMS-986165 in subjects with active PsA. A total of approximately 180 subjects with active PsA will be randomized in Part A. This Phase 2 study will be conducted in a mixed population of subjects with active PsA who have either not received prior treatment with a biologic (biologic-naïve, approximately 70%) or who have failed or been intolerant to 1 TNF-inhibitor (TNFi-experienced, approximately 30%). In addition, investigators will need to specify if the subject's phenotype is peripheral arthritis or peripheral plus psoriatic spondyloarthritis.

The total duration of participation in Part A is approximately 24 weeks and will be divided into the following periods: screening (up to 4 weeks), double-blind placebo-controlled treatment for 16 weeks (Week 1 to Week 16, Part A), and follow-up (up to 4 weeks). Subjects completing double-blind treatment in Part A will have an opportunity to enroll in an optional double-blind double-dummy Part B. Treatment in Part B will be given for up to 36 weeks (Week 16 to Week 52). For subjects completing both Part A and B of the study, the anticipated study duration is approximately 60 weeks: screening (up to 4 weeks), double-blind placebo-controlled treatment for 16 weeks (Week 1 to Week 16, Part A), double-blind double-dummy treatment for 36 weeks (Week 16 to Week 52, Part B), and follow-up (up to 4 weeks).

Efficacy and safety will be assessed throughout the study. [redacted]

Part A

Subjects will undergo screening evaluations to determine eligibility within 28 days prior to administration of study medication. Following the screening process, if subjects are eligible for randomization then subjects will be randomized in a 1:1:1 ratio (approximately 60 subjects per arm) to 1 of the following 3 treatment groups:

- Placebo
- BMS-986165 6 mg QD
- BMS-986165 12 mg QD

Randomization will be stratified by TNFi use (experienced/naïve) and body weight (≥ 90 kg and < 90 kg).

The primary endpoint is ACR 20 response at Week 16.

In Part A, subjects who discontinue study treatment early for any reason other than consent withdrawal will be expected to complete the early termination (ET) visit followed by the safety follow-up period.

Part B

At Week 16, subjects will have the option to continue to participate in the double-blind Part B of the study. All subjects who receive placebo in Part A will receive ustekinumab in Part B according to approved labeling for PsA; subjects who receive BMS-986165 in Part A and achieve MDA will continue treatment with BMS-986165 at the same dose in Part B, and subjects who receive BMS-986165 in Part A and fail to achieve MDA will receive ustekinumab in Part B. The treatment assignment in Part B will be double-blind, double-dummy as follows:

- Placebo in Part A: ustekinumab subcutaneous (SQ) injection plus placebo matching BMS-986165 QD in Part B
- BMS-986165 6 mg QD in Part A with MDA at Week 16: BMS-986165 6 mg QD plus placebo matching ustekinumab SQ injection in Part B
- BMS-986165 6 mg QD in Part A without MDA at Week 16: ustekinumab SQ injection plus placebo-matching BMS-986165 QD in Part B according to respective country product monographs (See Table 5, table note a)
- BMS-986165 12 mg QD in Part A with MDA at Week 16: BMS-986165 12 mg QD plus placebo matching ustekinumab SQ injection in Part B
- BMS-986165 12 mg QD in Part A without MDA at Week 16: ustekinumab SQ injection plus placebo matching BMS-986165 QD in Part B

In Part B at Week 28, at the discretion of the investigator, the study design provides for rescue therapy for relief of joint symptoms with NSAIDs, intra-articular injections of steroids, systemic glucocorticoids or DMARDs, as follows:

- NSAIDs may be added or the dose may be increased according to labeling guidelines
- A single oral tapering dose of glucocorticosteroid (no greater than 20 mg of prednisone [or prednisone equivalent]) per day, not to exceed 2 weeks
- An intra-articular dose of glucocorticoids (no greater than 40 mg methylprednisolone or 40 mg of triamcinolone [or methylprednisolone or triamcinolone equivalent]) into 1 joint or divided into 2 joints
- A single intramuscular dose of glucocorticoids (no greater than 40 mg methylprednisolone or 40 mg of triamcinolone [or methylprednisolone or triamcinolone equivalent])
- DMARD treatment may not be started; however:

- If already taking MTX, an increase in dose is allowed (maximum of 25 mg weekly)
- If already taking sulfasalazine, an increase in dose is allowed

Subjects who need rescue therapy or additional therapy for PsA and/or flares after the Week 28 timepoint of Part B will be discontinued from the study.

At Week 48, subjects will discuss with their investigator/treating physician plans for treatment with ustekinumab after study completion. In order to maintain the study blind and to ensure continuity of care for those electing to be treated with ustekinumab after the study completion (ie, completion of the Week 56 visit), the following Week 52 procedure should be performed:

- Subjects that **elect to be treated** with ustekinumab following study completion will receive the following treatment at Week 52:
  - Subjects that were on ustekinumab treatment in Part B will receive a placebo matching ustekinumab SQ injection
  - Subjects that were on BMS-986165 6 mg or BMS-986165 12 mg treatment in Part B will receive ustekinumab SQ injection
- Subjects that **elect not to be treated** with ustekinumab after the study will not receive any treatment at Week 52 (regardless of the treatment that they received in Part B).

Following completion of the Week 56 visit (ie, at the conclusion of the follow-up period of the study), subjects that elected to be treated with ustekinumab following study completion, will be due for their ustekinumab injection, as follows:

- Subjects that were on ustekinumab treatment in Part B will be due for their next scheduled (12-week) dose of ustekinumab SQ injection following completion of the Week 56 visit
- Subjects that were on BMS-986165 6 mg or BMS-986165 12 mg treatment in Part B will be due for their next scheduled (4-week) dose of ustekinumab SQ injection following completion of the Week 56 visit

**Note:** Ustekinumab treatment at Week 56 and beyond will be part of standard of care and will not be provided by the study Sponsor.

In Part B, subjects who discontinue study treatment early for any reason other than consent withdrawal will be expected to complete the ET visit followed by the safety follow-up period.

**Statistical Methods:**

**Sample Size and Power Determination:**

A total sample size of 180 subjects randomized in a blinded fashion at a 1:1:1 ratio to BMS-986165 6 mg QD arm, BMS-986165 12 mg QD arm, and placebo (approximately 60 subjects per arm) will provide 87.5% power to detect a significant dose-response trend for the primary endpoint of ACR 20 response at Week 16. Power determination is based on the assumption of a placebo response rate of 30% and BMS-986165 response rates of 50% and 55% in the 6 mg QD and 12 mg QD doses respectively, using a linear trend test with $\alpha$=0.05 (1-sided) or $\alpha$=0.10 (2-sided).

**General Methodology:**

The primary efficacy analysis population will be the Full Analysis Set (FAS). The FAS will include all randomized subjects who are dispensed study drug. Following the intent-to-treat principle, subjects will be analyzed according to the treatment assigned at randomization.

The primary efficacy analysis model for the binary endpoint of ACR 20 response (responder/non-responder) will use a logistic regression model to assess whether there is a dose-response trend between ACR 20 response and dose level. The model will include dose level (0, 6, 12) as a continuous variable, and the following covariates: TNFi use (experienced/naïve) and body weight (≥ 90 kg and < 90 kg) in the model. Odds ratios and the corresponding 2-sided 95% confidence intervals (CIs) will be provided.

The composite strategy as defined in ICH E9 R1 will be used to address the following intercurrent events:

- Subjects who discontinue the treatment or study early (ie, prior to Week 16),
- Start a protocol prohibited medication/therapy,
- Subjects who are lost to follow-up,
- Subjects who otherwise have missing endpoint data at or prior to Week 16.

Subjects with the above intercurrent events will be imputed using the non-responder imputation (NRI) method.

Additional sensitivity analyses will be conducted considering different strategies used for addressing intercurrent events. Supportive analyses on the primary endpoint will be conducted using the Per Protocol (PP) set. Tipping point analysis may be performed to assess the robustness of the primary imputation method.

The analysis model for binary secondary and additional endpoints will use a similar analysis model as the primary efficacy endpoint.

The analysis model for continuous secondary and additional endpoints will use analysis of covariance (ANCOVA) to assess the dose-response trend. The model will include dose level (0, 6, 12) as a continuous variable and the following covariates as fixed effects: TNFi use (experienced/naïve) and body weight (≥ 90 kg and < 90 kg). The baseline value will be added into the model as a covariate. Treatment differences based on least-squares (LS) means and the corresponding 2-sided 95% CIs will also be provided for contrast-based tests.

For continuous efficacy endpoints, the “Composite” and “While on Treatment” strategies will be used to address specific intercurrent events. For subjects who discontinue study treatment and/or study due to:

- Lack of efficacy
- Adverse events

or who start a protocol prohibited medication/therapy, the baseline observation will be used as the subject's Week 16 value. For all other intercurrent events, the last valid observation while on treatment will be used as the Week 16 value.

[redacted]

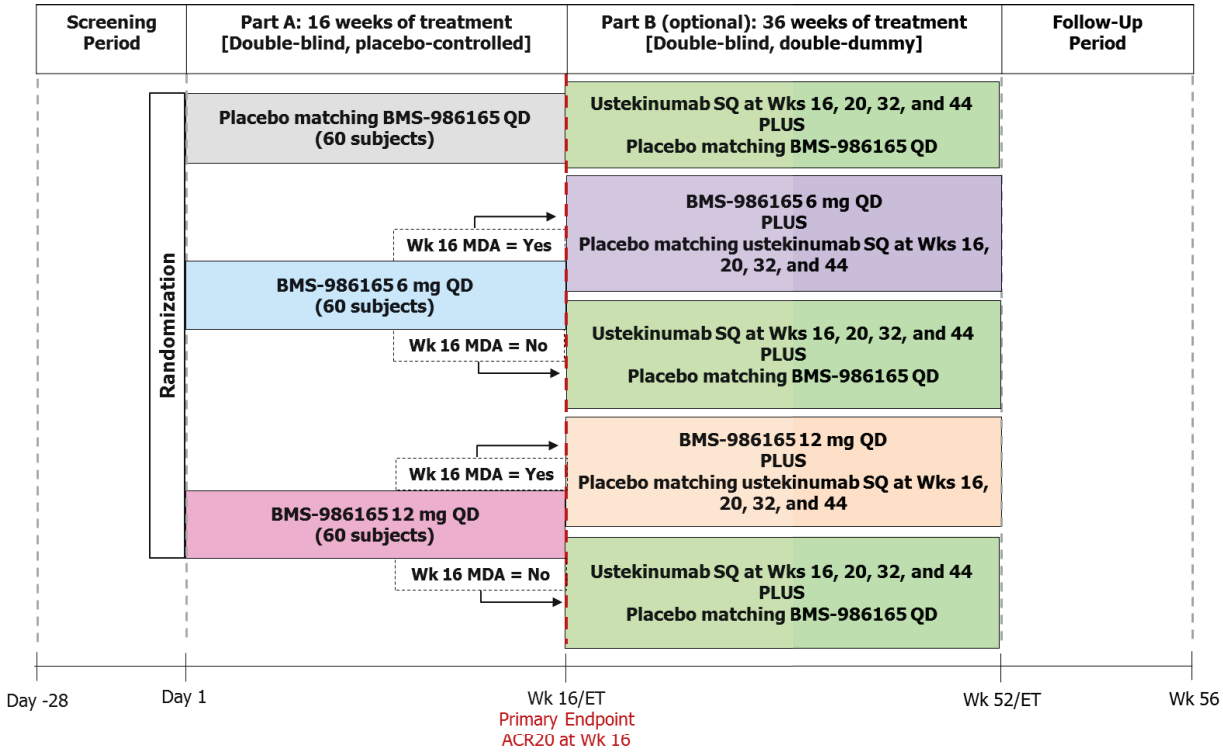
**Testing Strategy for Efficacy Endpoints:**

Statistical analysis of secondary endpoints will be performed in a hierarchical fashion. In order to preserve the overall Type I error rate, a fixed-sequence testing method will be implemented. Testing of secondary endpoints will occur sequentially and may only proceed to the next secondary endpoint if the null hypothesis is rejected at alpha = 0.10 (2-sided) for the prior endpoint showing a positive dose-response in that endpoint. If an endpoint fails at any step, then all subsequent p-values will be considered nominal.

**Safety Analysis:**

Treatment-emergent AEs (TEAEs) and SAEs will be summarized using counts and percentages of subjects experiencing the event as well as the number of events by system organ class, preferred term, and treatment group. Physical examination findings, vital signs, clinical laboratory test results, and ECG test results will be summarized using descriptive statistics (n, mean, standard deviation, median, minimum, and maximum) for continuous variables and frequency distributions (counts and percentages) for categorical variable.

## 1.2 Schema




Notes:
1) Subjects that complete Part A (16 weeks of treatment) will be offered the opportunity to enroll in Part B (36 weeks of treatment)
2) Completion of Week 16 of Part A and the start of Part B will occur on the same day
3) Subjects that complete Part A but decline Part B will proceed into the Follow-Up Period
4) Subjects who discontinue investigational product during Part A or Part B will have an Early Termination (ET) visit followed by the Follow-Up Period
5) Treatment assignment in Part B will depend on the subject's Part A randomized treatment as well as if the subject met MDA at Week 16 (Part A)
6) At Week 48, subjects will discuss with their Investigator/treating physician plans for treatment with ustekinumab following study completion. Subjects electing to take ustekinumab following study completion will receive either an ustekinumab SQ injection or placebo matching ustekinumab SQ injection at Week 52.

## 1.3 Schedule of Activities (SOA)

The schedules of assessments and procedures are documented in Table 1 for screening, Table 1 for baseline (Week 0) through Week 16 (Part A), and Table 3 for Week 16 through Week 52 (Part B).

**Table 1: Screening Procedural Outline IM011084**

| Procedure | Screening Visit | Notes |
|---|---|---|
| **Eligibility Assessments** | | |
| Informed Consent | X | A subject is considered enrolled only when a protocol-specific informed consent is signed |
| Enroll Subject in the interactive response technology (IRT) system | X | |
| Inclusion/Exclusion Criteria | X | Includes PsA Classification Criteria for Psoriatic Arthritis (CASPAR), active arthritis (tender/swollen joints), plaque psoriasis |
| PsA History, Treatment | X | PsA history to include investigator assessment of the subject's phenotype as peripheral arthritis or peripheral plus psoriatic spondyloarthritis.<br><br>History of: conventional synthetic DMARDs (e.g. MTX), biologic, and/or phototherapy.<br><br>For each therapy, include length of time on treatment and reason(s) for discontinuation (eg, lack of efficacy, intolerance, adverse events, loss of access to treatment) if applicable. |
| Other Medical History | X | See Section 5.1 for complete eligibility criteria associated with medical history. Of note, subjects need to be screened for: any current uncontrolled neuropsychiatric illness or history of suicidality; any history of TB; any congenital or acquired immunodeficiency; any significant drug allergy such as anaphylaxis; any cancer currently or in the previous 5 years. Investigators should check whether subjects have had preventive health measures such as cancer screening (eg, Pap smear, colonoscopy, mammograms) that are up-to-date according to local guidelines. Subjects who are not up to date should be encouraged to have up to date screenings conducted. |

**Table 1: Screening Procedural Outline IM011084**

| Procedure | Screening Visit | Notes |
|---|---|---|
| History of Tobacco Use | X | Include description of current tobacco use |
| [redacted] | X | [redacted] |
| **Safety Assessments** | | |
| Physical Examination | X | Complete PE |
| Physical Assessments | X | Includes height, weight, and BMI. |
| Vital Signs | X | Includes (ear or oral) body temperature, respiratory rate, and seated blood pressure and heart rate. Blood pressure and heart rate should be measured after the subject has been resting quietly for at least 5 minutes. |
| ECG | X | ECGs should be recorded after the subject has been supine for at least 5 minutes. |
| Chest Imaging (eg, Chest x-ray) | X | Chest imaging is required if not performed within 6 months of Screening visit, copy of radiology report must be on file and reviewed by the investigator. Section 8.4.4 |
| [redacted] | [redacted] | [redacted] |
| Serious Adverse Events Assessment | X | All SAEs must be collected from the date of subject's written consent until 28 days post discontinuation of dosing or subject's participation in the study. |
| Laboratory Tests | | Includes blood and urine samples. See Section 8.4.5. |
| Hematology | X | Complete Blood Count (CBC) with differential |
| Chemistry Panel | X | |

**Table 1: Screening Procedural Outline IM011084**

| Procedure | Screening Visit | Notes |
|---|---|---|
| Lipid Panel (Fasting) | X | Subjects are required to fast for at least 10 hours prior to collection |
| Urinalysis | X | |
| Hemoglobin A1c | X | |
| TSH | X | |
| hsCRP | X | |
| Serology | X | Includes HCV antibody, HBsAg, HBsAb, HBcAb, and HIV antibodies. |
| Tuberculosis Test | X | In accordance with QuantiFERON TB Gold. (details described in Section 8.4.4). |
| Pregnancy Test (Serum or Urine) | X | WOCBP only |
| FSH | X | For postmenopausal women only. Serum FSH level will be determined to confirm menopausal status (see APPENDIX 4) |
| [redacted] | | |
| [redacted] | [redacted] | |
| [redacted] | [redacted] | |
| [redacted] | [redacted] | |

BMI = body mass index; DMARD = disease-modifying antirheumatic drug; ECG = electrocardiogram; FSH = follicle-stimulating hormone; HBcAb = hepatitis B core antibody; HBsAb = hepatitis B surface antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; hsCRP = high-sensitivity C-reactive protein; PE = physical examination; PsA = psoriatic arthritis; RNA = ribonucleic acid; SAE = serious adverse event; TSH = Thyroid Stimulating Hormone; WOCBP = women of childbearing potential

**Table 1: Procedural Outline IM011084: Part A (Week 0 to Week 20)**

| Procedure | Week 0 D1 V2 | Week 1 D8 (± 3 d) V3 | Week 2 D15 (± 3 d) V4 | Week 4 D29 (± 3 d) V5 | Week 8 D57 (± 3 d) V6 | Week 12 D85 (± 3 d) V7 | Week 16 (or ET) D113 (± 3 d) V8 | Safety Follow-Up[e] (Week 20) D141 (±3 d) V9 | Notes |
|---|---|---|---|---|---|---|---|---|---|
| **Safety Assessments** | | | | | | | | | |
| Physical Examination | X | | | | | | | X | |
| Targeted Physical Examination | | X | X | X | X | X | X | | |
| Body Weight | X | | | | X | | X | X | |
| Vital Signs | X | X | X | X | X | X | X | X | |
| ECG | X | | | | | | X | | |
| [redacted] | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | |
| AE and SAE Assessment | X | X | X | X | X | X | X | X | |
| **Laboratory Tests** | | | | | | | | | |
| Hematology | X | X | X | X | X | X | X | X | |
| Chemistry Panel | X | X | X | X | X | X | X | X | Some visits may require fasting |
| Lipid Panel (Fasting) | X | | | X | | | X | | |
| Urinalysis | X | X | X | X | X | X | X | X | |
| Serum Immunoglobulin Levels (IgM, IgG, IgA, IgE) | X | | | | X | | X | | |
| Hemoglobin A1c | X | | | | | | X | | |
| Pregnancy Test (Urine or Serum) | X | | | X | X | X | X | X | WOCBP |
| TBNK | X | | | | X | | X | | |

**Table 1: Procedural Outline IM011084: Part A (Week 0 to Week 20)**

| Procedure | Week 0 D1 V2 | Week 1 D8 (± 3 d) V3 | Week 2 D15 (± 3 d) V4 | Week 4 D29 (± 3 d) V5 | Week 8 D57 (± 3 d) V6 | Week 12 D85 (± 3 d) V7 | Week 16 (or ET) D113 (± 3 d) V8 | Safety Follow-Up[e] (Week 20) D141 (±3 d) V9 | Notes |
|---|---|---|---|---|---|---|---|---|---|
| **Study Treatment** | | | | | | | | | |
| Randomize | X | | | | | | | | |
| Dispense Study Treatment | X | | X | X | X | X | | | |
| Study Treatment Compliance | X | X | X | X | X | X | X | | See Section 6.6 |
| [redacted] | | | | | | | | | |
| [redacted] | [redacted] | | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | | [redacted] |
| **Clinical Efficacy/Health Outcomes** | | | | | | | | | |
| ACR: Tender/Painful Joint Count (68) | X | X | X | X | X | X | X | | |
| ACR: Swollen Joint Count (66) | X | X | X | X | X | X | X | | |
| ACR: Subject Assessment of Pain | X | X | X | X | X | X | X | | |
| ACR: Physician Global Assessment of psoriatic arthritis | X | X | X | X | X | X | X | | |
| ACR: Subject Global Assessment of Disease Activity | X | X | X | X | X | X | X | | |

**Table 1: Procedural Outline IM011084: Part A (Week 0 to Week 20)**

| Procedure | Week 0 D1 V2 | Week 1 D8 (± 3 d) V3 | Week 2 D15 (± 3 d) V4 | Week 4 D29 (± 3 d) V5 | Week 8 D57 (± 3 d) V6 | Week 12 D85 (± 3 d) V7 | Week 16 (or ET) D113 (± 3 d) V8 | Safety Follow-Up[e] (Week 20) D141 (±3 d) V9 | Notes |
|---|---|---|---|---|---|---|---|---|---|
| ACR: hsCRP | X | X | X | X | X | X | X | | |
| ACR: HAQ-DI | X | X | X | X | X | X | X | | |
| Dactylitis (Count, LDI) | X | | | X | X | X | X | | |
| Enthesitis (LEI, SPARCC) | X | | | X | X | X | X | | |
| Nail Changes (PGA-F)[a] | X | | | X | X | X | X | | |
| PASI[b] | X | X | X | X | X | X | X | | |
| PASDAS | X | X | X | X | X | X | X | | |
| DAS 28 CRP | X | X | X | X | X | X | X | | |
| PsAID 12 | X | | X | X | | | X | | |
| MDA/VLDA | X | X | X | X | X | X | X | | |
| DAPSA | X | X | X | X | X | X | X | | |
| BASDAI[c] | X | X | X | X | X | X | X | | |
| SF-36 | X | | | | | | X | | |
| Fatigue (PROMIS-Fatigue or FACIT-Fatigue) | X | | | | | | X | | See Section 8.1.15 |
| WLQ (short form) | X | | | | | | X | | |
| RAPID3 | X | X | X | X | X | X | X | | |
| [redacted] | | | | | | | | | |
| [redacted] | [redacted] | | [redacted] | [redacted] | [redacted] | | [redacted] | | |

**Table 1: Procedural Outline IM011084: Part A (Week 0 to Week 20)**

| Procedure | Week 0 D1 V2 | Week 1 D8 (± 3 d) V3 | Week 2 D15 (± 3 d) V4 | Week 4 D29 (± 3 d) V5 | Week 8 D57 (± 3 d) V6 | Week 12 D85 (± 3 d) V7 | Week 16 (or ET) D113 (± 3 d) V8 | Safety Follow-Up[e] (Week 20) D141 (±3 d) V9 | Notes |
|---|---|---|---|---|---|---|---|---|---|
| [redacted] | ■ | | ■ | ■ | ■ | | ■ | | |
| [redacted] | ■ | | | | ■ | | ■ | | |
| [redacted] | ■ | | | | ■ | | ■ | | |
| [redacted] | ■ | | ■ | ■ | ■ | | ■ | | |

ACR = American College of Rheumatology; AE = adverse event; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; CV = cardiovascular; DAPSA = Disease Activity Index for Psoriatic Arthritis Score; DAS = Disease Activity Score; DNA = deoxyribonucleic acid; ECG = electrocardiogram; ET = early termination; FACIT = Functional Assessment of Chronic Illness Therapy; HAQ-DI = Health Assessment Questionnaire-Disability Index; hs-CRP = high-sensitivity C-reactive protein; LDI = Leeds Dactylitis Index; LEI = Leeds Enthesitis Index; MDA = Minimal Disease Activity; PASDAS = Psoriatic Arthritis Disease Activity Score; PASI = Psoriatic Area and Severity Index ; PGA-F = Physician Global Assessment-Fingernails; PROMIS = Patient Reported Outcome Measures Information System; PsA = psoriatic arthritis; PsAID = Psoriatic Arthritis Impact of Disease; RAPID3 = routine assessment of patient index data 3; RNA = ribonucleic acid; SAE = serious adverse events; SF-36 = Short Form Health Survey-36 Item; SPARCC = Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis index; TBNK = T cells, B cells, NK cells; V = visit; VLDA = very low disease activity; WLQ =Work limitation Questionnaire; WOCBP = women of childbearing potential

[a] In subjects with nail psoriasis at baseline

[b] In subjects with at least 3% body surface area (BSA) involvement at baseline

[c] In subjects with baseline evidence of PsA spondylitis

[d] If sample is missed, it may be taken at any visit once informed consent is obtained.

