Official Title of Study:

A Multi-center, Randomized, Double-blind, Placebo-controlled, Parallel Group, Phase 2 Study to Evaluate Clinical Efficacy and Safety of Deucravacitinib (BMS-986165) in Participants with Alopecia Areata

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CLINICAL PROTOCOL IM011134

A Multi-center, Randomized, Double-blind, Placebo-controlled, Parallel Group, Phase 2 Study to Evaluate Clinical Efficacy and Safety of Deucravacitinib (BMS-986165) in Participants with Alopecia Areata

Protocol Amendment 02

Brief Title: Efficacy and Safety of Deucravacitinib in Adults with Alopecia Areata

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DOCUMENT HISTORY

Document	Date of Issue	Summary of Changes
Protocol Amendment 02	29-Aug-2023	The primary purpose for Protocol Amendment 02 is to incorporate changes [redacted] as well as to add clarifications based on feedback from study investigators. Language from the Japan-specific protocol amendment 01 was incorporated.
Protocol Amendment 01	24-Mar-2022	The primary reason for Protocol Amendment 01 is to refine the endpoints based on recently available external data. Additional revisions include the addition of a summary of the completed Phase 3 psoriasis deucravacitinib trials; updates to the background section based on new compounds in development; update of the Protocol Summary to align with respective changes to the protocol; updated study contacts on the Title Page.
Original Protocol	13-Jan-2021	Not applicable

OVERALL RATIONALE FOR PROTOCOL AMENDMENT 02:

The primary purpose of this amendment is to incorporate changes [redacted] as well as to add clarifications based on feedback from study investigators.

Language from the Japan-specific Amendment 01, related to the interpretation of hepatitis B virus test results to assess eligibility and to clarify expectations for assessments and sample collections, has been incorporated into this global amendment.

Other edits were incorporated throughout the protocol to correct minor errors, add clarity, and improve consistency. Key changes are summarized below.

This protocol amendment applies to all participants.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 02		
Section Number & Title	**Description of Change**	**Brief Rationale**
Title page	Clinical Scientist contact information updated.	To reflect personnel change
Section 2, Table 2-2 and Table 2-3: Schedule of Activities	Added a line item to assess for adverse events (AEs) of suicidal ideation and behavior throughout the study.	To add a reminder to document AEs of suicidal ideation and behavior as described [redacted]
Section 2, Table 2-2 and Table 2-3: Schedule of Activities	Added hepatitis B virus (HBV) testing during the Treatment and Follow-up periods (Table 2-2 and Table 2-3).	To incorporate Japan-specific amendment language into the global amendment.
Section 6.2 Exclusion Criteria	Modified Exclusion Criteria 2) f)	
Section 8.1: Discontinuation from Study Intervention	Added category to clarify criteria related to HBV status.	
Appendix 9: Interpretation of Hepatitis Serologic Test Results	Added a new appendix.	
Appendix 4: Women of Childbearing Potential Definitions and Methods of Contraception	Modified language on contraceptive use to align with [redacted] requirements. Added "Note: Intravaginal and transdermal combined hormonal contraceptives are not approved by the Health Authority in Japan. Also, progestogen-only hormonal contraceptives are not approved by the Health Authority in Japan."	

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 02		
Section Number & Title	**Description of Change**	**Brief Rationale**
Table 4-1: Objectives and Endpoints	[redacted]	[redacted]
Section 6.2: Exclusion Criteria, 5e)	Replaced "tacrolimus" with "topical calcineurin inhibitors (applied to the scalp)".	To clarify that the criterion referred to the class rather than a single example (tacrolimus).
Section 7.7: Concomitant Therapy	Added that topical corticosteroids cannot be applied to the eyelids and eyebrows. Added that topical calcineurin inhibitors are permitted but cannot be applied on the eyelids, eyebrows, or scalp.	To clarify permitted concomitant medications.
Section 8.1: Discontinuation from Study Intervention	Added additional discontinuation criterium for suicidal ideation and behavior. with referral to a mental health professional	Text added [redacted]
Section 9.1: Efficacy Assessments	[redacted]	[redacted]
Section 9.2.6: Pregnancy	Replaced the text "including during and at least for 3 days after study product administration" with "and through the end of the saftey follow-up period".	To clarify reporting of pregnancies.
Section 10.3: Analysis Sets Section 10.4.1: General Considerations Section 10.4.2: Primary Efficacy Endpoints	Modified the population for all efficacy analyses from the Full Analysis Set (FAS) to the randomized population.	[redacted] updated to use intent-to-treat (ITT) population for efficacy analyses.
Section 10.3: Analysis Sets	Expanded analysis sets to include [redacted] populations.	Populations will be used for [redacted] summaries, respectively.
Section 10.4.5: Other Safety Analyses	Remove statement "An outlier analysis of ECG results will be conducted."	While ECG results will be summarized, no outlier test will be performed as data to be collected will be too limited to support this test. .

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 02		
Section Number & Title	**Description of Change**	**Brief Rationale**
All	Minor grammatical, formatting, and typographical corrections.	To correct minor errors.

TABLE OF CONTENTS

1 PROTOCOL SUMMARY

Protocol Title: A Multi-center, Randomized, Double-blind, Placebo-controlled, Parallel Group, Phase 2 Study to Evaluate Clinical Efficacy and Safety of Deucravacitinib (BMS-986165) in Participants with Alopecia Areata

Brief Title: Efficacy and Safety of Deucravacitinib in Adults with Alopecia Areata

Rationale:

Study IM011134 is a Phase 2, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of deucravacitinib (BMS-986165) in participants with alopecia areata (AA). Deucravacitinib will be compared to placebo to evaluate the efficacy of deucravacitinib versus placebo for the treatment of alopecia areata.

Alopecia areata is a chronic, relapsing, immune-mediated inflammatory disorder characterized by non-scarring hair loss. AA can affect nearly 2% of the general population at some point in their lifetime. The pathogenesis of AA is thought to involve autoimmune-mediated attack on the hair follicles (HF) leading to the inhibition of normal hair growth. The proximal portion of the HF constitutes an immune-privileged site, refractory to immune responses, similar to the anterior chamber of the eye. This immune privilege appears to be disrupted in AA with increased leukocyte trafficking into the dermis, enhanced antigen presentation, and migration of autoreactive T cells to be within close proximity of HFs in AA lesions. Cluster of differentiation (CD) 8+ and CD4+ T cells, mostly of the T1 type, comprise a significant portion of the infiltrate around the bulb of the HF and are considered to be the main drivers of pathology in this condition. Interleukin (IL)-12 made by antigen-presenting cells are thought to drive T1 responses in inflammation.

Tyrosine kinase 2 (TYK2) is a non-receptor tyrosine kinase associated with receptors for the p40-containing cytokines interleukin (IL)-12 and IL-23, as well as the type I interferon (IFN) receptor, and is required for the activation of their downstream signaling pathways. TYK2 catalyzes the phosphorylation of the intracellular receptor domains and signal transducer and activator of transcription (STAT) proteins, resulting in the activation of STAT-dependent transcription and functional responses specific for these cytokines. TYK2-dependent pathways and the cytokine networks they modulate have been implicated in the pathophysiology of multiple immune-mediated diseases.

Deucravacitinib (BMS-986165) is a selective TYK2 inhibitor with a unique mechanism of action distinct from related Janus kinase (JAK) 1-