[e] Subjects that complete treatment in Part A and opt to enroll in Part B, will complete the Safety Follow-Up following completion of Part B

When multiple assessments are conducted at a single visit, the following is the order in which they should be done:

1) Health outcomes assessments
2) Safety assessments (eg, vitals, AEs)
3) Clinical efficacy assessments
4) Laboratory tests (eg, safety laboratory tests, [redacted])

On fasting days, safety assessments can be done first followed by blood draws, and then health outcomes and finally efficacy assessments. The dose of the drug on a visit day is to be taken after blood draws

**Table 3: Procedural Outline IM011084: Part B – Optional (Week 16 to Week 56)**

| Procedure | Week 16 D113 (± 3 d) V8 | Week 20 D141 (± 3 d) V9 | Week 24 D169 (± 3 d) V10 | Week 28 D197 (± 3 d) V11 | Week 32 D225 (± 3 d) V12 | Week 36 D253 (± 3 d) V13 | Week 40 D281 (± 3 d) V14 | Week 44 D309 (± 3 d) V15 | Week 48 D337 (± 3 d) V16 | Week 52 (or ET) D365 (± 3 d) V17 | Safety Follow-Up Week 56 D393 (±3 d) V18 | Notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Part A to Part B Transition** | | | | | | | | | | | | |
| Informed Consent | X | | | | | | | | | | | |
| **Safety Assessments** | | | | | | | | | | | | |
| Physical Examination | | X | | | | | | | | X | X | |
| Targeted Physical Examination | | | X | X | X | X | X | X | X | X | | |
| Body Weight | | X | | | | | | | | X | X | |
| Vital Signs | | X | X | X | X | X | X | X | X | X | X | |
| ECG | | X | | | | | | | | X | | |
| [redacted] | | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | |
| AE and SAE Assessment | X | X | X | X | X | X | X | X | X | X | X | |
| **Laboratory Tests** | | | | | | | | | | | | |
| Hematology | | X | X | X | X | X | X | X | X | X | X | |
| Chemistry Panel | | X | X | X | X | X | X | X | X | X | X | |
| Lipid Panel (Fasting) | | X | | | | | | | | X | | |
| Urinalysis | | | | | | X | | | | X | X | |
| Serum Immunoglobulin Levels (IgM, IgG, IgA, IgE) | | | | | | X | | | | X | | |

**Table 3: Procedural Outline IM011084: Part B – Optional (Week 16 to Week 56)**

| Procedure | Week 16 D113 (± 3 d) V8 | Week 20 D141 (± 3 d) V9 | Week 24 D169 (± 3 d) V10 | Week 28 D197 (± 3 d) V11 | Week 32 D225 (± 3 d) V12 | Week 36 D253 (± 3 d) V13 | Week 40 D281 (± 3 d) V14 | Week 44 D309 (± 3 d) V15 | Week 48 D337 (± 3 d) V16 | Week 52 (or ET) D365 (± 3 d) V17 | Safety Follow-Up Week 56 D393 (±3 d) V18 | Notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hemoglobin A1c | | | | | | X | | | | X | | |
| hs-CRP | | X | X | X | X | X | X | X | X | X | | |
| Pregnancy Test (Urine or Serum) | | X | X | X | X | X | X | X | X | X | X | WOCBP |
| TBNK | | | | X | | | X | | | X | | |
| **Study Treatment** | | | | | | | | | | | | |
| Randomize | | | | | | | | | | | | |
| Dispense Study Treatment | X | X | X | X | X | X | X | X | X | | | |
| Study Treatment Compliance | | X | X | X | X | X | X | X | X | X | | See Section 6.6 |
| [redacted] | | | | | | | | | | | | |
| [redacted] | [redacted] | [redacted] | [redacted] | | [redacted] | | [redacted] | | [redacted] | [redacted] | | [redacted] |

**Table 3: Procedural Outline IM011084: Part B – Optional (Week 16 to Week 56)**

| Procedure | Week 16 D113 (± 3 d) V8 | Week 20 D141 (± 3 d) V9 | Week 24 D169 (± 3 d) V10 | Week 28 D197 (± 3 d) V11 | Week 32 D225 (± 3 d) V12 | Week 36 D253 (± 3 d) V13 | Week 40 D281 (± 3 d) V14 | Week 44 D309 (± 3 d) V15 | Week 48 D337 (± 3 d) V16 | Week 52 (or ET) D365 (± 3 d) V17 | Safety Follow-Up Week 56 D393 (±3 d) V18 | Notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Clinical Efficacy/Health Outcomes** | | | | | | | | | | | | |
| ACR: Tender/Painful Joint Count (68) | | X | X | | X | | X | | | X | | |
| ACR: Swollen Joint Count (66) | | X | X | | X | | X | | | X | | |
| ACR: Patient Assessment of Pain | | X | X | | X | | X | | | X | | |
| ACR: Physician Global Assessment of psoriatic arthritis | | X | X | | X | | X | | | X | | |
| ACR: Subject Global Assessment of Disease Activity | | X | X | | X | | X | | | X | | |
| ACR: hs-CRP | | X | X | | X | | X | | | X | | |
| ACR: HAQ-DI | | X | X | | X | | X | | | X | | |
| Dactylitis (Count, LDI) | | X | X | | X | | X | | | X | | |
| Enthesitis (LEI, SPARCC) | | X | X | | X | | X | | | X | | |
| Nail Changes (PGA-F)[a] | | X | X | | X | | X | | | X | | |
| PASI[b] | | X | X | | X | | X | | | X | | |
| PASDAS | | X | X | | X | | X | | | X | | |
| DAS 28 CRP | | X | X | | X | | X | | | X | | |

**Table 3: Procedural Outline IM011084: Part B – Optional (Week 16 to Week 56)**

| Procedure | Week 16 D113 (± 3 d) V8 | Week 20 D141 (± 3 d) V9 | Week 24 D169 (± 3 d) V10 | Week 28 D197 (± 3 d) V11 | Week 32 D225 (± 3 d) V12 | Week 36 D253 (± 3 d) V13 | Week 40 D281 (± 3 d) V14 | Week 44 D309 (± 3 d) V15 | Week 48 D337 (± 3 d) V16 | Week 52 (or ET) D365 (± 3 d) V17 | Safety Follow-Up Week 56 D393 (±3 d) V18 | Notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PsAID 12 | | X | X | | | | | | | X | | |
| MDA/VLDA | | X | X | | X | | X | | | X | | |
| DAPSA | | X | X | | X | | X | | | X | | |
| BASDAI[c] | | X | X | | X | | X | | | X | | |
| SF-36 | | X | | | | | | | | X | | |
| Fatigue (PROMIS-Fatigue or FACIT-Fatigue) | | X | X | | | | | | | X | | See Section 8.1.15 |
| WLQ (short form) | | | | | | | | | | X | | |
| RAPID3 | | X | X | | X | | X | | | X | | |
| [redacted] | | | | | | | | | | | | |
| [redacted] | | ■ | ■ | | ■ | | ■ | | | ■ | | |
| [redacted] | | ■ | ■ | | ■ | | ■ | | | ■ | | |
| [redacted] | | | ■ | | ■ | | | | | | | |
| [redacted] | | ■ | ■ | | ■ | | ■ | | | ■ | | |
| [redacted] | | ■ | ■ | | ■ | | ■ | | | ■ | | |
| **Post-study Completion Ustekinumab Treatment?** | | | | | | | | | | | | |
| Post-study Ustekinumab Evaluation | | | | | | | | | X | | | |

**Table 3: Procedural Outline IM011084: Part B – Optional (Week 16 to Week 56)**

| Procedure | Week 16 D113 (± 3 d) V8 | Week 20 D141 (± 3 d) V9 | Week 24 D169 (± 3 d) V10 | Week 28 D197 (± 3 d) V11 | Week 32 D225 (± 3 d) V12 | Week 36 D253 (± 3 d) V13 | Week 40 D281 (± 3 d) V14 | Week 44 D309 (± 3 d) V15 | Week 48 D337 (± 3 d) V16 | Week 52 (or ET) D365 (± 3 d) V17 | Safety Follow-Up Week 56 D393 (±3 d) V18 | Notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dispense/Administer appropriate study treatment for all subjects that elect to be treated with ustekinumab post-study completion | | | | | | | | | | X | | |

ACR = American College of Rheumatology; AE = adverse event; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; CV = cardiovascular; DAPSA = Disease Activity Index for Psoriatic Arthritis Score; DAS = Disease Activity Score; DNA = deoxyribonucleic acid; ECG = electrocardiogram; ET = early termination; FACIT = Functional Assessment of Chronic Illness Therapy; HAQ-DI = Health Assessment Questionnaire-Disability Index; hs-CRP = high-sensitivity C-reactive protein; LDI = Leeds Dactylitis Index; LEI = Leeds Enthesitis Index; MDA = Minimal Disease Activity; PASDAS = Psoriatic Arthritis Disease Activity Score; PASI = Psoriatic Arthritis Severity Index ; PGA-F = Physician Global Assessment-Fingernails; PROMIS = Patient Reported Outcome Measures Information System; PsA = psoriatic arthritis; PsAID = Psoriatic Arthritis Impact of Disease; RAPID3 = routine assessment of patient index data 3; RNA = ribonucleic acid; SAE = serious adverse events; SF-36 = Short Form Health Survey-36 Item; SPARCC = Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis index; TBNK = T cells, B cells, NK cells; TB = tuberculosis; V = visit; VLDA = very low disease activity; WLQ =Work limitation Questionnaire; WOCBP = women of childbearing potential

[a] In subjects with nail psoriasis at baseline

[b] In subjects with at least 3% body surface area (BSA) involvement at baseline

[c] In subjects with baseline evidence of PsA spondylitis

When multiple assessments are conducted at a single visit, the following is the order in which they should be done:

1) Health outcomes assessments
2) Safety assessments (eg, vitals, AEs)
3) Clinical efficacy assessments
4) Laboratory tests (eg, safety laboratory tests, [redacted])

On fasting days, safety assessments can be done first followed by blood draws, and then health outcomes and finally efficacy assessments. The dose of the drug on a visit day is to be taken after blood draws.

# STUDY ACKNOWLEDGMENT/DISCLOSURE

I understand that this protocol contains information that is confidential and proprietary to Bristol-Myers Squibb Company (BMS). Any supplemental information that may be added to this document is also confidential and proprietary to BMS and must be kept in confidence in the same manner as the contents of this protocol.

I have read the original protocol/revised protocol and agree that it contains all necessary details for carrying out the study as described. I will conduct this protocol as outlined therein and will make a reasonable effort to complete the study within the time designated.

I will provide copies of the protocol and access to all information furnished by BMS to study personnel under my supervision. I will discuss this material with them to ensure that they are fully informed about the investigational product and the study.

I will provide protocol information to my Institutional Review Board(s) [IRB(s)] or Independent Ethics Committee(s) [IEC(s]. I understand that original protocol/revised protocols must be reviewed by the Institutional Review Board or Independent Ethics Committee overseeing the conduct of the study and approved or given favorable opinion by all necessary Health Authorities before implementation unless to eliminate an immediate hazard to subjects.

I agree that the contents of the protocol may not be disclosed to any other person or entity or used for any other purpose without the prior written consent of BMS. The foregoing shall not apply to disclosure required by governmental regulations or laws; however, I will give prompt notice to BMS of any such disclosure.

I agree that the study data derived from this protocol may only be used and disclosed in furtherance of the protocol, for the medical treatment of a study subject or for publication of study results in accordance with the terms of the clinical trial agreement or as otherwise permitted by the terms of the clinical trial agreement.

I agree not to collect or use samples (eg, tissue, blood, serum, urine) or collect data (other than for diagnostic or treatment purposes) from the study subjects while enrolled in the study, except as expressly permitted by the protocol or the terms of the clinical trial agreement.

I understand that I may terminate or suspend enrollment of the study at any time if it becomes necessary to protect the best interests of the study subjects. Unless otherwise provided in the clinical trial agreement, the study may be terminated at any time by BMS, with or without cause.

Original Protocol: ☐ Revised Protocol: ☒

Protocol Number: IM011084 Site Number:

Date of Protocol or Revised Protocol: TBD

IND Number: 137,445 EUDRACT Number: 2018-004293-10

Investigator: Date:

(signature)

(printed name)

[redacted]

# 3 OBJECTIVES AND ENDPOINTS

**Table 2: Objectives and Endpoints**

| Objectives | Endpoints |
|---|---|
| **Efficacy** | |
| *Primary* | |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg once daily [QD]) at Week 16 in the treatment of subjects with active PsA | • ACR 20 response |
| *Secondary* | |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in daily functional activities | • Change from baseline in HAQ-DI score |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in reducing PsO severity | • PASI 75 response |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in Patient-reported Outcomes | • Change from baseline in the Physical Component Summary (PCS) score of the SF-36 Questionnaire |
| *Additional* | |
| • Assess the extent of the dose-response relationship of BMS-986165 treatment (6 or 12 mg QD) at Week 16 in active PsA | • ACR 50 response<br>• ACR 70 response |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in DAS 28 CRP | • DAS 28 CRP Low Disease Activity<br>• DAS 28 CRP Remission<br>• Change from baseline in DAS 28 CRP score |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in dactylitis | • Change from baseline in dactylitis count<br>• Change from baseline in LDI Basic<br>• Dactylitis resolution |

| | |
|---|---|
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in enthesitis | • Change from baseline in enthesitis count by LEI and SPARCC index<br>• Enthesitis resolution by LEI and SPARCC |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in Physician's global assessment – fingernails (PGA-F) PsO | • PGA-F response of 0/1 |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in minimal disease activity (MDA) | • MDA response |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in psoriatic arthritis activity | • PASDAS<br>• DAPSA<br>• Psoriatic Arthritis Response Criteria (PsARC) |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in ankylosing spondylitis activity | • Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in Patient-Reported Outcomes | • SF-36 Score<br>  • Mental Component Summary (MCS)<br>• PsAID 12<br>• PROMIS-Fatigue where available or FACIT-Fatigue where PROMIS is not available<br>• Work Limitation Questionnaire (WLQ short form) |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in daily functional activities | • HAQ-DI 0.35 response |
| • Assess the dose-response relationship of BMS-986165 (6 or 12 mg QD) at Week 16 in reducing PsO severity | • PASI 90 response |
| **Safety** | |
| • To assess the safety and tolerability of BMS-986165 in subjects with active PsA | • Incidence of adverse events (AEs), serious AEs (SAEs), AEs leading to study discontinuation, and target AEs of interest (AEIs)<br>• Change in laboratory, electrocardiogram (ECG), physical examination, and vital sign |

# 4 STUDY DESIGN

## 4.1 Overall Design

This is a 16-week (Part A) randomized, double-blind, placebo-controlled, multicenter study to evaluate the safety and efficacy of multiple doses of BMS-986165 in subjects with active PsA. A total of approximately 180 subjects with active PsA will be randomized in Part A. This Phase 2 study will be conducted in a mixed population of subjects with active PsA who have either not

received prior treatment with a biologic (biologic-naïve, approximately 70%) or who have failed or been intolerant to 1 TNF-inhibitor (TNFi-experienced, approximately 30%). In addition, investigators will need to specify if the subject's phenotype is peripheral arthritis or peripheral plus psoriatic spondyloarthritis.

The total duration of participation in Part A is approximately 24 weeks and will be divided into the following periods: screening (up to 4 weeks), double-blind placebo-controlled treatment for 16 weeks (Week 1 to Week 16, Part A), and follow-up (up to 4 weeks). Subjects completing double-blind treatment in Part A will have an opportunity to enroll in an optional double-blind double-dummy Part B. Treatment in Part B will be given for up to 36 weeks (Week 16 to Week 52). For subjects completing both Part A and B of the study, the anticipated study duration is approximately 60 weeks: screening (up to 4 weeks), double-blind placebo-controlled treatment for 16 weeks (Week 1 to Week 16, Part A), double-blind double-dummy treatment for 36 weeks (Week 16 to Week 52, Part B), and follow-up (up to 4 weeks).

Part A

Subjects will undergo screening evaluations to determine eligibility within 28 days prior to administration of study medication. Following the screening process, if subjects are eligible for randomization then subjects will be randomized in a 1:1:1 ratio (approximately 60 subjects per arm) to 1 of the following 3 treatment groups:

- Placebo
- BMS-986165 6 mg QD
- BMS-986165 12 mg QD

Randomization will be stratified by TNFi use (experienced/naïve) and body weight (≥ 90 kg and < 90 kg).

The primary endpoint is ACR 20 response at Week 16.

In Part A, subjects who discontinue study treatment early for any reason other than consent withdrawal will be expected to complete the ET visit followed by the safety follow-up period.

Part B

At Week 16, subjects will have the option to participate in the double-blind Part B of the study. All subjects who receive placebo in Part A will receive ustekinumab in Part B according to approved labeling for PsA; subjects who receive BMS-986165 in Part A and achieve MDA will continue treatment with BMS-986165 at the same dose in Part B, and subjects who receive BMS-986165 in Part A and fail to achieve MDA will receive ustekinumab in Part B. The treatment assignment in Part B will be double-blind, double-dummy as follows

- Placebo in Part A: ustekinumab subcutaneous (SQ) injection plus placebo matching BMS-986165 QD in Part B

- BMS-986165 6 mg QD in Part A with MDA at Week 16: BMS-986165 6 mg QD plus placebo matching ustekinumab SQ injection in Part B
- BMS-986165 6 mg QD in Part A without MDA at Week 16: ustekinumab SQ injection plus placebo matching BMS-986165 QD in Part B
- BMS-986165 12 mg QD in Part A with MDA at Week 16: BMS-986165 12 mg QD plus placebo matching ustekinumab SQ injection in Part B
- BMS-986165 12 mg QD in Part A without MDA at Week 16: ustekinumab SQ injection plus placebo matching BMS-986165 QD in Part B

In Part B at Week 28, at the discretion of the investigator, the study design provides for rescue therapy for relief of joint symptoms with nonsteroidal anti-inflammatory drugs (NSAIDs), intra-articular injections of steroids, systemic glucocorticoids, or DMARDs, as follows:

- NSAIDs may be added or the dose may be increased according to labeling guidelines
- A single oral tapering dose of glucocorticosteroid (no greater than 20 mg of prednisone [or prednisone equivalent]) per day, not to exceed 2 weeks
- An intra-articular dose of glucocorticoids (no greater than 40 mg methylprednisolone or 40 mg of triamcinolone [or methylprednisolone or triamcinolone equivalent]) into 1 joint or divided into 2 joints
- A single intramuscular dose of glucocorticoids (no greater than 40 mg methylprednisolone or 40 mg of triamcinolone [or methylprednisolone or triamcinolone equivalent])
- DMARD treatment may not be started; however:
    - If already taking MTX, an increase in dose is allowed (maximum of 25 mg weekly)
    - If already taking sulfasalazine, an increase in dose is allowed

Subjects who need rescue therapy or additional therapy for PsA and/or flares after the Week 28 timepoint of Part B will be discontinued from the study.

At Week 48, subjects will discuss with their investigator/treating physician plans for treatment with ustekinumab after study completion. In order to maintain the study blind and to ensure continuity of care for those electing to be treated with ustekinumab after the study completion (ie, completion of the Week 56 visit), the following Week 52 procedure should be performed:

- Subjects that **elect to be treated** with ustekinumab following study completion will receive the following treatment at Week 52:
    - Subjects that were on ustekinumab treatment in Part B will receive a placebo matching ustekinumab SQ injection
    - Subjects that were on BMS-986165 6 mg or BMS-986165 12 mg treatment in Part B will receive an ustekinumab SQ injection
- Subjects that **elect not to be treated** with ustekinumab after the study will not receive any treatment at Week 52 (regardless of the treatment that they received in Part B).

Following completion of the Week 56 visit (ie, at the conclusion of the follow-up period of the study), subjects that elected to be treated with ustekinumab following study completion, will be due for their ustekinumab injection, as follows:

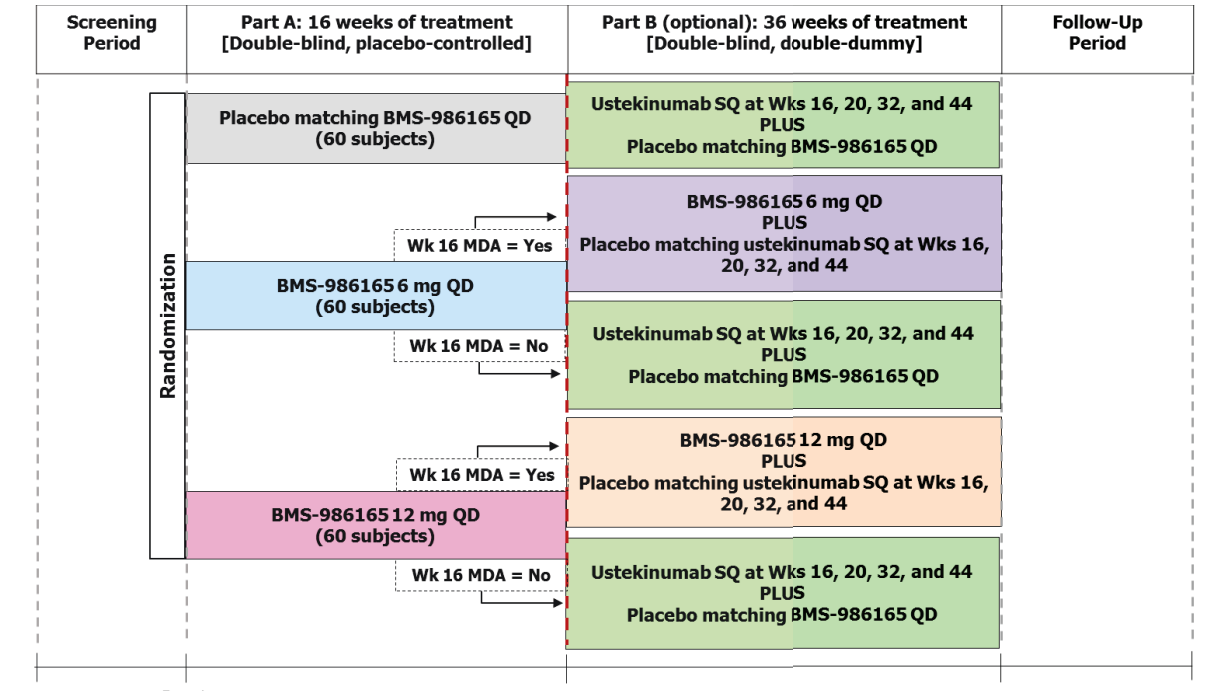
- Subjects that were on ustekinumab treatment in Part B will be due for their next scheduled (12-week) dose of ustekinumab SQ injection following completion of the Week 56 visit
- Subjects that were on BMS-986165 6 mg or BMS-986165 12 mg treatment in Part B will be due for their next scheduled (4-week) dose of ustekinumab SQ injection following completion of the Week 56 visit

**Note:** Ustekinumab treatment at Week 56 and beyond will be part of standard of care and will not be provided by the study Sponsor.

In Part B, subjects who discontinue study treatment early for any reason other than consent withdrawal will be expected to complete the ET visit followed by the safety follow-up period.

The study design schematic is presented in Figure 1.

**Figure 1 Study Design Schematic**




Notes:
1) Subjects that complete Part A (16 weeks of treatment) will be offered the opportunity to enroll in Part B (36 weeks of treatment)
2) Completion of Week 16 of Part A and the start of Part B will occur on the same day
3) Subjects that complete Part A but decline Part B will proceed into the Follow-Up Period
4) Subjects who discontinue investigational product during Part A or Part B will have an Early Termination (ET) visit followed by the Follow-Up Period
5) Treatment assignment in Part B will depend on the subject's Part A randomized treatment as well as if the subject met MDA at Week 16 (Part A)
6) At Week 48, subjects will discuss with their Investigator/treating physician plans for treatment with ustekinumab following study completion. Subjects electing to take ustekinumab following study completion will receive either an ustekinumab SQ injection or placebo matching ustekinumab SQ injection at Week 52.

### 4.1.1 Data Monitoring Committee and Other External Committees

#### 4.1.1.1 Data Monitoring Committee

An external independent Data Monitoring Committee (DMC) with multi-disciplinary representation will be established to evaluate safety data on a periodic basis. An independent reporting statistician not involved in the conduct of the study will be designated to provide the DMC with essential unblinded to treatment group safety data during the study.

Details of DMC responsibilities, timing of safety reviews, authorities, and procedures will be specified in the DMC charter.

#### 4.1.1.2 Infection Adjudication Committee

An independent Infection Adjudication Committee, composed of individuals with relevant expertise, will review and adjudicate infection AEs, such as opportunistic infections, influenza, herpes zoster, and TB, reported in the study. Additional information about these infections may be collected on the case report form (CRF) in order to characterize and understand them. The Adjudication Committee members will be blinded to the treatment assignment of subjects. The structure, responsibilities, and procedures of the Adjudication Committee will be outlined in a charter. The Adjudication Committee is distinct from the DMC and Adjudication Committee members will not be investigators on the study.

#### 4.1.1.3 Cardiovascular (CV) Adjudication Committee

An independent cardiovascular (CV) Adjudication Committee, composed of individuals with relevant expertise, will review and adjudicate CV and cerebrovascular AEs such as, but not limited to, Major Adverse Cardiovascular Events (MACE) that include death, nonfatal myocardial infarction, nonfatal stroke; revascularization procedures; heart failure; dysrhythmias; heart blocks; and thrombotic events reported in the study. Additional information about CV and cerebrovascular AEs may be collected on the CRF in order to characterize and understand them. The Adjudication Committee members will be blinded to the treatment assignment of subjects. The structure, responsibilities, and procedures of the Adjudication Committee will be outlined in a charter. The Adjudication Committee is distinct from the DMC and Adjudication Committee members will not be investigators on the study.

## 4.2 Number of Subjects

Approximately 180 qualified subjects will be randomized in a 1:1:1 ratio in Part A to BMS-986165 6 mg QD, BMS-986165 12 mg QD, or placebo matching BMS-986165 QD, respectively. Sample size considerations are described in Section 9.1. All subjects completing Part A will have the option to enroll in Part B.

## 4.3 End of Study Definition

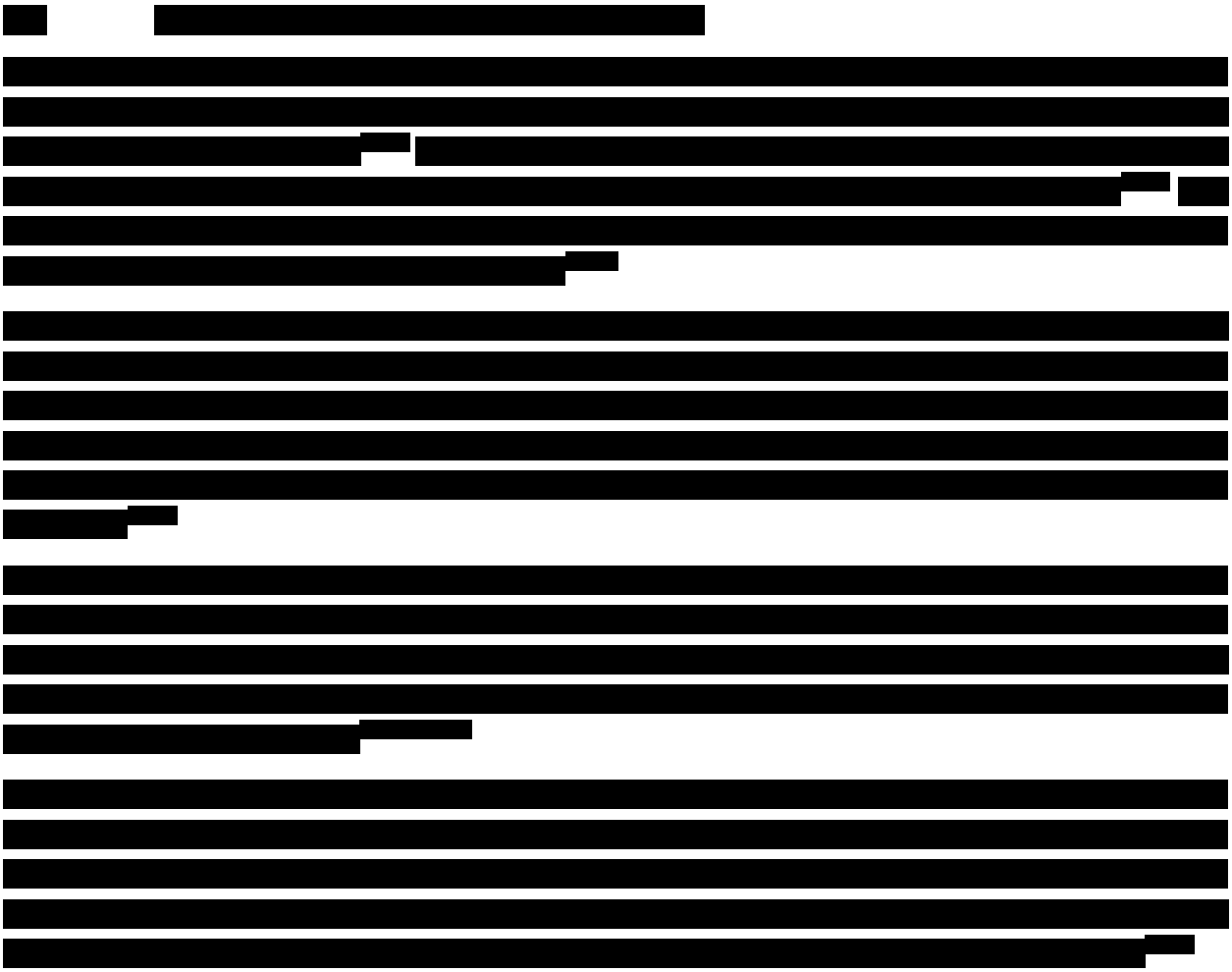
The duration of study participation in Part A for individual subjects is expected to be 24 weeks (168 days), which includes screening (up to 4 weeks), treatment (16 weeks) and follow-up (up to 4 weeks) periods.

For subjects who continue in Part B of the study, the total duration of study participation is expected to be up to 60 weeks (420 days), which includes screening (up to 4 weeks), double-blind treatment (16 weeks, Part A; 36 weeks, Part B), and follow-up (up to 4 weeks) periods.

The start of the study is defined as first visit for first subject screened. The end of the study is defined as the last visit or scheduled procedure shown in the Schedule of Activities (Section 1.3) for the last subject.

For subjects who do not continue in Part B of the study, study completion is defined as the final date on which data was or is expected to be collected (Week 20 for collection of potential SAEs).

For subjects who continue in Part B of the study, study completion is defined as the final date on which data was or is expected to be collected (Week 56 for collection of potential SAEs).



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# 5 STUDY POPULATION

## 5.1 Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

**1) Signed Written Informed Consent**

a) Subjects must be willing to participate in the study and sign the informed consent form (ICF)

**2) Type of Subject and Target Disease Characteristics**

a) Diagnosed with PsA for at least 6 months before screening, and who meet the Classification Criteria for Psoriatic Arthritis (CASPAR) at screening.

b) Subjects either (i) cannot have prior exposure to biologics (biologic-naïve) or (ii) have failed or been intolerant to 1 TNF-inhibitor (TNFi-experienced). Failure is defined as lack of response or loss of response with at least 3 months of therapy with an approved dose of a TNFi, as judged by the investigator. Failure must have occurred at least 2 months prior to Day 1. Note: If a prospective subject was previously exposed to a second TNFi and discontinued for reasons other than intolerance or lack of response (eg, used < 3 months), the Medical Monitor should be contacted to discuss whether the subject should be enrolled.

c) Subjects have at least 1 confirmed ≥ 2 cm lesion of plaque psoriasis at screening

d) Subjects have active arthritis as shown by a minimum of ≥ 3 swollen joints and ≥ 3 tender joints (66/68 joint counts) at screening and Day 1 (APPENDIX 5)

e) High sensitivity C-reactive protein (hsCRP) ≥ 3mg/L at screening

f) If on a conventional non-biologic DMARD (eg, MTX, leflunomide, sulfasalazine or hydroxychloroquine) subjects can only take 1 DMARD. The DMARD must have been used for at least 3 months with a stable dose for at least 28 days prior to Day 1

g) Have failed or been intolerant to at least 1 non-biologic DMARD (or had to stop because of pregnancy or lactation but still eligible for the trial), NSAID and/or corticosteroid

h) If using an NSAID, the dose must be stable for at least 14 days before Day 1 and consistent with labeling recommendations

i) If using oral corticosteroids (≤ 10 mg/day prednisone equivalent), the dose must be stable for at least 14 days before Day 1

j) Concurrent topical therapy for plaque psoriasis must have been stable for at least 14 days before Day 1. Note: Only low potency (Class V or higher) topical corticosteroids are permitted and restricted to use solely on the palms, soles, face and intertriginous areas.

Bland emollients (without urea or alpha or beta hydroxy acids, eg, salicylic acid) can be used on skin lesions. These should not be used within 24 hours prior to any study visit.

k) Treatment with targeted synthetic disease-modifying antirheumatic drugs (eg, apremilast) is not permitted during the study, but subjects who have previously received apremilast could be eligible if treatment has been discontinued at least 4 weeks prior to Day 1.

**3) Age and Reproductive Status**

a) Men and women aged ≥18 years at screening

b) Women of childbearing potential (WOCBP) must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of human chorionic gonadotropin [HCG]) within 24 hours prior to the start of study treatment.

c) Women must not be pregnant, lactating, breastfeeding or be planning pregnancy during the study period

d) Women of childbearing potential (WOCBP) must agree to follow instructions for method(s) of contraception (APPENDIX 4) for the duration of treatment with study drugs and until the end of relevant systemic exposure plus 5 half-lives of study drug plus 30 days (duration of ovulatory cycle) post-treatment completion. Therefore, in Part A, WOCBP must agree to follow instructions for methods of contraception for 33 days post-treatment completion and, in Part B, WOCBP must agree to follow instructions for methods of contraception for 190 days after completion of treatment.

i) Note:

(1) Local laws and regulations may require use of alternative and/or additional contraception methods; additionally, alternative and/or additional contraceptive may be required eg, based on background DMARDS the subject may be taking, such as methotrexate, leflunomide, etc.

(2) WOCBP who are continuously not heterosexually active are also exempt from contraceptive requirements, but must still undergo pregnancy testing as described in this section.

e) Males who are sexually active with WOCBP must also agree to follow instructions for method(s) of contraception (APPENDIX 4) for the duration of treatment with study drugs and until the end of relevant systemic exposure. Therefore, in Part A, male subjects must agree to follow instructions for methods of contraception for 93 days (5 half-lives of study treatment plus duration of sperm turnover) after end of treatment, and in Part B, for 250 days after end of treatment.

i) Note:

(1) Local laws and regulations may require use of alternative and/or additional contraception methods; eg, based on background DMARDS the subject may be taking, such as methotrexate, leflunomide, etc.

(2) Male subjects must be willing to refrain from sperm donation during this time.

Investigators shall counsel WOCBP, and male subjects who are sexually active with WOCBP, on the importance of pregnancy prevention and the implications of an unexpected pregnancy. Investigators shall advise on the use of highly effective methods of contraception, which have a failure rate of < 1% when used consistently and correctly.

## 5.2 Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

**1) Target Disease Exceptions**

a) Has non-plaque psoriasis (ie, guttate, inverse, pustular, erythrodermic or drug-induced psoriasis) at screening or Day 1

b) Has any other autoimmune condition such as rheumatoid arthritis, etc. There are exceptions for inflammatory bowel disease or uveitis as follows: currently active disease is excluded but, a history of no longer active disease for at least 12 months (including not being on medication) is allowed

c) Has active (ie currently symptomatic) fibromyalgia

**2) Infectious/Immune-related Exclusions**

a) History or evidence of active infection and/or febrile illness within 7 days prior to Day 1 (eg, bronchopulmonary, urinary, gastrointestinal, etc.)

b) History of recent serious bacterial, fungal, or viral infections requiring hospitalization and intravenous (IV) antimicrobial treatment within 90 days prior to screening, or any infection requiring antimicrobial treatment within 15 days prior to Day 1

c) Any bacterial infection within the last 60 days prior to screening, unless treated and resolved with antibiotics, or any chronic bacterial infection such as chronic pyelonephritis, osteomyelitis, and bronchiectasis

d) Received live vaccine(s) within 60 days prior to Day 1, or plans to receive a live vaccine during the study, or within 60 days after completing Part A, or within 15 weeks of receiving the last dose of Part B treatment

e) Presence of herpes simplex lesions or herpes zoster at screening or Day 1

f) History of severe herpes zoster or severe herpes simplex infection, which includes, but is not limited to, any episode of disseminated herpes simplex, multidermatomal herpes zoster, herpes encephalitis, ophthalmic herpes, or recurrent herpes zoster (defined as 2 episodes within 2 years)

g) Evidence of, or test positive for, hepatitis B. Positive hepatitis B lab testing is defined as 1) Positive Hepatitis B Surface Antigen (HbsAg+) or 2) Presence of Hepatitis B Virus DNA or 3) Positive anti-hepatitis B core antibody without concurrent positive hepatitis B surface antibody (HbcAb+ and HbsAb-) or 4) Positive anti-hepatitis B core antibody and

positive hepatitis B surface antibody with elevated liver transaminases (HbcAb+, HbsAb+, and abnormal ALT and AST)

h) Evidence of, or test positive for, hepatitis C virus (HCV). A positive test for HCV is defined as: 1) positive for hepatitis C antibody (anti-HCVAb), and 2) positive via a confirmatory test for HCV (for example, HCV polymerase chain reaction)

i) Positive for human immunodeficiency virus antibody (HIVAb) at screening

j) Any history of known or suspected congenital or acquired immunodeficiency state or condition that would compromise the subject's immune status (eg, infections with *Pneumocystis jirovecii* pneumonia, histoplasmosis, or coccidioidomycosis, history of splenectomy, primary immunodeficiency, etc.)

3) **Any of the following tuberculosis (TB) criteria:**

a) History of active TB prior to screening visit, regardless of completion of adequate treatment

b) Signs or symptoms of active TB (eg, fever, cough, night sweats, and weight loss) during screening as judged by the investigator

c) Any imaging of the chest (eg, chest x-ray, chest computed tomography [CT] scan) obtained during the screening period, or anytime within 6 months prior to Screening with documentation, showing evidence of current active or old pulmonary TB

d) Latent TB infection (LTBI) defined as positive IFN gamma release assay (IGRA), by QuantiFERON-TB Gold testing at screening, in the absence of clinical manifestations

Note: Subject may be eligible if (i) there are no current signs or symptoms of active TB and (ii) subject has received adequate documented treatment for LTBI within 5 years of screening or has initiated prophylactic treatment for LTBI per local guidelines and is rescreening now after 1 month of treatment. To continue in the study, subject must agree to complete a locally-recommended course of treatment for LTBI.

Note: An IGRA test that is indeterminate with no signs or symptoms of active TB must be re-tested for confirmation. If the second test is again indeterminate the subject will be excluded from the study. If the re-test is positive, the subject should be treated as having LTBI. If the re-test is negative, subject may be eligible provided no other exclusion criteria for TB are met.

**4) Medical History and Concurrent Diseases**

a) If the subject is biologic-experienced, the following exclusion criteria will apply:

i) History of use of antibodies to IL-12, IL-17, or IL-23 (eg, ustekinumab, secukinumab, bimekizumab, tildrakizumab, risankizumab, ixekizumab, or guselkumab)

ii) TNF-inhibitor(s) (eg, etanercept, adalimumab, infliximab, certolizumab, golimumab) within 2 months of Day 1

iii) History of use of agents that modulate lymphocyte trafficking (eg, natalizumab, efalizumab), or agents that modulate B cells or T cells (eg, alemtuzumab, abatacept, alefacept, or visilizumab)

b) If the subject is biologic-naïve: has received any biologic immunomodulatory treatment, eg, anti-TNF agents, anti-IL-23 agents, anti-IL-17 agents

c) Any major surgery within 4 weeks prior to Day 1, or any planned surgery during the study

d) Has donated blood > 500 mL within 4 weeks prior to Day 1, or intends to donate blood during the course of the study

e) Drug or alcohol abuse, as determined by the investigator within 6 months prior to Day 1 (Note: medical marijuana is not allowed)

f) Any major illness/condition or evidence of an unstable clinical condition (eg, renal, hepatic, hematologic, gastrointestinal, endocrine, pulmonary, psychiatric, immunologic, or local active infection/infectious illness) that, in the investigator's judgment or after consultation with the Medical Monitor, will substantially increase the risk to the subject if he or she participates in the study

g) Unstable CV disease, defined as a recent clinical deterioration (eg, unstable angina, myocardial infarction, stroke, rapid atrial fibrillation) in the last 3 months prior to screening, or a cardiac hospitalization within the 3 months prior to screening

h) Has uncontrolled arterial hypertension characterized by a systolic blood pressure (BP) > 160 mm Hg or diastolic BP > 100 mm Hg

Note: Determined by 2 consecutive elevated readings. If an initial BP reading exceeds this limit, the BP may be repeated once after the subject has rested sitting for ≥10 minutes. If the repeat value is less than the criterion limits, the second value may be accepted

i) Class III or IV congestive heart failure by New York Heart Association Criteria

j) History of cancer (solid organ or hematologic including myelodysplastic syndrome) or lymphoproliferative disease within the previous 5 years. Exception: subjects with resected cutaneous basal cell or squamous cell carcinoma, or carcinoma of cervix in situ that has been treated with no evidence of recurrence can be included

k) Any other sound medical, and/or social reason as determined by the investigator

l) Prior exposure to the investigational product (IP, ie, BMS-986165)

m) Has received any JAK inhibitors, eg baricitinib, tofacitinib, upadacitinib, etc

n) Has received systemic psoriasis medications other than biologics and/or any systemic immunosuppressants therapy (including, but not limited to, azathioprine, cyclosporine, 6-thioguanine, mercaptopurine, mycophenolate mofetil, hydroxyurea, tacrolimus, injectable corticosteroids, retinoids, 1,25-dihydroxy vitamin D3 and analogues, psoralens, or fumaric acid derivatives) within 4 weeks prior to Day 1

o) Use of any opioid analgesic at average daily doses of > 30 mg/day of morphine or its equivalent or use of variable doses of any opiate analgesic within 6 weeks prior to Day 1

p) Has received phototherapy (including either oral and topical psoralen ultraviolet A [PUVA] light therapy, ultraviolet B [UVB] or self-treatment with tanning beds or therapeutic sunbathing) within 4 weeks prior to Day 1

q) Has used topical medications/treatments that could affect psoriasis evaluation, including, but not limited to, high potency corticosteroids (Class I or higher), anthralin, calcipotriene, topical vitamin D derivatives, retinoids, tazarotene, methoxsalen, trimethylpsoralen, picrolimus, and tacrolimus, within 2 weeks of Day 1

Note: As stated above, low potency topical steroids (Class V and higher) are permitted on the palms, soles, face and intertriginous areas as well as bland emollients [without urea or alpha or beta hydroxy acids]); those should not be used within 24 hours prior to any study visit

r) Use of shampoos that contain corticosteroids, coal tar, or vitamin D3 analogues within 2 weeks prior to Day 1

s) Has received any experimental therapy or new investigational agent within 30 days or 5 half-lives (whichever is longer) prior to Day 1 or is currently enrolled in an investigational study

**5) Physical and Laboratory Test Findings**

a) Absolute white blood cell (WBC) count < 3000/$mm^3$ at screening

b) Absolute lymphocyte count < 500/$mm^3$ at screening

c) Absolute neutrophil count < 1000/$mm^3$ at screening

d) Platelet count < 100,000/$mm^3$ at screening

e) Hemoglobin < 9 g/dL at screening

f) ALT and/or AST > 2x upper limit of normal (ULN) at screening

g) Total, unconjugated, and/or conjugated bilirubin > 1.5 × upper limit of normal (ULN) at screening

h) Estimated glomerular filtration rate (eGFR) < 45 mL/min

i) Any other significant laboratory or procedure abnormalities that, in the opinion of the investigator, might place the subject at unacceptable risk for participation in this study

**6) Allergies and Adverse Drug Reactions**

a) History of any significant drug allergy or intolerance (such as anaphylaxis)

**7) Other Exclusion Criteria**

a) Prisoners or subjects who are involuntarily incarcerated. (Note: under certain specific circumstances a person who has been imprisoned may be included or permitted to continue as a subject. Strict conditions apply and BMS approval is required)

b) Subjects who are compulsorily detained for treatment of either a psychiatric or physical (eg, infectious disease) illness

c) Inability to comply with restrictions and prohibited activities/treatments as listed in Section 5.3.

d) Site personnel or their immediate family

## 5.3 Lifestyle Restrictions

General skin care measures (with above restrictions for topical treatments) are recommended that are standard for patients with plaque psoriasis. Subjects should avoid excessive sun exposure and avoid risks that are known to provoke flare of psoriasis.

### *5.3.1 Meals and Dietary Restrictions*

Study treatment may be taken without regard to meals, however, subjects are required to fast for a minimum of 10 hours before visits on which fasting lipid, fasting glucose, and post-dose PK samples will be drawn. Details are provided in Section 8.5.

### *5.3.2 Caffeine, Alcohol, and Tobacco*

No restrictions are required; however, extensive use of caffeine, alcohol, and tobacco should be avoided.

### *5.3.3 Activity*

No restrictions are required; however, unusual physical exertion should be avoided during the study.

## 5.4 Screen Failures

Screen failures are defined as subjects who consent to participate in the clinical study but who are not subsequently randomized in the study. A minimal set of screen failure information is required to ensure transparent reporting of screen failure subjects, to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements, as applicable, and to respond to queries from regulatory authorities. Minimal information includes date of consent, demography, screen failure details, eligibility criteria, and any serious AEs.

### *5.4.1 Retesting During Screening or Lead-in Period*

For laboratory parameters that initially do not meet eligibility requirements, a single retest within the 28-day screening period is permitted before subject is declared a screen failure. This is an effort to find all possible well-qualified subjects. Consultation with the Medical Monitor may be needed to identify whether repeat testing of any particular parameter would be clinically relevant.

The study permits the rescreening (after the end of the initial 28-day screening period) of a subject who discontinues the study as a pretreatment failure (ie, the subject fails to meet eligibility criteria and has not been treated). The subject must be reconsented, will be assigned a new identification number, and a full screening visit must be performed again. A subject can only be rescreened 1 time (ie, if the subject fails 1 rescreening attempt, no additional rescreening is allowed). Duration

of existing treatments and required discontinuation periods shall be considered relative to the new screening visit and/or randomization.

The most current result prior to randomization is the value by which study inclusion will be assessed, as it represents the subject's most current, clinical state.

Rescreening is allowed once with consultation with the Medical Monitor.

# 6 TREATMENT

Study treatment is defined as any investigational treatment(s), marketed product(s), placebo or medical device intended to be administered to a study subject according to the study randomization or treatment allocation.

Study treatment for IM011084 includes both Investigational [Medicinal] Product (IP/IMP) and Noninvestigational [Medicinal] Product (Non-IP/Non-IMP) as shown in Table 3.

An IP, also known as IMP in some regions, is defined as a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical study, including products already with a marketing authorization but used or assembled (formulated or packaged) differently than the authorized form, or used for an unauthorized indication, or when used to gain further information about the authorized form.

Other medications used as support or escape medication for preventative, diagnostic, or therapeutic reasons, as components of the standard of care for a given diagnosis, may be considered as non-IPs.

**Table 3: Study Treatments for IM011084**

| Product Description/ Class and Dosage Form | Potency | IP/Non-IMP | Blinded or Open Label | Packaging/ Appearance | Storage Conditions (per label) |
|---|---|---|---|---|---|
| BMS-986165 6 mg tablet | 6 mg | IP | Blinded | Blister Card | Store at 15 to 25°C; Protect from light |
| Placebo matching BMS-986165 6 mg tablet | n/a | IP | Blinded | Blister Card | Store at 15 to 25°C; Protect from light |
| BMS-986165 12 mg tablet | 12 mg | IP | Blinded | Blister Card | Store at 15 to 25°C; Protect from light |
| Placebo matching BMS-986165 12 mg tablet | n/a | IP | Blinded | Blister Card | Store at 15 to 25°C; Protect from light |
| Ustekinumab for subcutaneous injection[a] | 45 mg | IP | Blinded | Vials for Injection | Store at 2ºC to 8ºC, Protect from light, Do not freeze, Do not shake |
| Normal saline[a,b] | n/a | IP | Blinded | Per manufacturers specifications | Per manufacturers specifications |

[a] These products may be obtained by the investigational sites as local commercial products in certain countries if allowed by local regulations. In these cases, products may be in a different pack size/potency/pharmaceutical form than listed in the table. These products should be prepared/stored/administered in accordance with the package inserts or summaries of product characteristics

[b] Normal saline will be used as the placebo for ustekinumab

## 6.1 Treatments Administered

### *6.1.1 Dose Schedule for Part A*

In Part A, subjects will take BMS-986165 12 mg QD, 6 mg QD, or placebo matching BMS-986165over 16 weeks (Table 4).

Study treatment will be dispensed and administered in a double-blind fashion as described in Section 4.1. As the blister cards provided to the sites will be double-blind, all dispensing must be performed via the interactive response technology (IRT) system. Blister cards will be dispensed at Weeks 0, 2, 4, 8, and 12. An adequate supply of blister cards will be dispensed to cover the subject until their next scheduled visits.

The tablets will be arranged into sets and the subject will be instructed to take 2 tablets daily in the morning (total of 2 tablets daily). Any missed dose should be taken within the next 6 hours. If the subject is unable to take this dose within this time period, the subject should skip this dose. Any missed dose should be returned at the next study visit.

**Table 4: Part A – Treatment Group and Dosing**

| Treatment Group | Product Description | Potency | Blinded or Open Label | Frequency |
|---|---|---|---|---|
| **Placebo** | Placebo matching BMS-986165 6 mg | n/a | Blinded | Daily Morning |
| | Placebo matching BMS-986165 12 mg | n/a | Blinded | Daily Morning |
| **BMS-986165 6 mg QD** | BMS-986165 6 mg tablet | 6 mg | Blinded | Daily Morning |
| | Placebo matching BMS-986165 12 mg | n/a | Blinded | Daily Morning |
| **BMS-986165 12 mg QD** | Placebo matching BMS-986165 6 mg | n/a | Blinded | Daily Morning |
| | BMS-986165 12 mg tablet | 12 mg | Blinded | Daily Morning |

### 6.1.2 Dose Schedule for Part B

Subjects that complete Part A will have the option to enroll in Part B of the study to receive study drug in a double-blind, double-dummy fashion over 36 weeks (Table 5). The treatment group assignment in Part B will depend on the treatment the subject received in Part A as well as if the subject achieved MDA at Week 16 (Part A). Subjects will be assigned to 1 of 3 treatment groups:

- Ustekinumab SQ injection PLUS Placebo matching BMS-986165
- BMS-986165 6 mg PLUS Placebo matching ustekinumab injection
- BMS-986165 12 mg PLUS Placebo matching ustekinumab injection

Study treatment will be dispensed and administered in a double-blind, double-dummy fashion as described in Section 4.1.

BMS-986165 6 mg, 12 mg, or placebo matching BMS-986165 tablets:

As the blister cards provided to the sites will be double-blind, all dispensing must be performed via the IRT system. Blister cards will be dispensed at Weeks 16, 20, 24, 28, 32, 36, 40, 44, and 48. An adequate supply of blister cards will be dispensed to cover the subject until their next scheduled visits.

The tablets will be arranged into sets and the subject will be instructed to take 2 tablets daily in the morning (total of 2 tablets daily). Any missed doses should be returned at the next study visit.

Ustekinumab or placebo matching ustekinumab:

The ustekinumab or placebo matching ustekinumab will be administered SQ at Weeks 16, 20, 32, and 44. Additionally another dose of ustekinumab or placebo matching ustekinumab will be administered at Week 52 based on the investigator/treating physician's and subject's decision to take ustekinumab post-study completion (ie, following Week 56 visit completion).

The ustekinumab vials provided by the Sponsor will be open-label. Normal saline will be used as the placebo for ustekinumab. An unblinded pharmacist (or appropriate drug preparation person) will need to prepare the SQ injection based on the subject's treatment assignment (ie, ustekinumab SQ injection or placebo matching ustekinumab SQ injection). The syringe used for administration of ustekinumab or placebo must be identical. However, the color and viscosity of the solutions may be different. Even though the subject will not be able to distinguish the difference, study personnel who administer both preparations may be able to perceive the difference. For this reason, the person designated as the unblinded drug administrator will not be involved in any other study conduct. Depending on the site, the unblinded pharmacist (or appropriate drug preparation person) and the unblinded study drug administrator may be the same person.

Guidance on the preparation of the ustekinumab or placebo matching ustekinumab SQ injection is contained in the Pharmacy Manual.

**Table 5: Part B -- Treatment Group and Dosing**

| Treatment Group | Product Description | Dosage in mg | Frequency of Administration[a] |
|---|---|---|---|
| **Ustekinumab SQ injection PLUS Placebo matching BMS-986165** | Placebo matching BMS-986165 6 mg | n/a | Daily Morning |
| | Placebo matching BMS-986165 12 mg | n/a | Daily Morning |
| | Ustekinumab | 45 mg / 90 mg[b] | Weeks 16, 20, 32, and 44 |
| **BMS-986165 6 mg PLUS Placebo matching ustekinumab injection** | BMS-986165 6 mg | 6 mg | Daily Morning |
| | Placebo matching BMS-986165 12 mg | n/a | Daily Morning |
| | Normal saline | n/a | Weeks 16, 20, 32, and 44 |
| **BMS-986165 12 mg PLUS Placebo matching ustekinumab injection** | BMS-986165 12 mg | 12 mg | Daily Morning |
| | Placebo matching BMS-986165 6 mg | n/a | Daily Morning |
| | Normal saline | n/a | Weeks 16, 20, 32, and 44 |

[a] Based on the Week 48 Post-study Ustekinumab Evaluation, for subjects that elect to be treated with ustekinumab after the study completion (ie, completion of the Week 56 visit), the following treatment will be administered at Week 52: 1) subjects that were on ustekinumab treatment in Part B will receive a placebo matching ustekinumab SQ injection, or 2) subjects that were on BMS-986165 6 mg or BMS-986165 12 mg treatment in Part B will receive ustekinumab SQ injection

[b] Ustekinumab is weight based dosing. Two vials will be used for injections to create 90 mg doses. Dosing will be in quick succession and different syringes will be needed

## 6.2 Method of Treatment Assignment

At the time of the screening visit, before any study-related procedures are performed, the investigative site will access the enrollment option of the IRT system for assignment of a subject number. This number is assigned sequentially by the system and will be unique across all sites. If a potential subject is rescreened, a new identification number will be used.

At Week 0 (Day 1) of Part A, subjects who meet all criteria for enrollment at Screening and Day 1 will be centrally randomized in a 1:1:1 ratio to BMS-986165 6 mg QD, BMS-986165 12 mg QD, or placebo matching BMS-986165, as determined by a computer-generated randomization schedule using IRT. The randomization lists will be generated by the IRT vendor using a permuted block design within each combination of stratum level. Randomization will be stratified by TNFi use (experienced/naïve) and body weight (< 90 kg and ≥ 90 kg). After all inclusion/exclusion criteria have been met for a subject, the investigative site will access the IRT

on Day 1 for the purposes of randomizing a subject. 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 number will be assigned to the subject corresponding to the treatment assignment.

Subjects completing Part A will have the option to enroll into Part B of the study. Treatment assignment in Part B will be based on the subject's treatment assignment in Part A as well as the patient's MDA score at Week 16. Similar to Part A, blister cards will be dispensed to create a 1-month supply.

## 6.3 Blinding

### *6.3.1 Maintaining the Blind*

Treatment assignments and study drug dispensing in Part A and in Part B will be managed using IRT. Investigative site staff, the Sponsor, and subject will remain blinded to treatment assignment with the exception of an unblinded pharmacist (or appropriate drug preparation person), an unblinded study drug administrator (Part B), and an unblinded site monitor who will be involved only with drug accountability in Part B. Depending on the site, the unblinded pharmacist (or appropriate drug preparation person) and the unblinded study drug administrator may be the same person.

BMS-986165 6 mg, 12 mg tablets, or placebo matching BMS-986165:

Each strength of BMS-986165 (6 mg or 12 mg) will have a matching placebo. The tablets will be provided to the sites in blister cards and each subject will need to take 2 tablets daily.

Ustekinumab or placebo matching ustekinumab:

Ustekinumab vials for SQ injection will be provided by the Sponsor. Normal saline will be used as the placebo for ustekinumab and will be procured by the site. An unblinded pharmacist (or appropriate drug preparation person) will need to prepare the SQ injection based on the subject's treatment assignment (i.e. ustekinumab SQ injection or placebo matching ustekinumab SQ injection). The syringe used for administration of ustekinumab or placebo must be identical; however, the color and viscosity of the solutions may be different. Even though the subject will not be able to distinguish the difference, study personnel who administer both preparations may be able to perceive the difference. For this reason, the person is designated as the unblinded drug administrator and will not be involved in any other study conduct. Depending on the site, the unblinded pharmacist (or appropriate drug preparation person) and the unblinded study drug administrator may be the same person.

Guidance on the preparation of the ustekinumab or placebo matching ustekinumab SQ injection is contained in the Pharmacy Manual.

### 6.3.2 Circumstances for Unblinding

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 IP 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, ie, that it will alter the subject's immediate management. In many cases, particularly when the emergency is clearly not related to the IP, 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 case of an emergency, the investigator has unrestricted access to randomization information via IRT and is capable of breaking the blind through the IRT system without prior approval from the Sponsor. After the unblinding, the investigator shall notify the Medical Monitor and/or study director. The method of unblinding for emergency purposes is described in the IRT manual. Subject and unblinded treatment information and the reason for the blind being broken must be recorded on the appropriate study status page of the electronic case report form (eCRF). In addition, the information that is requested on the emergency unblinding envelope must be completed. After unblinding via IRT, the investigator shall notify the Medical Monitor.

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 nonemergency purposes must be discussed with the Medical Monitor.

The DMC will assess safety and risk benefit on an ongoing basis, and will have access to unblinded treatment codes for individual subjects An analysis team, including a reporting statistician and programming support, who are not involved with the conduct of the study, will provide analyses to the DMC. The procedures to be respected and the reasons for unblinding of the DMC are discussed in the DMC charter.

In addition, an unblinded analysis of the safety and endpoint data will be performed after all subjects complete their Week 16 visit (Part A). The analysis will be performed by an independent statistical team who are not involved in the conduct of the study and reviewed by non-study team members who will use the data to support Phase 3 development decision making. Study team members will remain blinded as subjects move into Part B.

A bioanalytical scientist in the Bioanalytical Sciences department of BMS Research & Development (or a designee in the external central bioanalytical laboratory) will be unblinded to the randomized treatment assignments in order to minimize unnecessary bioanalytical analysis of samples.

If a subject is unblinded for any reason, the subject will be discontinued from treatment.

## 6.4 Dosage Modification

There is no provision for dose-modification of study treatment. If a subject interrupts treatment due to an AE, study treatment can be restarted in consultation with the Medical Monitor.

## 6.5 Preparation/Handling/Storage/Accountability

The IP should be stored in a secure area according to local regulations. It is the responsibility of the investigator to ensure that IP is only dispensed to study subjects. The IP must be dispensed only from official study sites by authorized personnel according to local regulations.

The product storage manager should ensure that the study treatment is stored in accordance with the environmental conditions (temperature, light, and humidity) as determined by BMS. If concerns regarding the quality or appearance of the study treatment arise, the study treatment should not be dispensed and contact BMS immediately.

Study treatment not supplied by BMS will be stored in accordance with the package insert.

IP documentation (whether supplied by BMS or not) must be maintained that includes all processes required to ensure drug is accurately administered. This includes documentation of drug storage, administration and, as applicable, storage temperatures, reconstitution, and use of required processes (eg, required diluents, administration sets).

Further guidance and information for final disposition of unused study treatment are provided in APPENDIX 2.

The unblinded pharmacist (or appropriate drug preparation person) will obtain treatment assignment by IRT in Part B and prepare the ustekinumab or placebo injection.

[redacted]

## 6.6 Treatment Compliance

Study treatment compliance will be periodically monitored using standard drug accountability procedures (comparing the number of tablets returned to number dispensed, considering the expected regimen and any reported missed doses). Drug accountability will be reviewed by the investigative site staff at each visit to confirm treatment compliance. Site staff will discuss any discrepancies with the subject and remind the subject of the importance of compliance with the assigned regimen. A real-time monitoring platform may be used.

[redacted]

[redacted]

[redacted]

## 6.8 Treatment After the End of the Study

At the end of the study, BMS will not continue to provide BMS-supplied study treatment to subjects/investigators unless BMS chooses to extend the study. The investigator should ensure that the subject receives appropriate standard of care to treat the condition under study.

# 7 DISCONTINUATION CRITERIA

## 7.1 Discontinuation from Study Treatment

Subjects MUST discontinue IP (and non-IP at the discretion of the investigator) for any of the following reasons:

- Subject's request to stop study treatment. Subjects who request to discontinue study treatment will remain in the study and must continue to be followed for protocol specified follow-up procedures. The only exception to this is when a subject specifically withdraws consent for any further contact with him/her or persons previously authorized by subject to provide this information
- Any clinical AE, laboratory abnormality or intercurrent illness which, in the opinion of the investigator, indicates that continued participation in the study is not in the best interest of the subject
- Termination of the study by BMS
- Loss of ability to freely provide consent through imprisonment or involuntarily incarceration for treatment of either a psychiatric or physical (eg, infectious disease) illness
- eGFR <45 mL/min confirmed on a repeat assessment within 7 days
- Abnormal liver tests suggestive of drug-induced liver injury (DILI), as defined in Section 8.2.8 or if the investigator believes that it is in the best interest of the subject
- The subject develops a malignancy, with the exception of a subject who develops nonmelanoma skin cancer who may continue in the study at the discretion of the investigator
- Pregnancy, positive pregnancy test, or subject expresses an interest in becoming pregnant (refer to Section 8.2.6)
- Subject develops active TB during the study or prematurely discontinues treatment for LTBI, or subject is noncompliant with LTBI therapy (refer to Section 8.4.4)
- Unblinding of a subject's treatment assignment for any reason (emergency or nonemergency)
- Inability or failure to comply with protocol requirements in the opinion of the investigator
- Clinically significant worsening of disease, while taking study treatment, that requires the use of medications listed as prohibited in the protocol

Refer to the Schedule of Activities for data to be collected at the time of treatment discontinuation and follow-up and for any further evaluations that can be completed.

In the case of pregnancy, the investigator must immediately, within 24 hours of awareness of the pregnancy, notify the Medical Monitor/designee of this event. In most cases, the study treatment will be permanently discontinued in an appropriate manner (eg, dose tapering if necessary for subject safety). Refer to Section 8.2.6 Pregnancy.

All subjects who discontinue study treatment should comply with protocol-specified follow-up procedures as outlined in the Schedule of Activities, Section 1.3. The only exception to this requirement is when a subject withdraws consent for all study procedures including post-treatment

study follow-up or loses the ability to consent freely (ie, is imprisoned or involuntarily incarcerated for the treatment of either a psychiatric or physical illness).

If study treatment is discontinued prior to the subject's completion of the study, the reason for the discontinuation must be documented in the subject's medical records and entered on the appropriate CRF page.

### *7.1.1 Post-Study Treatment Study Follow Up*

Subjects who discontinue study treatment will be followed through the scheduled 30-day safety follow-up period or longer, as required, and in line with Section 8.2.4.

## 7.2 Discontinuation from the Study

Subjects who request to discontinue study treatment will remain in the study and must continue to be followed for protocol-specified follow-up procedures. The only exception to this is when a subject specifically withdraws consent for any further contact with him/her or persons previously authorized by subject to provide this information.

- Subjects should notify the investigator of the decision to withdraw consent from future follow-up **in writing**, whenever possible.
- The withdrawal of consent should be explained in detail in the medical records by the investigator and entered on the appropriate CRF page.
- In the event that vital status (whether the subject is alive or dead) is being measured, publicly available information should be used to determine vital status only as appropriately directed in accordance with local law.
- If the subject withdraws consent for disclosure of future information, the Sponsor may retain and continue to use any data collected before such a withdrawal of consent.
- During part B of the study (Week 16 to Week 52), and after 12 weeks of treatment (at Week 28 only), for subjects who do not achieve MDA, the study design provides for rescue therapy for relief of joint symptoms with NSAIDs, intra-articular injections of steroids, systemic glucocorticoids or DMARDs. After Week 28, subjects who need rescue therapy or additional therapy for PsA and/or flares will be discontinued from the study.

## 7.3 Lost to Follow-Up

- All reasonable efforts must be made to locate subjects to determine and report their ongoing status. This includes follow-up with persons authorized by the subject.
- Lost to follow-up is defined by the inability to reach the subject after a minimum of **three** documented phone calls, faxes, or emails as well as lack of response by subject to one registered mail letter. All attempts should be documented in the subject's medical records.
- If it is determined that the subject has died, the site will use permissible local methods to obtain date and cause of death.
- If investigator's use of third-party representative to assist in the follow-up portion of the study has been included in the subject's informed consent, then the investigator may use a Sponsor retained third-party representative to assist site staff with obtaining subject's contact

information or other public vital status data necessary to complete the follow-up portion of the study.

- The site staff and representative will consult publicly available sources, such as public health registries and databases, in order to obtain updated contact information.
- If after all attempts, the subject remains lost to follow-up, then the last known alive date as determined by the investigator should be reported and documented in the subject's medical records.

# 8 STUDY ASSESSMENTS AND PROCEDURES

- Study procedures and timing are summarized in the Schedule of Activities (Section 1.3).
- Protocol waivers or exemptions are not allowed.
- All immediate safety concerns must be discussed with the Medical Monitor immediately upon occurrence or awareness to determine if the subject should continue or discontinue treatment.
- Adherence to the study design requirements, including those specified in the Schedule of Activities, is essential and required for study conduct.
- All screening evaluations must be completed and reviewed to confirm that potential subjects meet all eligibility criteria before randomization. The investigator will maintain a screening log to record details of all subjects screened and to confirm eligibility or record reasons for screening failure, as applicable.
- Procedures conducted as part of the subject's routine clinical management (eg, blood count) and obtained before signing of informed consent may be utilized for screening or baseline purposes provided the procedure meets the protocol-defined criteria and has been performed within the timeframe defined in the Schedule of Activities.

## 8.1 Efficacy Assessments

### *8.1.1 Rater Qualification*

All rheumatologic and dermatologic evaluations must be performed by a qualified assessor that is blinded to the subject's safety data, previous efficacy data, and treatment. Every effort must be made to ensure the same assessor will complete the clinical efficacy/health outcome assessments for each subject at all visits at approximately the same time throughout the study, according to the Schedule of Activities (Section 1.3). Visits should be scheduled with the availability of the evaluator(s) taken into account. If the assessor is unable to complete the evaluation, then another qualified individual can take the place of the initial evaluator, but the substitute evaluator should have examined and reviewed the subject with the initial evaluator in order to assure overlapping experience (consistency between subject evaluations). Documentation of who performed the evaluation is to be recorded in source notes.

To be an eligible Joint Assessor, individuals must receive the standardized joint count training provided by PRA/BMS or be trained by an individual who did receive the standardized training (documentation filed in the Investigator File and the Study File). Such individuals should have appropriate medical credentials and/or should be individuals with appropriate scientific/medical background who are experienced in performing joint assessments. If the individual does not have

medical credentials, documentation of their experience (preferably on a curriculum vitae) must be provided to the study site manager, and their eligibility as joint assessor must be confirmed by the PRA or BMS medical monitor before the individual's participation in the study as joint assessor.

The Joint Assessor may also perform the enthesitis and dactylitis, as well as assess the Target Lesion and conduct the PASI scoring. Training in these assessments will be provided by BMS or PRA and is required in order to perform this function.

Individuals performing the Physician's Global Assessment of psoriatic arthritis must be a physician or other healthcare professional who is competent to perform the assessment.

Subjects will complete all subject reported questionnaires, which will be considered source documents in this study. All subject reported outcomes must be performed prior to all other assessments, including phlebotomy, physical exam, joint and skin assessments.

### *8.1.2 American College of Rheumatology (ACR) Improvement Criteria*

The ACR 20, ACR 50 or ACR 70 definition of improvement is a 20%, 50% or 70% improvement, respectively, over baseline in tender and swollen joint counts and a 20%, 50% or 70% improvement, respectively, in 3 of the 5 remaining core data set measures (APPENDIX 5):

≥ 20%, 50% or 70% improvement from baseline in the number of tender joints (68 joint count)

≥ 20%, 50% or 70% improvement from baseline in the number of swollen joints (66 joint count)

≥ 20%, 50% or 70% improvement from baseline in 3 of the following 5 domains:

- Subject Global Assessment of disease activity (APPENDIX 7)
- Physician Global Assessment of psoriatic arthritis
- Subject global assessment of pain (APPENDIX 8)
- Health Assessment Questionnaire-Disability Index (HAQ-DI, APPENDIX 6)
- hsCRP

### *8.1.3 Health Assessment Questionnaire-Disability Index (HAQ-DI)*

The HAQ-DI is a patient-reported outcome measure that assesses the degree of difficulty a subject has experienced during the past week in 8 domains of daily living activities: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and other activities. Each activity category consists of 2 to 3 items. For reach item in the questionnaire the level of activity is cored from 0 to 3 with 0 representing "no difficulty", 1 as "some difficulty", 2 as much "difficulty", and 3 has "unable to do". Any activity that requires assistance from another individual or requires the use of an assistive device adjusts to a minimum score of 2 to represent a more limited functional status (see APPENDIX 6).

### 8.1.4 Psoriasis Area and Severity Index (PASI)

The PASI is a measure of the average erythema, induration thickness and scaling of psoriatic skin lesions (each graded on a 0 to 4 scale), weighted by the area of involvement (head, arms, trunk to groin, and legs to top of buttocks).[26] The PASI produces a numeric score that can range from 0 to 72, with higher PASI scores denoting more severe disease activity. The PASI can also be used to assess response to treatment. The PASI 50 is the proportion of subjects who experience at least a 50% improvement in PASI score as compared with the baseline value. The PASI 75, PASI 90, and PASI 100 are defined similarly. BMS will host a training session prior to initiation of the study to demonstrate proper PASI scoring. All PASI assessments should be performed by a trained assessor experienced in the assessment of psoriasis patients (see APPENDIX 9).

### 8.1.5 Disease Activity Score 28 CRP

A Disease Activity Score (DAS) can be used to assess patients' PsA disease activity, to determine whether it is under control, and if any treatment adjustments are required. It can also assist in establishing a target score to aim for, to help inform treatment decisions, and optimize disease management.

DAS 28 CRP is a composite outcome measure that assesses:

- How many joints in the hands (including metacarpophalangeal and proximal interphalangeal joints , but excluding distal interphalangeal joints), wrists, elbows, shoulders, and knees are swollen and/or tender over a total of 28
- CRP in the blood to measure the degree of inflammation
- Subject Global Assessment of disease activity (APPENDIX 7)

The results are combined to produce the DAS 28 CRP score, which correlates with the extent of disease activity:

- < 2.6: Disease remission
- 2.6 – 3.2: Low disease activity
- 3.2 – 5.1: Moderate disease activity
- >5.1: High disease activity

### 8.1.6 Dactylitis

The number of digits in hands and feet with dactylitis will be counted by a blinded assessor. The Leads Dactylitis Index (LDI) Basic is a quantitative measurement of dactylitis in the 20 digits using a dactylometer. The circumference of the affected and contralateral digits, and tenderness of the affected digits are measured to generate a total score. A higher score indicates worse dactylitis and is based on the current evaluation. Training will be provided so dactylitis will be evaluated in a consistent manner throughout the study.[77]

### 8.1.7 Enthesitis

The number of sites with enthesitis will be evaluated by a blinded assessor using the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis index and the Leeds Enthesitis index (LEI).

The SPARCC Enthesitis Index has a 0 to 16 score that is derived from the evaluation of 8 locations: the greater trochanter (R/L), quadriceps tendon insertion into the patella (R/L), patellar ligament insertion into the patella and tibial tuberosity (R/L), Achilles tendon insertion (R/L), plantar fascia insertion (R/L), medial and lateral epicondyles (R/L), and the supraspinatus insertion (R/L). A higher count indicates a higher enthesitis burden based on the current evaluation. It has been validated in ankylosing spondylitis and correlates well with the LDI.[78]

The LEI was developed specifically for PsA. An overall score of 0 to 6 is derived from the presence or absence of tenderness at 6 entheseal sites (right and left: lateral epicondyle, medial femoral condyle, and Achilles tendon insertion) at the time of evaluation. A higher count indicates a greater enthesitis burden.[79]

### 8.1.8 Physicians Global Assessment-Fingernails (PGA-F)

In this assessment, 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 Physician's Global Assessment – fingernails (PGA-F) will be performed only in subjects with psoriatic fingernail involvement to assess severity and subsequent improvement. An example is provided in APPENDIX 10. The PGA-F should be performed by an appropriately trained assessor experienced in the assessment of psoriasis patients.

### 8.1.9 Minimal Disease Activity (MDA) and Very Low Disease Activity (VLDA)

Minimal Disease Activity (MDA) response is where an MDA responder is defined as a subject fulfilling 5 of 7 of the following outcomes:

- tender joint count ≤ 1
- swollen joint count ≤ 1
- PASI ≤ 1 or body surface area (BSA) ≤ 3%
- Subject Global Assessment of pain ≤ 15 (APPENDIX 8)
- Subject Global Assessment of disease activity ≤ 20 (APPENDIX 7)
- HAQ-DI ≤ 0.5
- Tender entheseal points ≤ 1

Very low disease activity (VLDA) response is where a VLDA responder is defined as a subject fulfilling all 7 of 7 of the MDA outcomes.

### 8.1.10 Psoriatic Arthritis Disease Activity Score

A composite measure calculated from the Physician Global Assessment of psoriatic arthritis, the Subject Global Assessment of disease activity, the Short Form Health Survey-36 Item (SF-36) Physical Component Summary (PCS), the swollen joint count, the tender joint count, the LEI, the LDI (Basic), and the hsCRP.

### 8.1.11 Disease Activity Index for Psoriatic Arthritis Score

The Disease Activity Index for Psoriatic Arthritis Score (DAPSA) is a composite measure to assess peripheral joint involvement that is based upon numerical summation of 5 variables of disease activity: tender/painful joint count, swollen joint count, Subject Global Assessment of disease activity (APPENDIX 7), Subject Global Assessment of pain (APPENDIX 8), and CRP.

### 8.1.12 PsA Response Criteria (PsARC)

The Psoriatic Arthritis Response Criteria (PsARC) consists of 4 measurements: tender/painful joint count, swollen joint count, Physician Global Assessment of psoriatic arthritis, and Subject Global Assessment of pain ≤ 15 (APPENDIX 8).

In order to be classified as a PsARC responder, subjects must achieve improvement in 2 of 4 measures, one of which must be joint pain or swelling, without worsening in any measure.

### 8.1.13 Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

In subjects with baseline evidence of PsA spondylitis, symptoms will be evaluated using the BASDAI (APPENDIX 11), which consists of a 0 to 100 scale measuring discomfort, pain, and fatigue in response to 6 questions pertaining to the 5 major symptoms of ankylosing spondylitis:

- Fatigue (medical)
- Spinal pain
- Joint pain and swelling
- Areas of localized tenderness
- Morning stiffness duration
- Morning stiffness severity

A higher count indicates worse disease. The recall period is one week.

### 8.1.14 Short Form Health Survey-36 Item (SF-36)

The SF-36 is a patient-reported outcome measure in clinical practice and research. The instrument includes 36 items in a Likert-type format to measure the following 8 health dimensions over the past week: 1) limitations in physical activities, such as bathing or dressing; 2) limitations in social activities because of physical or emotional problems; 3) limitations in usual role activities because of physical health problems; 4) bodily pain; 5) general mental health (psychological distress and

well-being); 6) limitations in usual role activities because of emotional problems; 7) vitality (energy and fatigue); and 8) general health perceptions. Scores for each domain range from 0 to 100, with high scores indicating a better status. An example of the SF-36 is provided in APPENDIX 11.

### 8.1.15 Patient Reported Outcome Measures Information System-Fatigue (PROMIS-FATIGUE) and Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-Fatigue)

The Patient-Reported Outcome Measures Information System-Fatigue (PROMIS-Fatigue) and Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-Fatigue) instruments evaluate a range of self-reported symptoms over the past week, from mild subjective feelings of tiredness to an overwhelming, debilitating, and sustained sense of exhaustion that likely decreases one's ability to execute daily activities and function normally in family or social roles. Fatigue is divided into the experience of fatigue (frequency, duration, and intensity) and the impact of fatigue on physical, mental, and social activities. The first 13 questions of the PROMIS-Fatigue questionnaire comprise the FACIT-Fatigue questionnaire.

The PROMIS-Fatigue questionnaire is not yet available in all languages and will be administered at sites where it is available in the local language. In countries where the PROMIS-Fatigue questionnaire is not available in the local language, sites will administer the FACIT-Fatigue questionnaire to start the protocol. Once the PROMIS-Fatigue questionnaire is available in the local language, and with approval from the ethics committee, any newly enrolled subjects will complete the PROMIS-Fatigue questionnaire. Subjects who were administered the FACIT-Fatigue at Day 1 will continue to be administered the FACIT-Fatigue throughout the study. The PROMIS-Fatigue Short Form 13a (FACIT-Fatigue), along with 5 supplemental fatigue items from the PROMIS item bank, is provided in APPENDIX 13.

### 8.1.16 Work Limitation Questionnaire (WLQ)

The Work Limitation Questionnaire (WLQ) is a 25-item self-report that measures the on-the-job impact of chronic health conditions and treatment over the past 2 weeks. It focuses on assessing limitations while performing specific job demands from the following 4 domains:

1) Time management: difficulty with handling time and scheduling demands (5 items)
2) Physical demands: ability to perform job tasks that involve bodily strength, movement, endurance, coordination, and flexibility (6 items)
3) Mental-interpersonal demands: cognitively demanding tasks and on-the-job social interactions (9 items)
4) Output demands: concerns reduced work productivity (5 items)

The score can be used to calculate a percent of lost work productivity due to a particular disease state. The WLQ Short Form will be used in this study. An example is provided in APPENDIX 14).

### 8.1.17 Psoriatic Arthritis Impact of Disease (PsAID)

The Psoriatic Arthritis Impact of Disease (PsAID) is a 12-item self-report that measures psoriatic arthritis symptoms and impact of disease. Each item is scored on a 0 to 10 numeric rating scale with a one week recall period. The PsAID has a total score, with a higher value indicating worse health (APPENDIX 15).

### 8.1.18 Routine Assessment of Patient Index Data 3 (RAPID3)

RAPID3 (routine assessment of patient index data 3) is a pooled index of the 3 patient-reported ACR Core Data Set measures: function, Subject Global Assessment of pain, and Subject Global Assessment of disease activity. Each of the 3 individual measures is scored 0 to 10, for a total of 30. Disease severity may be classified on the basis of RAPID3 scores: >12 = high; 6.1-12 = moderate; 3.1-6 = low; < or =3 = remission. RAPID3 scores are correlated with the disease activity score 28 (DAS 28) in clinical trials and clinical care, and are comparable to DAS 28 scores in the capacity to distinguish active from control treatments in clinical trials.[80]

### 8.1.19 Imaging Assessment for the Study

Not applicable.

## 8.2 Adverse Events

The definitions of an AE or SAE can be found in APPENDIX 3.

AEs will be reported by the subject (or, when appropriate, by a caregiver, surrogate, or the subject's legally authorized representative).

The investigator and any designees are responsible for detecting, documenting, and reporting events that meet the definition of an AE or SAE and remain responsible for following up AEs that are serious, considered related to the study treatment or the study, or that caused the subject to discontinue before completing the study.

**Contacts for SAE reporting specified in APPENDIX 3.**

### 8.2.1 Adverse Events of Interest

Adverse events of interest (AEIs) are AEs for a particular product or class of products that a Sponsor may wish to monitor carefully. AEIs may be serious or nonserious. Such events may require further investigation to better characterize and understand them. In the BMS-986165 clinical development program, certain skin-related AEs (eg, acne), infection AEs, and creatine kinase (CK) elevation have been identified as potential AEIs; however, there has been no definitive assessment on the causal relationship between these events and treatment with BMS-986165. Additionally, given a potential association between treatment for immune-mediated diseases and increased risk for cancer, malignancy has been identified as a potential AEI. Therefore, additional information about certain skin-related AEs, infection AEs, CK elevation, MACE, and malignancy may be collected on the CRF in order to better characterize and understand them.

### 8.2.2 Time Period and Frequency for Collecting AE and SAE Information

The collection of nonserious AE information should begin at initiation of study treatment until discharge, at the timepoints specified in the Schedule of Activities (Section 1.3). Nonserious AE information should also be collected from the start of a placebo lead-in period or other observational period intended to establish a baseline status for the subjects. The Reference Safety Information in Sections 5.6.1 and 5.6.2 of the Investigator's Brochure (IB) should be used to determine the expectedness of SAEs for expedited reporting.

All SAEs must be collected from the time of signing the consent, including those thought to be associated with protocol-specified procedures and within 30 days of discontinuation of dosing.

The investigator must report any SAE that occurs after these time periods and that is believed to be related to study drug or protocol-specified procedure (eg, a follow-up skin biopsy).

- Medical occurrences that begin before the start of study treatment but after obtaining informed consent will be recorded on the appropriate section of the eCRF module.
- All SAEs will be recorded and reported to Sponsor or designee within 24 hours, as indicated in APPENDIX 3.
- The investigator will submit any updated SAE data to the Sponsor or designee within 24 hours of updated information being available.

Investigators are not obligated to actively seek AEs or SAEs in former study subjects. However, if the investigator learns of any SAE, including a death, at any time after a subject has been discharged from the study, and he/she considers the event reasonably related to the study treatment or study participation, the investigator must promptly notify the Sponsor.

The method of evaluating, and assessing causality of AEs and SAEs and the procedures for completing and reporting/transmitting SAE reports are provided in APPENDIX 3.

### 8.2.3 Method of Detecting AEs and SAEs

Adverse events can be spontaneously reported or elicited during open-ended questioning, examination, or evaluation of a subject. (In order to prevent reporting bias, subjects should not be questioned regarding the specific occurrence of one or more AEs.)

### 8.2.4 Follow-up of AEs and SAEs

- Nonserious AEs should be followed to resolution or stabilization, or reported as SAEs if they become serious (see APPENDIX 3).
- Follow-up is also required for nonserious AEs that cause interruption or discontinuation of study treatment and for those present at the end of study treatment as appropriate.
- All identified nonserious AEs must be recorded and described on the nonserious AE page of the CRF. Completion of supplemental CRFs may be requested for AEs and/or laboratory abnormalities that are reported/identified during the course of the study.

All SAEs will be followed until resolution, until the condition stabilizes, until the event is otherwise explained, or until the subject is lost to follow-up (as defined in Section 7.3).

Further information on follow-up procedures is given in APPENDIX 3.

### 8.2.5 Regulatory Reporting Requirements for SAEs

- Prompt notification by the investigator to the Sponsor of SAEs is essential so that legal obligations and ethical responsibilities towards the safety of subjects and the safety of a product under clinical investigation are met.
- An investigator who receives an investigator safety report describing SAEs or other specific safety information (eg, summary or listing of SAEs) from the Sponsor will file it along with the IB and will notify the IRB/IEC, if appropriate according to local requirements.

Sponsor or designee will be reporting AEs to regulatory authorities and ethics committees according to local applicable laws including European Directive 2001/20/EC and FDA Code of Federal Regulations 21 CFR Parts 312 and 320. A Suspected, Unexpected Serious Adverse Reaction (SUSAR) is a subset of SAEs and will be reported to the appropriate regulatory authorities and investigators following local and global guidelines and requirements.

### 8.2.6 Pregnancy

If, following initiation of the study treatment, it is subsequently discovered that a subject is pregnant or may have been pregnant at the time of study exposure, including during at least 5 half-lives after product administration, the investigator must immediately notify PRA Drug Safety of this event and complete and forward a Pregnancy Surveillance Form to PRA Drug Safety within 24 hours of awareness of the event and in accordance with SAE reporting procedures described in APPENDIX 3.

If the investigator determines a possible favorable benefit/risk ratio that warrants continuation of study treatment, or re-initiation of study treatment, a discussion between the investigator and the BMS Medical Monitor/designee must occur.

Protocol-required procedures for study discontinuation and follow-up must be performed on the subject.

Follow-up information regarding the course of the pregnancy, including perinatal and neonatal outcome and, where applicable, offspring information, must be reported on the Pregnancy Surveillance Form.

Any pregnancy that occurs in a female partner of a male study subject should be reported to PRA Drug Safety. In order for Sponsor or designee to collect any pregnancy surveillance information from the female partner, the female partner must sign an ICF for disclosure of this information. Information on this pregnancy will be collected on the Pregnancy Surveillance Form.

### 8.2.7 Laboratory Test Result Abnormalities

The following laboratory test result abnormalities should be captured on the AE eCRF page.

- Any laboratory test result that is clinically significant or meets the definition of an AE or SAE
- Any laboratory test result abnormality that required the subject to have study treatment discontinued or interrupted

- Any laboratory test result abnormality that required the subject to receive specific corrective therapy

If a laboratory test result meets the definition of an AE or SAE, the laboratory test result should be reported as an AE or SAE and submitted to PRA Drug Safety, as specified in APPENDIX 3.

It is expected that wherever possible, the clinical rather than laboratory term would be used by the reporting investigator (eg, anemia versus low hemoglobin value).

### *8.2.8 Potential Drug-Induced Liver Injury (DILI)*

Wherever possible, timely confirmation of initial liver-related laboratory abnormalities should occur prior to the reporting of a potential DILI event. All occurrences of potential DILIs, meeting the defined criteria, must be reported as SAEs (see Section 8.2 and APPENDIX 3 for reporting details).

Potential DILI is defined as:

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 AT elevation and hyperbilirubinemia, including, but not limited to, viral hepatitis, pre-existing chronic or acute liver disease, or the administration of other drug(s) known to be hepatotoxic.

### *8.2.9 Other Safety Considerations*

Any significant worsening noted during interim or final physical examinations, ECG, x-ray filming, any other potential safety assessment required or not required by protocol should also be recorded as a nonserious or SAE, as appropriate, and reported accordingly.

## 8.3 Overdose

For this study, taking more than 2 days' worth of study treatment within a 24-hour time period will be considered an overdose.

In the event of an overdose the investigator should:

**1)** Contact the Medical Monitor immediately

**2)** Closely monitor the subject for AEs/SAEs and laboratory abnormalities

Decisions regarding dose interruptions or modifications will be made by the investigator in consultation with the Medical Monitor based on the clinical evaluation of the subject.

## 8.4 Safety

Planned time points for all safety assessments are listed in the Schedule of Activities (Section 1.3).

### 8.4.1 Physical Examinations

Refer to Schedule of Activities (Section 1.3). A complete physical examination will include general appearance, vital signs, eyes, ears, nose mouth, throat, neck, respiratory, CV, respiratory, gastrointestinal/abdomen, lymphatic, musculoskeletal, skin, psychiatric, and neurologic exams. A targeted physical examination will include any organ system associated with an AE or a laboratory abnormality.

### 8.4.2 Vital Signs

Refer to Schedule of Activities (Section 1.3).

### 8.4.3 Electrocardiograms

Refer to Schedule of Activities. A 12-lead ECG will be performed at the visits indicated in the Schedule of Activities (Section 1.3). The subject will remain supine for 5 to 10 minutes prior to the ECG and must have their lab work done after the tracing so that the ECG results remain as accurate as possible. The ECG results will be read by the primary study investigator or a designee.

### 8.4.4 Tuberculosis Screening and Chest Imaging

Chest imaging results and physical examinations are part of the process to assess a subject's eligibility, as outlined in Section 1.3 and as defined in exclusion criterion 3.c, Section 5.2. Chest imaging (eg, chest x-ray, chest CT scan) at the screening visit is required if not already performed and documented within 6 months of obtaining written informed consent. A subject must not have active signs or symptoms of TB, as judged by the investigator, to be eligible for the study.

In addition to a complete PE and medical history to evaluate exposure to TB, all subjects will have a screening test, an IGRA (eg, QuantiFERON®-TB Gold) performed centrally. If unable to obtain central laboratory results, an IGRA test could be obtained locally, after consultation with the PRA Medical Monitor. A subject with an indeterminate IGRA test result must be re-tested for confirmation. If the second result is again indeterminate, the subject will be excluded from the study. If the second result is positive, the subject should be considered as having LTBI provided there are no signs or symptoms of active TB. If the second result is negative, the subject may be eligible provided no other exclusion criterion for TB is met.

### 8.4.5 Clinical Safety Laboratory Assessments

Investigators must document their review of each laboratory safety report.

A central/local laboratory will perform the analyses and will provide reference ranges for these tests.

| | |
|---|---|
| **Hematology** | |
| Hemoglobin | |
| Hematocrit | |
| Total leukocyte count, including differential | |
| Platelet count | |
| **Chemistry** | |
| Aspartate aminotransferase (AST)<br>Alanine aminotransferase (ALT)<br>Total bilirubin<br>Direct bilirubin<br>Alkaline phosphatase<br>Lactate dehydrogenase (LDH)<br>Creatinine<br>Blood Urea Nitrogen (BUN)<br>Uric acid<br>Glucose (fasting at some visits) | Total Protein<br>Albumin<br>Sodium<br>Potassium<br>Chloride<br>Calcium<br>Phosphorus<br>Creatine kinase (CK)*<br>Estimated Glomerular Filtration Rate (eGFR) |
| **Urinalysis** | |
| Protein | |
| Glucose | |
| Blood | |
| Leukocyte esterase | |
| Specific gravity | |
| pH | |
| Microscopic examination (reflex if abnormal) | |
| **Lipid Panel** | |
| Cholesterol (total) | |
| High Density Lipoprotein (HDL) | |
| Low Density Lipoprotein (LDL) | |
| Triglycerides | |
| **Serologies** | |
| Hepatitis C Antibody with reflex to Hepatitis C RNA if positive | |
| Hepatitis B Surface Antigen (HbsAg) | |
| Hepatitis B Surface Antibody (HbsAb) | |
| Hepatitis B Core Antibody (HbcAb) | |
| HIV antibody | |
| **Other Analyses** | |
| Pregnancy test (WOCBP only: serum or HCG test at Screening, prior to first study drug administration, and every 4 weeks thereafter) | |
| Follicle-Stimulating Hormone (FSH) (Screening only for WOCBP only) | |
| Hemoglobin A1C | |
| Thyroid-Stimulating Hormone (TSH) | |
| High-Sensitivity C-Reactive Protein (hs-CRP) | |
| Serum Immunoglobulins (IgM, IgG, IgA, IgE) | |

*If CK > 2.5 × ULN, then reflex testing (ie, CK-MB, Troponin I) will be required.

#### 8.4.5.1 Estimated Glomerular Filtration Rate (eGFR)

Glomerular filtration rate will be estimated using the Modification of Diet in Renal Disease (MDRD) equation at screening and during the study at select visits.

The MDRD equation is as follows:

$$eGFR = 175 \times \text{standardized } SCr^{-1.154} \times age^{-0.203} \times 1.212 \text{ [if black] or } 0.742 \text{ [if female]}$$

Note: GFR is expressed as mL/min/1.73 $m^2$ of BSA and SCr (serum creatinine) is expressed in mg/dL.

Subjects with an eGFR <45 mL/min will be excluded from participation.

### 8.4.6 Imaging Safety Assessment

Not applicable.

[redacted]

[redacted]

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|---|---|---|---|---|
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# 9 STATISTICAL CONSIDERATIONS

## 9.1 Sample Size Determination

Sample size considerations are based on providing exposure in a sufficient number of subjects for 2 dose levels of BMS-986165, 6 mg QD and 12 mg QD, to be able to observe a true dose-response trend that is significantly greater than placebo in the primary endpoint of ACR 20 after 16 weeks of treatment.

BMS-986165 is expected to provide similar PsA efficacy as observed in current biological trials. With this assumption, the expected overall placebo response rate is assumed to be 30% and BMS-986165 response rates to be 50% and 55% in the 6 mg QD and 12 mg QD doses respectively.

A total sample size of 60 subjects per arm randomized in a blinded fashion at a 1:1:1 ratio to BMS-986165 6 mg QD arm, BMS-986165 12 mg QD arm, and placebo will provide 87.5% power in a mixed population to detect a significant dose-response trend compared to placebo for the primary endpoint of ACR 20 response at Week 16 using a trend test with $\alpha = 0.05$ (1-sided) or with $\alpha = 0.10$ (2-sided).

## 9.2 Populations for Analyses

For purposes of analysis, the following analysis sets will be used in this trial:

| Population | Description |
|---|---|
| Enrolled Population | All subjects who sign informed consent. |
| Full Analysis Set (FAS) | All randomized subjects who are dispensed study drug. Following the intent-to-treat principle, subjects will be analyzed according to the treatment assigned at randomization. The FAS will be the primary efficacy analysis population. This is the same as the intent-to-treat population. |
| Per Protocol Set (PPS) | A subset of the FAS who are compliant with the study treatment (compliance criteria will be defined in the SAP) and who do not have any important protocol deviations that may impact the primary efficacy endpoint assessments. The PPS will be a supportive efficacy analysis population. |
| Safety Set (All Treated) | All randomized subjects who receive at least one dose of double-blind study treatment. Subjects will be analyzed according to treatment received. |
| [redacted] | [redacted] |

| Population | Description |
|---|---|
| [redacted] | [redacted] |

## 9.3 Endpoints

### *9.3.1 Primary Endpoint*

The primary endpoint is the ACR 20 response at Week 16. A subject is considered an ACR 20 responder if the following 3 conditions are met:

- ≥ 20% improvement from baseline in the number of tender joints (68 joint count)
- ≥ 20% improvement from baseline in the number of swollen joints (66 joint count)
- ≥ 20% improvement from baseline in **at least** 3 of the following 5 domains:
    - Subject Global Assessment of disease activity (APPENDIX 7)
    - Physician Global Assessment of psoriatic arthritis
    - Subject Global Assessment of pain (APPENDIX 8)
    - HAQ-DI
    - hsCRP

### *9.3.2 Secondary Endpoints*

The secondary endpoints assessed at Week 16 include the following:

- Change from baseline in HAQ-DI score
- PASI 75 response in subjects with at least 3% BSA involvement at baseline
- Change from baseline in SF-36 PCS score

### *9.3.3 Additional Endpoints*

Additional endpoints at Week 16 include:

- ACR 50/70 response
- HAQ-DI 0.35 response, where HAQ-DI 0.35 responder is defined as a subject with an improvement from baseline in HAQ-DI score of 0.35
- PASI 90 response in subjects with at least 3% BSA involvement at baseline
- Dactylitis mean change from baseline (dactylitis count)
- Dactylitis change from baseline (LDI)

- Dactylitis resolution, where resolution is defined as a dactylitis count of 0 in subjects with dactylitis count ≥ 1 at baseline
- Enthesitis mean change from baseline
- Enthesitis resolution, where resolution is defined as a LEI score of 0, in subjects with LEI ≥ 1 at baseline
- Change from baseline in SPARCC enthesitis index
- Enthesitis resolution, where resolution is defined as a SPARCC enthesitis index score of 0, in subjects with SPARCC ≥ 1 at baseline
- MDA response, where an MDA responder is based on a subject fulfilling at least 5 of the below outcomes:
    - Tender joint count ≤ 1
    - Swollen joint count ≤ 1
    - PASI ≤ 1 or BSA ≤ 3%
    - Subject Global Assessment of pain ≤ 15 (APPENDIX 8)
    - Subject Global Assessment of disease activity ≤ 20 (APPENDIX 7)
    - HAQ-DI ≤ 0.5
    - Tender entheseal points ≤ 1
- PGA-F 0/1, assessed as a proportion of subjects with a PGA-F score of 0 or 1 in subjects with a baseline PGA-F score ≥ 3
- Change from baseline in PASDAS
- Change from baseline in DAPSA
- PsARC response
- DAS 28 CRP response:
    - Proportion of subjects with Low Disease Activity defined as DAS 28 CRP score < 3.2
    - Proportion of subjects in remission and time to remission, remission is defined as a DAS 28 CRP score < 2.6
- Change from baseline in DAS 28 CRP score
- Change from baseline in PsAID score
- Change from baseline in BASDAI, in subjects with baseline evidence of PsA spondylitis
- Change from baseline in SF-36 MCS score
- Change from baseline in PROMIS-Fatigue or FACIT-Fatigue score

- Change from baseline in WLQ score
- Change from baseline in RAPID3 score

[redacted]

## 9.4 Statistical Analyses

A description of the subject population will be included in a statistical output report, including subgroups of age, gender, and race.

### *9.4.1 Efficacy Analyses*

Categorical data will be summarized as frequency counts and percentages. Continuous data will be summarized using n, mean, standard deviation, median, minimum, and maximum unless otherwise specified. Efficacy data will be primarily summarized using the FAS population unless otherwise stated. Variables will be summarized for all visits in which the variable is assessed. Complete details of the planned analyses will be documented in the SAP and finalized before database lock.

During the first 16 weeks of treatment, data will be presented for the following treatments:

- BMS-986165 6 mg QD
- BMS-986165 12 mg QD
- Placebo

#### *9.4.1.1 Primary Endpoint Analyses*

The primary efficacy analysis model for binary endpoints (responder/non-responder) will use a logistic regression model to assess whether there is a dose-response trend between ACR 20 response and dose level. The model will include dose level (0, 6, 12) as a continuous variable, and the following covariates: TNFi use (experienced/naïve) and body weight (≥ 90 kg and < 90 kg) in

the model. The odds ratio and the corresponding 2-sided 95% confidence interval (CI) will be provided.

#### *9.4.1.1.1 Imputation Methods for Primary Endpoint*

The estimand of interest is to assess the dose-response of multiple doses of BMS-986165 on subject response to ACR 20 criteria at Week 16 for all randomized subjects receiving at least one dose of study treatment. Occurrence of intercurrent events such as:

- Subjects who discontinue the treatment or study early (ie, prior to Week 16)
- Start a protocol prohibited medication/therapy
- Subjects who are lost to follow-up
- Subjects who otherwise have missing endpoint data at or prior to Week 16 will use the "Composite Strategy" as defined in ICH E9 R1 addendum and will be considered as a measure of non-response to treatment. Non-responder imputation (NRI) will be used for binary endpoints for the above intercurrent events

### *9.4.1.2 Sensitivity Analyses for the Primary Endpoint*

The following strategies for addressing intercurrent events will be used in sensitivity analyses of the primary efficacy endpoint:

1. While on Treatment Strategy – the last observation while the subject was on blinded treatment will be considered as their Week 16 value. This is essentially the last observation carried forward (LOCF) imputation methodology.
2. For subjects with an intercurrent event at Week 16, "While on Treatment" strategy will be used for placebo subjects and "Composite" strategy will be used for BMS-986165 subjects. Therefore, placebo subjects with an intercurrent event will be imputed using the LOCF method and BMS-986165 subjects will be imputed using the NRI method in this analysis.

Furthermore, tipping point analysis may be performed to assess the robustness of the primary imputation method. The goal of this analysis is to identify assumptions about the missing data under which the conclusions change. Further details of this procedure may be described in the SAP.

#### *9.4.1.2.1 Supportive Analyses for the Primary Endpoint*

The primary efficacy endpoint will also be analyzed for the PPS using the analysis described in Section 9.4.1.1.

#### *9.4.1.2.2 Subgroup Analyses for the Primary Endpoint*

Subgroup analyses will be conducted for the primary efficacy endpoint for the FAS using the analysis model described in Section 9.4.1.1 as well as the imputation method described in Section 9.4.1.1.1. Subgroups will not be further stratified based on the factors used for randomization. Subgroups that may be evaluated include the following:

- Gender
- Age categories (< 65, ≥ 65)
- Race
- Body weight categories (< 90 kg; ≥ 90 kg)
- TNFi use (experienced/naïve)
- Glucocorticosteroid use (yes/no)
- Geographic region
- Country
- DMARD use (yes/no)

In addition, additional subgroups defined for descriptive summaries will be specified in the SAP.

#### *9.4.1.3 Secondary Endpoint Analyses*

The secondary endpoint of PASI 75 response at Week 16 will be assessed in a dose-response analysis. The binary endpoint (responder/non-responder) will use a logistic regression analysis similar to the primary analysis.

The secondary continuous endpoints will be assessed at Week 16 using dose-response linear regression analysis. The change from baseline score will be calculated at Week 16 and analyzed using an analysis of covariance (ANCOVA). Dose level (0, 6, 12) will be assessed in the model as a continuous variable and the following covariates as fixed effects: TNFi use (experienced/naïve) and body weight (< 90 kg and ≥ 90 kg). The baseline value will be added into the model as a covariate. Treatment differences based on least-squares (LS) means and the corresponding 2-sided 95% CIs will be provided.

##### *9.4.1.3.1 Imputation Methods for Secondary Endpoints*

Similar strategies for addressing intercurrent events will be used for binary secondary efficacy endpoints.

For continuous secondary efficacy endpoints, the "Composite" and "While on Treatment" strategies will be used to address specific intercurrent events. For subjects who discontinue study treatment and/or study due to:

- Lack of efficacy
- Adverse events

or who start a protocol prohibited medication/therapy, the baseline observation will be used as the subject's Week 16 value. For all other intercurrent events, the last valid observation while on treatment will be used as the Week 16 value.

#### 9.4.1.4 Adjustment for Multiplicity of Primary and Key Secondary Endpoints

Statistical analysis of secondary endpoints will be performed in a hierarchical fashion. In order to preserve the overall Type I error rate, a fixed-sequence testing method will be implemented. Testing of secondary endpoints will occur sequentially and may only proceed to the next secondary endpoint if the null hypothesis is rejected at alpha = 0.10 (2-sided) for the prior endpoint showing a positive dose-response in that endpoint. If an endpoint fails at any step, then all subsequent p-values will be considered nominal.

Secondary Family – Secondary endpoints will be tested for a positive dose-response trend in the following order:

a. Change from baseline in HAQ-DI score at Week 16
b. PASI 75 response at Week 16
c. Change from baseline in SF-36 PCS score at Week 16

There will be no multiplicity adjustment for testing of additional endpoints. Nominal p-values will be provided as descriptive statistics.

### 9.4.2 Safety Analyses

Safety data will be analyzed for AEs, SAEs, laboratory analytes, physical exam, vital signs, and ECGs. Safety will be summarized using the Safety population. Categorical data will be summarized as frequency counts and percentages. Continuous data will be summarized using n, mean, standard deviation, median, minimum, and maximum unless otherwise specified. Safety data for Part A and B will be summarized separately.

During the first 16 weeks of treatment, data will be presented for the following treatments:

- BMS-986165 6 mg QD
- BMS-986165 12 mg QD
- Placebo

After Week 16, subjects continuing in Part B of the study will have their data presented depending on MDA response in Part A, as follows:

- BMS-986165 6 mg QD → BMS-986165 6 mg QD
- BMS-986165 12 mg QD → BMS-986165 12 mg QD
- Placebo → Ustekinumab injection
- BMS-986165 6 mg QD → Ustekinumab injection
- BMS-986165 12 mg QD → Ustekinumab injection

#### 9.4.2.1 Adverse Events

Treatment-emergent adverse events (TEAEs), SAEs and deaths, and AEs leading to study treatment discontinuation, AEs by maximum severity, and AEs by relationship will be summarized

by the Medical Dictionary for Regulatory Activities (MedDRA) system organ class and preferred term. All TEAEs, AEIs, as well as MACE (cardiac death, nonfatal myocardial infarction, nonfatal stroke) will be summarized by preferred term sorted by decreasing frequency.

#### *9.4.2.2 Vital Signs, ECGs and Physical Examinations*

Vital signs and ECGs will be summarized as raw, change from baseline, and change from maximum postbaseline value. Incidence of abnormal ECG and physical examination findings will also be summarized.

#### *9.4.2.3 Clinical Laboratory Tests*

Laboratory analytes will be summarized as raw, change from baseline, and change from maximum post-baseline value. Incidence of abnormal, high, or low values will be summarized. Shift tables will also be provided.

### *9.4.3 Other Analyses*

#### *9.4.3.1 Demographics and Other Baseline Characteristics*

Demographics and other baseline characteristics will be summarized by treatment for each applicable analysis set. Categorical data will be summarized as frequency counts and percentages. Continuous data will be summarized using n, mean, standard deviation, median, minimum, and maximum unless otherwise specified.

Baseline demographic and disease characteristic comparability of the randomized treatment groups will be assessed. Categorical variables will be evaluated by a Fisher's exact test and continuous variables will be evaluated by a t-test. These tests of comparability are performed for descriptive purposes only.

[redacted]

#### *9.4.3.3 Relevant Protocol Deviations*

The impact of relevant protocol deviations on the efficacy results will be assessed by excluding subjects from the PPS in supportive analyses of the primary efficacy endpoint. Relevant protocol deviations to be considered regarding exclusion of subjects from the PPS may include but are not limited to the following:

- Subject did not take study drug per protocol
- Subject failed to meet study inclusion criteria but was entered into the study
- Subject met study exclusion criteria but was entered into the study

- Subject took prohibited concomitant medication
- Subject did not have a Week 16 assessment

Relevant protocol deviations will be summarized descriptively by treatment.

[redacted]

#### *9.4.3.6 PROMIS-Fatigue and FACIT-Fatigue*

PROMIS-Fatigue score will be summarized by treatment and time point for subjects who were administered PROMIS-Fatigue. FACIT-Fatigue scores will be similarly presented as a pooled analysis, which will include FACIT-Fatigue scores combined with scores from the first 13 PROMIS-Fatigue questions.

[redacted]

[redacted]

### *9.4.4 Interim Analyses*

No interim analysis is currently planned.

## 9.5 Analysis and Reporting

A database lock (16-week database lock) will occur once all randomized subjects have completed the Week 16 efficacy assessments or have discontinued prior to Week 16. Analyses of the collected efficacy and safety results during the 16-week Part A will be performed in order to aid in planning for subsequent clinical development. Details of these analyses will be described in the SAP. The study team responsible for managing the study, including medical monitors, will remain blinded to treatment assignment and the results of this analysis throughout the study.

# 11 APPENDICES

# APPENDIX 1 ABBREVIATIONS AND TRADEMARKS

| Term | Definition |
|---|---|
| AE | adverse event |
| AEI | adverse event of interest |
| ALT | alanine aminotransferase |
| ANCOVA | analysis of covariance |
| AST | aspartate aminotransferase |
| AT | aminotransaminases |
| AUC(TAU) | area under the concentration-time curve in one dosing interval |
| β-HCG | beta-human chorionic gonadotrophin |
| BASDAI | Bath Ankylosing Spondylitis Disease Activity Index |
| BID | bis in die, twice daily |
| BMI | body mass index |
| BMS | Bristol-Myers Squibb |
| BP | blood pressure |
| BSA | Boy surface area |
| BUN | blood urea nitrogen |
| CASPAR | Classification Criteria for Psoriatic Arthritis |
| CBC | complete blood count |
| CFR | Code of Federal Regulations |
| CI | confidence interval |
| CK | creatine kinase |
| cm | centimeter |
| CMH | Cochran-Mantel-Haenszel |
| Cmax, CMAX | maximum observed concentration |
| CNS | Central nervous system |
| CRF | Case Report Form, paper or electronic |
| CS | corticosteroid |
| CT | computed tomography |
| Ctrough | Trough observed plasma concentration |
| CV | cardiovascular |

| Term | Definition |
|---|---|
| DAPSA | Disease Activity Index for Psoriatic Arthritis Score |
| DAS | Disease Activity Score |
| dL | deciliter |
| DMARD | disease-modifying antirheumatic drug |
| DILI | drug-induced liver injury |
| DMC | data monitoring committee |
| DSM IV | Diagnostic and Statistical Manual of Mental Disorders (4th Edition) |
| ECG | electrocardiogram |
| eCRF | Electronic Case Report Form |
| eg | exempli gratia (for example) |
| eGFR | Estimated glomerular filtration rate |
| ESR | erythrocyte sedimentation rate |
| ET | early termination |
| E-R | exposure-response |
| FAS | Full Analysis Set |
| FDA | Food and Drug Administration |
| FSH | follicle stimulating hormone |
| g | gram |
| GCP | Good Clinical Practice |
| GFR | glomerular filtration rate |
| h | hour |
| HAQ-DI | Health Assessment Questionnaire-Disability Index |
| HBcAb | hepatitis B core antibody |
| HBsAb | hepatitis B surface antibody |
| HBsAg | hepatitis B surface antigen |
| HBV | hepatitis B virus |
| HCV | hepatitis C virus |
| HIV | Human Immunodeficiency Virus |
| HR | heart rate |
| HRT | hormone replacement therapy |

| Term | Definition |
|---|---|
| hsCRP | high-sensitivity C-reactive protein |
| ICH | International Conference on Harmonisation |
| ie | id est (that is) |
| IEC | Independent Ethics Committee |
| IGRA | IFN gamma release assay |
| IMP | investigational medicinal products |
| IND | Investigational New Drug Exemption |
| IRB | Institutional Review Board |
| IRT | Interactive Response Technology |
| IV | intravenous |
| kg | kilogram |
| L | liter |
| LDH | lactate dehydrogenase |
| LDI | Leeds Dactylitis Index |
| LEI | Leeds Enthesitis Index |
| LOCF | Last observation carried forward |
| LS | least-squares |
| LTBI | Latent TB Infection |
| LTE | long term extension |
| MDA | Minimal Disease Activity |
| MDRD | Modification of Diet in Renal Disease |
| mg | milligram |
| min | minute |
| mL | milliliter |
| µg | microgram |
| MTX | methotrexate |
| N | number of subjects or observations |
| n/a | not applicable |
| NRI | non-responder imputation |
| NSAID | nonsteroidal anti-inflammatory drug |

| Term | Definition |
|---|---|
| PASI | Psoriasis Area and Seventy Index |
| PASDAS | Psoriatic Arthritis Disease Activity Score |
| PD | pharmacodynamics |
| PGA-F | Physician's Global Assessment-Fingernails |
| PK | pharmacokinetics |
| PO | per os (by mouth route of administration) |
| PP | Per Protocol |
| PPS | Per Protocol Set |
| PRO | Patient Reported Outcome |
| PROMIS | Patient Reported Outcome Measurement Information System |
| PsA | psoriatic arthritis |
| PsAID | Psoriatic Arthritis Impact of Disease |
| PsARC | Psoriatic Arthritis Response Criteria |
| PsO | psoriasis |
| QD | quaque die, once daily |
| QSP | quantitative systems pharmacology |
| RAPID3 | routine assessment of patient index data 3 |
| RBC | red blood cell |
| SAE | serious adverse event |
| SAP | statistical analysis plan |
| SCr | serum creatinine |
| SF-36 | Short Form Health Survey-36 Item |
| SPARCC | Spondyloarthritis Research Consortium of Canada |
| SQ | subcutaneous |
| STAT | signal transducer and activator of transcription |
| SUSAR | Suspected, Unexpected Serious Adverse Reaction |
| TB | tuberculosis |
| TEAE | treatment emergent adverse event |
| $T_H$ | T-helper |
| TNF | tumor necrosis factor |

| Term | Definition |
|---|---|
| TNFi | TNF-inhibitor |
| TYK2 | tyrosine kinase 2 |
| Tmax | time of maximum observed concentration |
| TNF | tumor necrosis factor |
| ULN | upper limit of normal |
| VLDA | Very Low Disease Activity |
| WBC | white blood cell |
| WHO | World Health Organization |
| WLQ | work limitation questionnaire |
| WOCBP | women of childbearing potential |

# APPENDIX 2 STUDY GOVERNANCE CONSIDERATIONS

The term 'Subject' is used in the protocol to refer to a person who has consented to participate in the clinical research study. The term 'Subject' used in the eCRF is intended to refer to a person (Subject) who has consented to participate in the clinical research study.

## REGULATORY AND ETHICAL CONSIDERATIONS

## GOOD CLINICAL PRACTICE

This study will be conducted in accordance with:

- Good Clinical Practice (GCP),
- as defined by the International Council on Harmonisation (ICH)
- in accordance with the ethical principles underlying European Union Directive 2001/20/EC
- United States Code of Federal Regulations, Title 21, Part 50 (21CFR50)
- applicable local requirements.

The study will be conducted in compliance with the protocol. The protocol and any amendments and the subject informed consent will receive approval/favorable opinion by Institutional Review Board/Independent Ethics Committee (IRB/IEC), and regulatory authorities according to applicable local regulations prior to initiation of the study.

All potential serious breaches must be reported to Sponsor or designee immediately. A serious breach is a breach of the conditions and principles of GCP in connection with the study or the protocol, which is likely to affect, to a significant degree, the safety or physical or mental integrity of the subjects of the study or the scientific value of the study.

Personnel involved in conducting this study will be qualified by education, training, and experience to perform their respective tasks.

This study will not use the services of study personnel where sanctions have been invoked or where there has been scientific misconduct or fraud (eg, loss of medical licensure, debarment).

## INSTITUTIONAL REVIEW BOARD/INDEPENDENT ETHICS COMMITTEE

Before study initiation, the investigator must have written and dated approval/favorable opinion from the IRB/IEC for the protocol, consent form, subject recruitment materials (eg, advertisements), and any other written information to be provided to subjects. The investigator or BMS should also provide the IRB/IEC with a copy of the Investigator Brochure or product labeling information to be provided to subjects and any updates.

The investigator, Sponsor or designee should provide the IRB/IEC with reports, updates and other information (eg, expedited safety reports, amendments, and administrative letters) according to regulatory requirements or institution procedures.

## COMPLIANCE WITH THE PROTOCOL AND PROTOCOL REVISIONS

The investigator should not implement any deviation or change to the protocol without prior review and documented approval/favorable opinion of an amendment from the IRB/IEC (and if applicable, also by local health authority) except where necessary to eliminate an immediate hazard(s) to study subjects.

If a deviation or change to a protocol is implemented to eliminate an immediate hazard(s) prior to obtaining relevant approval/favorable opinion(s) the deviation or change will be submitted, as soon as possible to:

- IRB/IEC for
- Regulatory Authority(ies), if applicable by local regulations (per national requirements)

Documentation of approval/favorable opinion signed by the chairperson or designee of the IRB(s)/IEC(s) and if applicable, also by local health authority must be sent to BMS.

If an amendment substantially alters the study design or increases the potential risk to the subject: (1) the consent form must be revised and submitted to the IRB(s)/IEC(s) for review and approval/favorable opinion; (2) the revised form must be used to obtain consent from subjects currently enrolled in the study if they are affected by the amendment; and (3) the new form must be used to obtain consent from new subjects prior to enrollment.

If the revision is done via an administrative letter, investigators must inform their IRB(s)/IEC(s).

## FINANCIAL DISCLOSURE

Investigators and sub-Investigators will provide the Sponsor with sufficient, accurate financial information in accordance with local regulations to allow the Sponsor to submit complete and accurate financial certification or disclosure statements to the appropriate health authorities. Investigators are responsible for providing information on financial interests during the course of the study and for 1 year after completion of the study.

## INFORMED CONSENT PROCESS

Investigators must ensure that subjects are clearly and fully informed about the purpose, potential risks, and other critical issues regarding clinical studies in which they volunteer to participate.

In situations where consent cannot be given to subjects, their legally acceptable representatives (as per country guidelines) are clearly and fully informed about the purpose, potential risks, and other critical issues regarding clinical studies in which the subject volunteers to participate.

Sponsor or designee will provide the investigator with an appropriate (ie, Global or Local) sample informed consent form which will include all elements required by ICH, GCP and applicable regulatory requirements. The sample informed consent form will adhere to the ethical principles that have their origin in the Declaration of Helsinki.

Investigators must:

- Provide a copy of the consent form and written information about the study in the language in which the subject is most proficient prior to clinical study participation. The language must be non-technical and easily understood.
- Allow time necessary for subject or subject's legally acceptable representative to inquire about the details of the study.
- Obtain an informed consent signed and personally dated by the subject or the subject's legally acceptable representative and by the person who conducted the informed consent discussion.
- Obtain the IRB/IEC's written approval/favorable opinion of the written informed consent form and any other information to be provided to the subjects, prior to the beginning of the study, and after any revisions are completed for new information.

If informed consent is initially given by a subject's legally acceptable representative or legal guardian, and the subject subsequently becomes capable of making and communicating his or her informed consent during the study, consent must additionally be obtained from the subject.

Revise the informed consent whenever important new information becomes available that is relevant to the subject's consent. The investigator, or a person designated by the investigator, should fully inform the subject or the subject's legally acceptable representative or legal guardian, of all pertinent aspects of the study and of any new information relevant to the subject's willingness to continue participation in the study. This communication should be documented.

The confidentiality of records that could identify subjects must be protected, respecting the privacy and confidentiality rules applicable to regulatory requirements, the subjects' signed ICF and, in the US, the subjects' signed HIPAA Authorization.

The consent form must also include a statement that BMS and regulatory authorities have direct access to subject records.

Subjects unable to give their written consent (e.g., stroke or subjects with or severe dementia) may only be enrolled in the study with the consent of a legally acceptable representative. The subject must also be informed about the nature of the study to the extent compatible with his or her understanding, and should this subject become capable, he or she should personally sign and date the consent form as soon as possible. The explicit wish of a subject who is unable to give his or her written consent, but who is capable of forming an opinion and assessing information to refuse participation in, or to be withdrawn from, the clinical study at any time should be considered by the investigator.

The rights, safety, and well-being of the study subjects are the most important considerations and should prevail over interests of science and society.

## SOURCE DOCUMENTS

The Investigator is responsible for ensuring that the source data are accurate, legible, contemporaneous, original and attributable, whether the data are hand-written on paper or entered electronically. If source data are created (first entered), modified, maintained, archived, retrieved, or transmitted electronically via computerized systems (and/or any other kind of electronic

devices) as part of regulated clinical trial activities, such systems must be compliant with all applicable laws and regulations governing use of electronic records and/or electronic signatures. Such systems may include, but are not limited to, electronic medical/health records (EMRs/EHRs), adverse event tracking/reporting, protocol required assessments, and/or drug accountability records).

When paper records from such systems are used in place of electronic format to perform regulated activities, such paper records should be certified copies. A certified copy consists of a copy of original information that has been verified, as indicated by a dated signature, as an exact copy having all of the same attributes and information as the original.

## STUDY TREATMENT RECORDS

Records for study treatments (whether supplied by BMS, its vendors, or the site) must substantiate study treatment integrity and traceability from receipt, preparation, administration, and through destruction or return. Records must be made available for review at the request of BMS/designee or a Health Authority.

| If | Then |
|---|---|
| Supplied by BMS (or its vendors): | Records or logs must comply with applicable regulations and guidelines and should include:<br>• amount received and placed in storage area<br>• amount currently in storage area<br>• label identification number or batch number<br>• amount dispensed to and returned by each subject, including unique subject identifiers<br>• amount transferred to another area/site for dispensing or storage<br>• nonstudy disposition (e.g., lost, wasted)<br>• amount destroyed at study site, if applicable<br>• amount returned to BMS<br>• retain samples for bioavailability/bioequivalence, if applicable<br>• dates and initials of person responsible for Investigational Product dispensing/accountability, as per the Delegation of Authority Form. |
| Sourced by site, and not supplied by BMS or its vendors (examples include IP sourced from the sites stock or commercial supply, or a specialty pharmacy) | The investigator or designee accepts responsibility for documenting traceability and study treatment integrity in accordance with requirements applicable under law and the SOPs/standards of the sourcing pharmacy.<br>These records should include:<br>• label identification number or batch number<br>• amount dispensed to and returned by each subject, including unique subject identifiers<br>• dates and initials of person responsible for Investigational Product dispensing/accountability, as per the Delegation of Authority Form. |

BMS or designee will provide forms to facilitate inventory control if the investigational site does not have an established system that meets these requirements.

## CASE REPORT FORMS

An investigator is required to prepare and maintain adequate and accurate case histories designed to record all observations and other data pertinent to the investigation on each individual treated or entered as a control in the investigation. Data that are derived from source documents and reported on the CRF must be consistent with the source documents or the discrepancies must be explained. Additional clinical information may be collected and analyzed in an effort to enhance understanding of product safety. CRFs may be requested for AEs and/or laboratory abnormalities that are reported or identified during the course of the study.

For sites using the Sponsor or designee electronic data capture tool, electronic CRFs will be prepared for all data collection fields except for fields specific to SAEs and pregnancy, which will be reported on the electronic SAE form and paper Pregnancy Surveillance form, respectively. If electronic SAE form is not available, a paper SAE form can be used.

The confidentiality of records that could identify subjects must be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

The investigator will maintain a signature sheet to document signatures and initials of all persons authorized to make entries and/or corrections on CRFs.

The completed CRF, SAE/pregnancy CRFs, must be promptly reviewed, signed, and dated by the investigator or qualified physician who is a subinvestigator and who is delegated this task on the Delegation of Authority Form. Subinvestigators in Japan may not be delegated the CRF approval task. For electronic CRFs, review and approval/signature is completed electronically through the electronic data capture tool. The investigator must retain a copy of the CRFs including records of the changes and corrections.

Each individual electronically signing electronic CRFs must meet Sponsor or designee training requirements and must only access the electronic data capture tool using the unique user account provided by Sponsor or designee. User accounts are not to be shared or reassigned to other individuals

## MONITORING

Sponsor or designee representatives will review data centrally to identify potential issues to determine a schedule of on-site visits for targeted review of study records.

Representatives of BMS must be allowed to visit all study site locations periodically to assess the data quality and study integrity. On site they will review study records and directly compare them with source documents, discuss the conduct of the study with the investigator, and verify that the facilities remain acceptable Certain CRF pages and/or electronic files may serve as the source documents:

In addition, the study may be evaluated by Sponsor or designee internal auditors and government inspectors who must be allowed access to CRFs, source documents, other study files, and study facilities. BMS audit reports will be kept confidential.

The investigator must notify BMS promptly of any inspections scheduled by regulatory authorities, and promptly forward copies of inspection reports to Sponsor or designee.

## RECORDS RETENTION

The investigator (or head of the study site in Japan) must retain all study records and source documents for the maximum period required by applicable regulations and guidelines, or institution procedures, or for the period specified by BMS or designee, whichever is longer. The investigator (or head of the study site in Japan) must contact BMS prior to destroying any records associated with the study.

BMS or designee will notify the investigator (or head of the study site in Japan) when the study records are no longer needed.

If the investigator withdraws from the study (eg, relocation, retirement), the records shall be transferred to a mutually agreed upon designee (eg, another investigator, study site, IRB). Notice of such transfer will be given in writing to BMS or designee.

## RETURN OF STUDY TREATMENT

For this study, study treatments (those supplied by BMS, a vendor or sourced by the investigator) such as partially used study treatment containers, vials and syringes may be destroyed on site.

| If.. | Then |
|---|---|
| Study treatments supplied by BMS (including its vendors | Any unused study treatments supplied by BMS can only be destroyed after being inspected and reconciled by the responsible Study Monitor unless study treatments containers must be immediately destroyed as required for safety, or to meet local regulations (eg, cytotoxics or biologics).<br><br>If study treatments will be returned, the return will be arranged by the responsible Study Monitor. |
| Study treatments sourced by site, not supplied by BMS (or its vendors) (examples include study treatments sourced from the sites stock or commercial supply, or a specialty pharmacy) | It is the investigator's or designee's responsibility to dispose of all containers according to the institutional guidelines and procedures. |

It is the investigator's or designee's responsibility to arrange for disposal, provided that procedures for proper disposal have been established according to applicable federal, state, local, and institutional guidelines and procedures, and provided that appropriate records of disposal are kept. The following minimal standards must be met:

- On-site disposal practices must not expose humans to risks from the drug.
- On-site disposal practices and procedures are in agreement with applicable laws and regulations, including any special requirements for controlled or hazardous substances.
- Written procedures for on-site disposal are available and followed. The procedures must be filed with the site's SOPs and a copy provided to BMS upon request.
- Records are maintained that allow for traceability of each container, including the date disposed of, quantity disposed, and identification of the person disposing the containers. The method of disposal, ie, incinerator, licensed sanitary landfill, or licensed waste disposal vendor must be documented.
- Accountability and disposal records are complete, up-to-date, and available for the Monitor to review throughout the clinical trial period.

It is the investigator's or designee's responsibility to arrange for disposal of all empty containers.

If conditions for destruction cannot be met the responsible Study Monitor will make arrangements for return of study treatments provided by BMS (or its vendors). Destruction of non-study treatments sourced by the site, not supplied by BMS, is solely the responsibility of the investigator or designee.

## CLINICAL STUDY REPORT AND PUBLICATIONS

A Signatory Investigator must be selected to sign the clinical study report.

For this protocol, the Signatory Investigator will be selected as appropriate based on the following criteria:

- External Principal Investigator designated at protocol development
- National Coordinating Investigator
- Study Steering Committee chair or their designee
- Subject recruitment (eg, among the top quartile of enrollers)
- Involvement in trial design
- Regional representation (eg, among top quartile of enrollers from a specified region or country)
- Other criteria (as determined by the study team)

The data collected during this study are confidential and proprietary to Sponsor or designee. Any publications or abstracts arising from this study must adhere to the publication requirements set forth in the clinical trial agreement (CTA) governing [Study site or Investigator] participation in the study. These requirements include, but are not limited to, submitting proposed publications to Sponsor or designee at the earliest practicable time prior to submission or presentation and otherwise within the time period set forth in the CTA.

# APPENDIX 3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS: DEFINITIONS AND PROCEDURES FOR RECORDING, EVALUATING, FOLLOW UP AND REPORTING

## ADVERSE EVENTS

**Adverse Event Definition:**

An adverse event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation subject administered study drug and that does not necessarily have a causal relationship with this treatment.

An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug.

**Events Meeting the AE Definition**

- Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or results from other safety assessments (eg, ECG, radiological scans, vital signs measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator. Note that abnormal lab tests or other safety assessments should only be reported as AEs if the final diagnosis is not available. Once the final diagnosis is known, the reported term should be updated to be the diagnosis.
- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition.
- New conditions detected or diagnosed after study intervention administration even though it may have been present before the start of the study.
- Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction.
- Signs, symptoms, or the clinical sequelae of a suspected overdose of either study intervention or a concomitant medication. Overdose, as a verbatim term (as reported by the investigator), should not be reported as an AE/SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae and should specify "intentional overdose" as the verbatim term.

**Events <u>NOT</u> Meeting the AE Definition**

- Medical or surgical procedure (eg, endoscopy, appendectomy): the condition that leads to the procedure is the AE.
- Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).

### DEFINITION OF SAE

If an event is not an AE per definition above, then it cannot be an SAE even if serious conditions are met.

## SERIOUS ADVERSE EVENTS

| **Serious Adverse Event Definition: Any untoward medical occurrence that, at any dose:** |
|---|
| Results in death |
| Is life-threatening (defined as an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe) |
| Requires inpatient hospitalization or causes prolongation of existing hospitalization (see note below)<br>Note: The following hospitalizations are not considered SAEs in BMS clinical studies:<br>• a visit to the emergency room or other hospital department < 24 hours, that does not result in admission (unless considered an important medical or life-threatening event)<br>• elective surgery, planned prior to signing consent<br>• admissions as per protocol for a planned medical/surgical procedure<br>• routine health assessment requiring admission for baseline/trending of health status (eg, routine colonoscopy)<br>• medical/surgical admission other than to remedy ill health and planned prior to entry into the study. Appropriate documentation is required in these cases.<br>• admission encountered for another life circumstance that carries no bearing on health status and requires no medical/surgical intervention (eg, lack of housing, economic inadequacy, caregiver respite, family circumstances, administrative reason)<br>• admission for administration of anticancer therapy in the absence of any other SAEs (applies to oncology protocols) |
| Results in persistent or significant disability or permanent damage |
| Is a congenital anomaly/birth defect |
| Is an important medical event (defined as a medical event(s) that may not be immediately life-threatening or result in death or hospitalization but, based upon appropriate medical and scientific judgment, may jeopardize the subject or may require intervention [eg, medical, surgical] to prevent one of the other serious outcomes listed in the definition above). Examples of such events include, but are not limited to, intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalization. Potential drug-induced liver injury (DILI) is also considered an important medical event (see Section 8.2.7 for the definition of potential DILI). |

Pregnancy and potential DILI must follow the same transmission timing and processes to BMS as used for SAEs (see Section 8.2.5 for reporting pregnancies).

Any component of a study endpoint that is considered related to study therapy should be reported as SAE (eg, death is an endpoint, if death occurred due to anaphylaxis, anaphylaxis must be reported).

## EVALUATING AEs AND SAEs

**Assessment of Intensity**

The intensity of AEs is determined by a physician and will use the following levels:

- Mild: An event that is easily tolerated by the subject, causing minimal discomfort, and not interfering with everyday activities.
- Moderate: An event that causes sufficient discomfort and interferes with normal everyday activities.
- Severe: An event that prevents normal everyday activities. An AE that is assessed as severe should not be confused with an SAE. Severe is a category utilized for rating the intensity of an event; and both AEs and SAEs can be assessed as severe.

**Assessment of Causality**

- The investigator is obligated to assess the relationship between study intervention and each occurrence of each AE/SAE. A "reasonable possibility of a relationship" conveys that there are facts, evidences, and/or arguments to suggest a causal relationship rather than a relationship cannot be ruled out.
- The investigator will use clinical judgment to determine the relationship.
- Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study intervention administration will be considered and investigated.
- The investigator will also consult the Investigator's Brochure (IB) and/or Product Information, for marketed products, in his/her assessment.
- For each AE/SAE, the investigator must document in the medical notes that he/she has reviewed the AE/SAE and has provided an assessment of causality.
- There may be situations in which an SAE has occurred and the investigator has minimal information to include in the initial report to Sponsor. However, it is very important that the investigator always make an assessment of causality for every event before the initial transmission of the SAE data to Sponsor.
- The investigator may change his/her opinion of causality in light of follow-up information and send a SAE follow-up report with the updated causality assessment.
- The causality assessment is one of the criteria used when determining regulatory reporting requirements.

**Follow-up of AEs and SAEs**

If only limited information is initially available, follow-up reports are required. Note: Follow-up SAE reports must include the same investigator term(s) initially reported.

If an ongoing SAE changes in its intensity or relationship to study drug or if new information becomes available, the SAE report must be updated and submitted within 24 hours to BMS (or designee) using the same procedure used for transmitting the initial SAE report.

All SAEs must be followed to resolution or stabilization.

## REPORTING OF SAES TO SPONSOR OR DESIGNEE

SAEs, whether related or not related to study drug, and pregnancies must be reported to PRA Drug Safety within 24 hours of awareness of the event.

SAEs must be recorded on the SAE Report Form. For studies capturing SAEs through electronic data capture (EDC), electronic submission is the required method for reporting. In the event the electronic system is unavailable for transmission, paper forms must be used and submitted immediately. When paper forms are used, the original paper forms are to remain on site.

Pregnancies must be recorded on a paper Pregnancy Surveillance Form and transmitted via email or confirmed facsimile (fax) transmission to:

**SAE Email Address:** BMSSafety@prahs.com

**SAE Fax Number:**

**Americas:** 1-888-772-6919 (or 1-434- 951-3482)

**Europe/East Asia Pacific:** +44-1792-525-720

**SAE Telephone Contact -** For questions on SAE/pregnancy reporting, please call:

**Americas:** 1-800 772 2215 (or 1-434-951-3489)

**Europe/East Asia Pacific:** +49-621-878-2154.

# APPENDIX 4 WOMEN OF CHILDBEARING POTENTIAL DEFINITIONS AND METHODS OF CONTRACEPTION

## DEFINITIONS

### Woman of Childbearing Potential (WOCBP)

A woman is considered fertile following menarche and until becoming post-menopausal unless permanently sterile. Permanent sterilization methods include hysterectomy, bilateral salpingectomy, and bilateral oophorectomy.

### Women in the following categories are not considered WOCBP

- Premenarchal
- Premenopausal female with 1 of the following:
  - Documented hysterectomy
  - Documented bilateral salpingectomy
  - Documented bilateral oophorectomy

Note: Documentation can come from the site personnel's review of the subject's medical records, medical examination, or medical history interview.

- Postmenopausal female
  - A postmenopausal state is defined as 12 months of amenorrhea in a woman over age 45 years in the absence of other biological or physiological causes. In addition, females under the age of 55 years must have a serum follicle stimulating hormone, (FSH) level > 40 mIU/mL to confirm menopause.

Note: Females treated with hormone replacement therapy, (HRT) are likely to have artificially suppressed FSH levels and may require a washout period in order to obtain a physiologic FSH level. The duration of the washout period is a function of the type of HRT used. The duration of the washout period below are suggested guidelines and the investigators should use their judgement in checking serum FSH levels.

- 1 week minimum for vaginal hormonal products (rings, creams, gels)
- 4 week minimum for transdermal products
- 8 week minimum for oral products

Other parenteral products may require washout periods as long as 6 months. If the serum FSH level is > 40 mIU/ml at any time during the washout period, the woman can be considered postmenopausal.

## CONTRACEPTION GUIDANCE FOR FEMALE SUBJECTS OF CHILD BEARING POTENTIAL

One of the highly effective methods of contraception listed below, in conjunction with the required restrictions in Inclusion Criterion Sec 5.1 (3d) of the protocol, is required during study duration and until the end of relevant systemic exposure plus 30 days. As such, in Part A WOCBP must

agree to follow instructions for methods of contraception for 33 days post-treatment completion, and in Part B WOCBP must agree to follow instructions for methods of contraception for 190 days post-treatment completion.

Local laws and regulations may require use of alternative and/or additional contraception methods. Additionally, alternative and/or additional contraception methods may be required based on background DMARDS the subject may be taking (eg, methotrexate, leflunomide, etc.)

| **Highly Effective Contraceptive Methods That Are User Dependent**<br><br>*Failure rate of <1% per year when used consistently and correctly.*[a] |
|---|
| • Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation[b]<br>– oral<br>– intravaginal<br>– transdermal |
| • Progestogen-only hormonal contraception associated with inhibition of ovulation[b]<br>– oral<br>– injectable |
| **Highly Effective Methods That Are User Independent** |
| • Implantable progestogen-only hormonal contraception associated with inhibition of ovulation [b]<br>• Intrauterine device (IUD)[c]<br>• Intrauterine hormone-releasing system (IUS)[c]<br>• Bilateral tubal occlusion |
| • Vasectomized partner<br><br>*A vasectomized partner is a highly effective contraception method provided that the partner is the sole male sexual partner of the WOCBP and the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used.* |
| • Sexual abstinence<br><br>*Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatment. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the subject.*<br><br>• It is not necessary to use any other method of contraception when complete abstinence is elected.<br>• WOCBP subjects who choose complete abstinence must continue to have pregnancy tests, as specified in Section 2.<br>• Acceptable alternate methods of highly effective contraception must be discussed in the event that the WOCBP subjects chooses to forego complete abstinence |

NOTES:

[a] Typical use failure rates may differ from those when used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for subjects participating in clinical studies.

[b] Hormonal contraception may be susceptible to interaction with the study treatment, which may reduce the efficacy of the contraceptive method. Hormonal contraception is permissible only when there is sufficient evidence that the IMP and other study medications will not alter hormonal exposures such that contraception would be ineffective or result in increased exposures that could be potentially hazardous. In this case, alternative methods of contraception should be utilized.

[c] Intrauterine devices and intrauterine hormone releasing systems are acceptable methods of contraception in the absence of definitive drug interaction studies when hormone exposures from intrauterine devices do not alter contraception effectiveness

| **Less Than Highly Effective Contraceptive Methods That Are User Dependent**<br>*Failure rate of >1% per year when used consistently and correctly.* |
|---|
| • Male or female condom with or without spermicide. Male and female condoms cannot be used simultaneously<br>• Diaphragm with spermicide<br>• Cervical cap with spermicide<br>• Vaginal Sponge with spermicide<br>• Progestogen-only oral hormonal contraception, where inhibition of ovulation is not the primary mechanism of action |
| **Unacceptable Methods of Contraception** |
| • Periodic abstinence (calendar, symptothermal, post-ovulation methods)<br>• Withdrawal (coitus interruptus).<br>• Spermicide only<br>• Lactation amenorrhea method (LAM) |

## CONTRACEPTION GUIDANCE FOR MALE SUBJECTS WITH PARTNER(S) OF CHILD BEARING POTENTIAL.

Male subjects with female partners of childbearing potential are eligible to participate if they agree to the following during the treatment and until the end of relevant systemic exposure.

- Inform any and all partner(s) of their participation in a clinical drug study and the need to comply with contraception instructions as directed by the investigator.
- Male subjects are required to use a condom for study duration and for 93 days post-treatment completion in Part A and 250 days post-treatment completion in Part B.
- Female partners of males participating in the study to consider use of effective methods of contraception for 93 days after the end of treatment in the male subject in Part A and 250 days after the end of treatment in the male subject in Part B.

- Male subjects with a pregnant or breastfeeding partner must agree to remain abstinent from penile vaginal intercourse or use a male condom during each episode of penile penetration during the treatment and for 93 days after the end of treatment in Part A and 250 days after the end of treatment in Part B.
- Refrain from donating sperm for the duration of the study treatment and for 93 days after the end of treatment in Part A and 250 days after the end of treatment in Part B.

## COLLECTION OF PREGNANCY INFORMATION

Guidance for collection of Pregnancy Information and outcome of pregnancy on the Pregnancy Surveillance Form is provided in Section 8.2.5 and APPENDIX 3.

# APPENDIX 5 AMERICAN COLLEGE OF RHEUMATOLOGY CORE DATASET AND RESPONSE DEFINITIONS

| ACR core data set component | Validated Measurement Tool |
|---|---|
| Tender joint count | Standardized 68 joint count |
| Swollen joint count | Standardized 66 joint count |
| Subject global assessment of pain | A 0-100 mm visual analog scale |
| Subject global assessment of disease activity | A 0-100 mm visual analog scale |
| Physician global assessment of psoriatic arthritis | A 0-100 mm visual analog scale |
| Subject assessment of physical function | Health Assessment Questionnaire (HAQ) |
| Acute phase reactant value | ESR (Westergren) and C-reactive protein |

The ACR 20, ACR 50, or ACR 70 definition of improvement is a 20%, 50%, or 70% improvement, respectively, over baseline in tender and swollen joint counts (#1 and #2) and a 20%, 50%, or 70% improvement, respectively, in 3 of the 5 remaining core data set measures (components #3 to #7).

# APPENDIX 6 AMERICAN COLLEGE OF RHEUMATOLOGY SUBJECT ASSESSMENT OF PHYSICAL FUNCTION SCALE: HEALTH ASSESSMENT QUESTIONNAIRE (HAQ)

## HEALTH ASSESSMENT QUESTIONNAIRE

In this section we are interested in learning how your illness affects your ability to function in daily life. Please feel free to add any comments on the back of this page.

**Please check the response which best describes your usual abilities OVER THE PAST WEEK:**

| | Without ANY Difficulty (0) | With SOME Difficulty (1) | With MUCH Difficulty (2) | UNABLE To Do (3) |
|---|---|---|---|---|
| **DRESSING & GROOMING**<br>Are you able to: | | | | |
| - Dress yourself, including tying shoelaces and doing buttons? | __0 | __1 | __2 | __3 |
| - Shampoo your hair? | __0 | __1 | __2 | __3 |
| | | | | |
| **ARISING**<br>Are you able to: | | | | |
| - Stand up from a straight chair? | __0 | __1 | __2 | __3 |
| - Get in and out of bed? | __0 | __1 | __2 | __3 |
| | | | | |
| **EATING**<br>Are you able to: | | | | |
| - Cut your meat? | __0 | __1 | __2 | __3 |
| - Lift a full cup or glass to your mouth? | __0 | __1 | __2 | __3 |
| - Open a new milk carton? | __0 | __1 | __2 | __3 |
| | | | | |
| **WALKING**<br>Are you able to: | | | | |
| - Walk outdoors on flat ground? | __0 | __1 | __2 | __3 |
| - Climb up five steps? | __0 | __1 | __2 | __3 |

**Please check any AIDS OR DEVICES that you usually use for any of these activities:**

| | |
|---|---|
| _____Cane | _____Devices used for dressing (button hook, zipper pull, long-handled shoe horn, etc.) |
| _____Walker | _____Built up or special utensils |
| _____Crutches | _____Special or built up chair |
| _____Wheelchair | _____Other (Specify:_____) |

**Please check any categories for which you usually need HELP FROM ANOTHER PERSON:**

| | |
|---|---|
| _____Dressing and Grooming | _____Eating |
| _____Arising | _____Walking |

**Please check the response which best describes your usual abilities OVER THE PAST WEEK:**

| | Without ANY Difficulty (0) | With SOME Difficulty (1) | With MUCH Difficulty (2) | UNABLE To Do (3) |
|---|---|---|---|---|
| **HYGIENE**<br>Are you able to: | | | | |
| - Wash and dry your body? | __0 | __1 | __2 | __3 |
| - Take a tub bath? | __0 | __1 | __2 | __3 |
| - Get on and off the toilet? | __0 | __1 | __2 | __3 |
| **REACH**<br>Are you able to: | | | | |
| - Reach and get down a 5 pound object (such as a bag of sugar) from just above your head? | __0 | __1 | __2 | __3 |
| - Bend down to pick up clothing from the floor? | __0 | __1 | __2 | __3 |
| | | | | |
| **GRIP**<br>Are you able to: | | | | |
| - Open car doors? | __0 | __1 | __2 | __3 |
| - Open jars which have been previously opened? | __0 | __1 | __2 | __3 |
| - Turn faucets on and off? | __0 | __1 | __2 | __3 |
| **ACTIVITIES**<br>Are you able to: | | | | |
| - Run errands and shop? | __0 | ____ | __2 | __3 |
| - Get in and out of a car? | __0 | __1 | __2 | __3 |
| - Do chores such as vacuuming or yardwork? | __0 | __1 | __2 | __3 |

**Please check any AIDS OR DEVICES that you usually use for any of these activities:**

| | |
|---|---|
| ____Raised toilet seat | ____Bathtub bar |
| ____Bathtub seat | ____Long-handled appliances for reach |
| ____Jar opener (for jars previously opened) | ____Long-handled appliances in bathroom |
| | ____Other (Specify: |

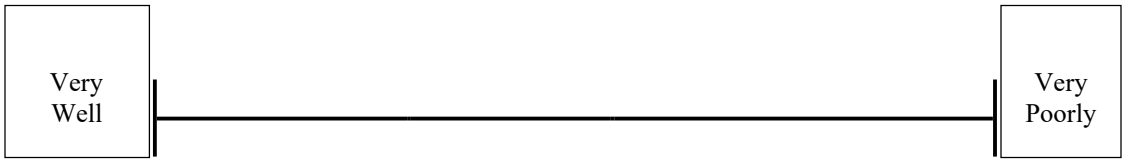
**Please check any categories for which you usually need HELP FROM ANOTHER PERSON:**

| | |
|---|---|
| ____Hygiene | ____Gripping and opening things |
| ____Reach | ____Errands and chores |

# APPENDIX 7 AMERICAN COLLEGE OF RHEUMATOLOGY SUBJECT ASSESSMENT OF DISEASE ACTIVITY VISUAL ASSESSMENT SCALE

Measure with a metric ruler. Line on Case Report Form is exactly 10 cm long. Scores should be recorded in millimeter format. DO NOT USE THIS APPENDIX AS SOURCE DOCUMENT OR CASE REPORT FORM.

In all the ways in which your psoriatic arthritis as a whole, affects you, how would you rate the way you felt over the past week ?



# APPENDIX 8 AMERICAN COLLEGE OF RHEUMATOLOGY SUBJECT ASSESSMENT OF PAIN SCALE

Measure with a metric ruler. Line on Case Report Form is exactly 10 cm long. Scores should be recorded in millimeter format. DO NOT USE THIS APPENDIX AS SOURCE DOCUMENT OR CASE REPORT FORM.

How much pain have you had because of your psoriatic arthritis over the past week? Place a mark on the line below to indicate how severely your pain has been:

# APPENDIX 9 PSORIASIS AREA AND SEVERITY INDEX (PASI)

Psoriasis Area and Severity Index (PASI); a quantitative rating scale for measuring the severity of psoriatic lesions based on area coverage and plaque appearance. Please complete **all** sections of the table.

| **Plaque Characteristic** | **Rating score** | **Body region (and weighting factor)** | | | |
|---|---|---|---|---|---|
| | | **Head** | **Upper Extremities** | **Trunk** | **Lower Extremities** |
| Erythema (Redness) | 0 = None<br>1 = Slight<br>2 = Moderate<br>3 = Severe<br>4 = Very severe | | | | |
| Infiltration (Thickness) | | | | | |
| Desquamation (Scaling) | | | | | |
| Add together each of the 3 scores for each of the body regions to give 4 separate sub totals. | | | | | |
| Sub Totals | | A1 = | A2 = | A3 = | A4 = |
| Multiply each subtotal by amount of body surface area represented by that region i.e. A1 x 0.1 for head, A2 x 0.2 for upper extremities, A3 x 0.3 for trunk, A4 x 0.4 for lower extremities to give a value B1, B2, B3 and B4 for each body region respectively | | | | | |
| | | A1 x 0.1 = B1 | A2 x 0.2 = B2 | A3 x 0.3 = B3 | A4 x 0.4 = B4 |
| | | B1 = | B2 = | B3 = | B4 = |
| Degree of involvement as % for each body region affected; (score each region with score between 0-6) | 0 = None<br>1 = 1-9 %<br>2 = 10-29%<br>3 = 30-49%<br>4 = 50 -69%<br>5 = 70-89%<br>6 = 90-100% | | | | |
| *For each body region multiply sub total B1, B2, B3 and B4 by the score (0-6) of the % of body region involved to give 4 subtotals C1, C2, C3 and C4* | | | | | |
| | | B1 x score = C1 | B2 x score = C2 | B3 x score = C3 | B4 x score = C4 |
| | | C1 = | C2 = | C3 = | C4 = |
| **The patient's PASI score is the sum of C1 + C2 + C3 + C4** | | | | **PASI=** | |

# APPENDIX 10 PHYSICIAN'S GLOBAL ASSESSMENT-FINGERNAILS (PGA-F)

For this assessment in subjects with psoriasis fingernail involvement, the overall condition of the fingernails is rated by the investigator on a 0-4 (5-point) scale. The overall score assigned based on the higher of the nail bed/nail matrix score:

| | | Nail Bed Signs | Nail Matrix Signs |
|---|---|---|---|
| Clear | 0 | Onycholysis- consistent with a normal nail<br>**AND**<br>Hyperkeratosis- none<br>**AND**<br>Splinter Hemorrhages-consistent with non-psoriatic splinter hemorrhages<br>**AND**<br>Nail Bed Erythema- none | No non-psoriatic nail plate irregularities including pitting, crumbling, Beau's lines, senile onychorrhexis, and non-psoriatic leukonychia |
| Minimal | 1 | Onycholysis- < 10% involved on all nails<br>**OR**<br>Hyperkeratosis- present, but barely detectable elevation of nail plate<br>**OR**<br>Nail Bed Erythema- faint<br>**AND**<br>Splinter Hemorrhages- consistent with non-psoriatic splinter hemorrhages | No more than 5 pits or psoriatic leukonychia on any nail<br>**AND**<br>No crumbling |
| Mild | 2 | Onycholysis- >10% on five or more nails<br>**OR**<br>Hyperkeratosis- present with mild elevation of nail plate<br>**OR**<br>Splinter Hemorrhages- present on four or fewer nails<br>**OR**<br>Nail Bed Erythema- mild | Five or more nails with mild pitting (eg, >10 pits/nail) or psoriatic leukonychia<br>**AND**<br>No crumbling |
| Moderate | 3 | Onycholysis- >30% on at least one nail<br>**OR**<br>Hyperkeratosis- present with moderate elevation of nail plate<br>**OR**<br>Splinter Hemorrhages- scattered and present on five or more nails<br>**OR**<br>Nail Bed Erythema- moderate | Five or more nails with moderate pitting (eg, >25 pits/nail)<br>**AND**<br>≤25% crumbling on any nails |
| Severe | 4 | Onycholysis- >50% on at least one nail<br>**OR**<br>Hyperkeratosis- present with severe elevation of nail plate<br>**OR**<br>Splinter Hemorrhages- numerous and present on five or more nails<br>**OR**<br>Nail Bed Erythema- severe | Five or more nails with severe pitting (>50 pits/nail)<br>**AND**<br>>25% crumbling on any nail |

# APPENDIX 11 THE BATH ANKYLOSING SPONDYLITIS DISEASE ACTIVITY INDEX (BASDAI)

Please place a mark on each line below to indicate your answer to each question relating to the past week

1. How would you describe the overall level of fatigue/tiredness you have experienced?

NONE_____VERY SEVERE

2. How would you describe the overall level of AS neck, back or hip pain you have had?

NONE_____VERY SEVERE

3. How would you describe the overall level of pain/swelling in joints other than neck, back, hips you have had?

NONE_____VERY SEVERE

4. How would you describe the overall level of discomfort you have had from any areas tender to touch or pressure?

NONE_____VERY SEVERE

5. How would you describe the overall level of morning stiffness you have had from the time you wake up?

NONE_____VERY SEVERE

6. How long does your morning stiffness last from the time you wake up?

_____

0 hrs ½ 1 1½ 2 or more hours

# APPENDIX 12 SHORT FORM HEALTH SURVEY-36 ITEM (SF-36)

This survey asks for your views about your health. This information will help you keep track of how you feel and how well you are able to do your usual activities.

Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully, and click on the circle that best describes your answer. *Thank you for completing this survey!*

---

**1) In general, would you say your health is:**

| Excellent | Very good | Good | Fair | Poor |
|---|---|---|---|---|
| ○ | ○ | ○ | ○ | ○ |

---

**2) Compared to one year ago, how would you rate your health in general now?**

| Much better now than one year ago | Somewhat better now than one year ago | About the same as one year ago | Somewhat worse now than one year ago | Much worse now than one year ago |
|---|---|---|---|---|
| ○ | ○ | ○ | ○ | ○ |

---

**3) The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?**

| | Yes, limited a lot | Yes, limited a little | No, not limited at all |
|---|---|---|---|
| a. Vigorous Activities, such as running, lifting heavy objects, participating in strenuous sports | ○ | ○ | ○ |
| b. Moderate Activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf | ○ | ○ | ○ |
| c. Lifting or carrying groceries | ○ | ○ | ○ |
| d. Climbing several flights of stairs | ○ | ○ | ○ |
| e. Climbing one flight of stairs | ○ | ○ | ○ |
| f. Bending, kneeling, or stooping | ○ | ○ | ○ |
| g. Walking more than a mile | ○ | ○ | ○ |
| h. Walking several hundred yards | ○ | ○ | ○ |
| i. Walking one hundred yards | ○ | ○ | ○ |
| j. Bathing or dressing yourself | ○ | ○ | ○ |

**4) During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?**

| | All of the time | Most of the time | Some of the time | A little of the time | None of the time |
|---|---|---|---|---|---|
| a. Cut down on the amount of time you spent on work or other activities | ○ | ○ | ○ | ○ | ○ |
| b. Accomplished less than you would like | ○ | ○ | ○ | ○ | ○ |
| c. Were limited in the kind of work or other activities | ○ | ○ | ○ | ○ | ○ |
| d. Had difficulty performing the work or other activities (for example, it took extra effort) | ○ | ○ | ○ | ○ | ○ |

---

**5) During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?**

| | All of the time | Most of the time | Some of the time | A little of the time | None of the time |
|---|---|---|---|---|---|
| a. Cut down on the amount of time you spent on work or other activities | ○ | ○ | ○ | ○ | ○ |
| b. Accomplished less than you would like | ○ | ○ | ○ | ○ | ○ |
| c. Did work or activities less carefully than usual | ○ | ○ | ○ | ○ | ○ |

---

**6) During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?**

| Not at all | Slightly | Moderately | Quite a bit | Extremely |
|---|---|---|---|---|
| ○ | ○ | ○ | ○ | ○ |

---

**7) How much bodily pain have you had during the past 4 weeks?**

| None | Very Mild | Mild | Moderate | Severe | Very Severe |
|---|---|---|---|---|---|
| ○ | ○ | ○ | ○ | ○ | ○ |

---

**8) During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?**

| Not at all | A little bit | Moderately | Quite a bit | Extremely |
|---|---|---|---|---|
| ○ | ○ | ○ | ○ | ○ |

---

**9) These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...**

| | All of the time | Most of the time | Some of the time | A little of the time | None of the time |
|---|---|---|---|---|---|
| a. Did you feel full of life? | ○ | ○ | ○ | ○ | ○ |
| b. Have you been very nervous? | ○ | ○ | ○ | ○ | ○ |
| c. Have you felt so down in the dumps that nothing could cheer you up? | ○ | ○ | ○ | ○ | ○ |
| d. Have you felt calm and peaceful? | ○ | ○ | ○ | ○ | ○ |
| e. Did you have a lot of energy? | ○ | ○ | ○ | ○ | ○ |
| f. Have you felt downhearted and depressed? | ○ | ○ | ○ | ○ | ○ |
| g. Did you feel worn out? | ○ | ○ | ○ | ○ | ○ |
| h. Have you been happy? | ○ | ○ | ○ | ○ | ○ |
| i. Did you feel tired? | ○ | ○ | ○ | ○ | ○ |

**10) During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?**

| All of the time | Most of the time | Some of the time | A little of the time | None of the time |
|---|---|---|---|---|
| ○ | ○ | ○ | ○ | ○ |

**11) How TRUE or FALSE is each of the following statements for you?**

| | Definitely true | Mostly true | Don't know | Mostly false | Definitely false |
|---|---|---|---|---|---|
| a. I seem to get sick a little easier than other people | ○ | ○ | ○ | ○ | ○ |
| b. I am as healthy as anybody I know | ○ | ○ | ○ | ○ | ○ |
| c. I expect my health to get worse | ○ | ○ | ○ | ○ | ○ |
| d. My health is excellent | ○ | ○ | ○ | ○ | ○ |

## APPENDIX 13 PROMIS-FATIGUE

### Fatigue – Short Form 13a (FACIT-Fatigue) and 5 Supplemental Item Bank Items

**Please respond to each question or statement by marking one box per row.**

| | During the past 7 days… | Not at all | A little bit | Somewhat | Quite a bit | Very much |
|---|---|---|---|---|---|---|
| HI7 | I feel fatigued ..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| HI12 | I feel weak all over ..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| AN1 | I feel listless ("washed out")..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| AN2 | I feel tired ..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| AN3 | I have trouble starting things because I am tired..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| AN4 | I have trouble finishing things because I am tired..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| AN5 | I have energy ..... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| AN7 | I am able to do my usual activities... | ☐ 5 | ☐ 4 | ☐ 3 | ☐ 2 | ☐ 1 |
| AN8 | I need to sleep during the day..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| AN12 | I am too tired to eat ..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| AN14 | I need help doing my usual activities ..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| AN15 | I am frustrated by being too tired to do the things I want to do..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| AN16 | I have to limit my social activity because I am tired..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |

| | During the past 7 days… | Not at all | A little bit | Somewhat | Quite a bit | Very much |
|---|---|---|---|---|---|---|
| FATEXP36 | How exhausted were you on average?..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| FATIMP2 | To what degree did your fatigue make you feel slowed down in your thinking?..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| FATIMP36 | To what degree did your fatigue make it difficult to make decisions? | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| FATIMP52 | To what degree did your fatigue make you feel less alert?..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |
| FATIMP44 | To what degree did your fatigue make you more forgetful?..... | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |

20 February 2017

## APPENDIX 14 WORK LIMITATIONS QUESTIONNAIRE (WLQ)

Are you currently employed (working for pay)? If you have more than one job, report on your main job only.

_____NO ____ YES

*If NO, check "NO" and skip to question 4.*

The next two questions are about the **past seven days**, not including today.

During the past seven days, how many hours did you miss from work because of your health problems? *Include hours you missed on sick days, times you went in late, left early, etc., because of your health problems. Do not include time you missed to participate in this study.*

_____HOURS

During the past seven days, how many hours did you actually work?

_____HOURS

# WLQ Instructions

Health problems can make it difficult for working people to perform certain parts of their jobs. We are interested in learning about how your health may have affected you at work during the past 2 weeks.

(1) The questions will ask you to think about your physical health or emotional problems. These refer to any ongoing or permanent medical conditions you may have and the effects of any treatments you are taking for these. Emotional problems may include feeling depressed or anxious.

(2) The questions are multiple choice. They ask you to answer by placing a mark in a box.

For example:

a. How satisfied are you with your local schools?

(*Mark one box.*)

| | |
|---|---|
| **Not At All Satisfied** | ☐ |
| **Moderately Satisfied** | ☐ |
| **Very Satisfied** | ■ |

b. How satisfied are you with your local police department?

(*Mark one box.*)

| | |
|---|---|
| **Not At All Satisfied** | ☐ |
| **Moderately Satisfied** | ■ |
| **Very Satisfied** | ☐ |

These marks tell us you are very satisfied with your local schools and moderately satisfied with your local police department.

Questions 1 through 5 ask about how your health has affected you at work during the past 2 weeks. Please answer these questions even if you missed some workdays.

- *Mark the "Does not apply to my job" box only if the question describes something that is not part of your job.*
- *If you have more than one job, report on your **main** job only.*

1a. In the past 2 weeks, how much of the time did your physical health or emotional problems make it **difficult** for you to get going easily at the beginning of the workday?

(*Mark one box.*)

| | |
|---|---|
| **Difficult** all of the time (100%) | ☐ |
| **Difficult** most of the time | ☐ |
| **Difficult** some of the time (about 50%) | ☐ |
| **Difficult** a slight bit of the time | ☐ |
| **Difficult** none of the time (0%) | ☐ |
| Does not apply to my job | ☐ |

1b. In the past 2 weeks, how much of the time did your physical health or emotional problems make it **difficult** for you to start on your job as soon as you arrived at work?

(*Mark one box.*)

| | |
|---|---|
| **Difficult** all of the time (100%) | ☐ |
| **Difficult** most of the time | ☐ |
| **Difficult** some of the time (about 50%) | ☐ |
| **Difficult** a slight bit of the time | ☐ |
| **Difficult** none of the time (0%) | ☐ |
| Does not apply to my job | ☐ |

These questions ask you to rate the amount of time you were able to handle certain parts of your job without difficulty.

2a. In the past 2 weeks, how much of the time were you **able** to sit, stand, or stay in one position for longer than 15 minutes while working, without difficulty caused by physical health or emotional problems?

(*Mark one box.*)

| | |
|---|---|
| **Able** all of the time (100%) | ☐ |
| **Able** most of the time | ☐ |
| **Able** some of the time (about 50%) | ☐ |
| **Able** a slight bit of the time | ☐ |
| **Able** none of the time (0%) | ☐ |
| Does not apply to my job | ☐ |

2b. In the past 2 weeks, how much of the time were you **able** to repeat the same motions over and over again while working, without difficulty caused by physical health or emotional problems?

(*Mark one box.*)

| | |
|---|---|
| **Able** all of the time (100%) | ☐ |
| **Able** most of the time | ☐ |
| **Able** some of the time (about 50%) | ☐ |
| **Able** a slight bit of the time | ☐ |
| **Able** none of the time (0%) | ☐ |
| Does not apply to my job | ☐ |

This question asks about difficulties you may have had at work.

3. In the past 2 weeks, how much of the time did your physical health or emotional problems make it **difficult** for you to concentrate on your work?

(*Mark one box.*)

| | |
|---|---|
| **Difficult** all of the time (100%) | ☐ |
| **Difficult** most of the time | ☐ |
| **Difficult** some of the time (about 50%) | ☐ |
| **Difficult** a slight bit of the time | ☐ |
| **Difficult** none of the time (0%) | ☐ |
| Does not apply to my job | ☐ |

The next question asks about difficulties in relation to the people you came in contact with while working. These may include employers, supervisors, coworkers, clients, customers, or the public.

*4.* In the past 2 weeks, how much of the time did your physical health or emotional problems make it **difficult** for you to speak with people in-person, in meetings or on the phone?

(*Mark one box.*)

| | |
|---|---|
| **Difficult** all of the time (100%) | ☐ |
| **Difficult** most of the time | ☐ |
| **Difficult** some of the time (about 50%) | ☐ |
| **Difficult** a slight bit of the time | ☐ |
| **Difficult** none of the time (0%) | ☐ |
| Does not apply to my job | ☐ |

These questions ask about how things went at work overall.

5a. In the past 2 weeks, how much of the time did your physical health or emotional problems make it **difficult** for you to handle the workload?

(*Mark one box.*)

| | |
|---|---|
| **Difficult** all of the time (100%) | ☐ |
| **Difficult** most of the time | ☐ |
| **Difficult** some of the time (about 50%) | ☐ |
| **Difficult** a slight bit of the time | ☐ |
| **Difficult** none of the time (0%) | ☐ |
| Does not apply to my job | ☐ |

5b. In the past 2 weeks, how much of the time did your physical health or emotional problems make it **difficult** for you to finish work on time?

(*Mark one box.*)

| | |
|---|---|
| **Difficult** all of the time (100%) | ☐ |
| **Difficult** most of the time | ☐ |
| **Difficult** some of the time (about 50%) | ☐ |
| **Difficult** a slight bit of the time | ☐ |
| **Difficult** none of the time (0%) | ☐ |
| Does not apply to my job | ☐ |

# APPENDIX 15 THE EULAR PSORIATIC ARTHRITIS IMPACT OF DISEASE: PsAID 12 FOR CLINICAL PRACTICE

We want you to indicate how much your psoriatic arthritis impacts your health.
Please tell us how you have been feeling this last week.

**1. Pain**

Circle the number that best describes the pain you felt due to your psoriatic arthritis during the last week:

| None | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

For office use only
Result x3 ☐

**2. Fatigue**

Circle the number that best describes the overall level of fatigue due to your psoriatic arthritis you have experienced during the last week:

| No fatigue | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Totally exhausted |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

Result x2 ☐

**3. Skin problems**

Circle the number that best describes the skin problems including itching you felt due to your psoriatic arthritis during the last week:

| None | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

Result x2 ☐

**4. Work and/or leisure activities**

Circle the number that best describes the difficulties you had to participate fully in work and/or leisure activities due to your psoriatic arthritis during the last week:

| None | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

Result x2 ☐

**5. Functional capacity**

Circle the number that best describes the difficulty you had in doing daily physical activities due to your psoriatic arthritis during the last week:

| No difficulty | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme difficulty |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

Result x2 ☐

**6. Discomfort**

Circle the number that best describes the feeling of discomfort and annoyance with everyday tasks due to your psoriatic arthritis during the last week:

| None | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

Result x2 ☐

**7. Sleep disturbance**

Circle the number that best describes the sleep difficulties (i.e., resting at night) you felt due to your psoriatic arthritis during the last week:

| No difficulty | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme difficulty |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

Result x2 ☐

**8. Coping**

Considering your psoriatic arthritis overall, how well did you cope (manage, deal, make do) with your psoriatic arthritis during the last week?

| Very well | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Very poorly |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

For office use only
Result x1 ☐

**9. Anxiety, fear and uncertainty**

Circle the number that best describes the level of anxiety, fear and uncertainty (for example about the future, treatments, fear of loneliness) due to your psoriatic arthritis you have experienced during the last week:

| None | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

Result x1 ☐

**10. Embarrassment and/or shame**

Considering your psoriatic arthritis overall, circle the number that best describes the level of embarrassment and/or shame due to your appearance experienced during the last week:

| None | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

Result x1 ☐

**11. Social participation**

Circle the number that best describes the difficulties you had to participate fully in social activities (including relationships with family and/or people very close to you) due to your psoriatic arthritis during the last week:

| None | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

Result x1 ☐

**12. Depression**

Circle the number that best describes the level of depression due to your psoriatic arthritis you have experienced during the last week:

| None | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

Result x1 ☐

**THANK YOU FOR ANSWERING THIS QUESTIONNAIRE**

Final PsAID out of 20

Add up the ☐ and divide by 10:

☐

## PsAID12 SCORING AND CALCULATION RULES

**The PsAID is calculated based on 12 Numerical rating scales (NRS) questions. Each NRS is assessed as a number between 0 and 10.**

### Calculation

PsAID final value =

(PsAID1 (pain) NRS value (range 0-10) x 3)

+ (PsAID2 (fatigue) NRS value (range 0-10) x 2)

+ (PsAID3 (skin) NRS value (range 0-10) x 2)

+ (PsAID4 (Work and/or leisure activities) NRS value (range 0-10) x 2)

+ (PsAID5 (function) NRS value (range 0-10) x 2)

+ (PsAID6 (discomfort) NRS value (range 0-10) x 2)

+ (PsAID7 (sleep) NRS value (range 0-10) x 2)

+ (PsAID8 (coping) NRS value (range 0-10) x 1)

+ (PsAID9 (anxiety) NRS value (range 0-10) x 1)

+ (PsAID10 (embarrassment) NRS value (range 0-10) x 1)

+ (PsAID11 (social life) NRS value (range 0-10) x 1)

+ (PsAID12 (depression) NRS value (range 0-

10) x 1) The total is divided by 20.

Thus, the range of the final PsAID value is 0-10 where higher figures indicate worse status.

### Missing data imputation

If one of the 12 NRS values composing the PsAID is missing, the imputation is as follows: calculate the mean value of the 11 other (non-missing) NRS (range, 0-10)

impute this value for the missing NRS

Then, calculate the PsAID as explained above.

If 2 or more of the NRS are missing, the PsAID is considered as missing value (no imputation).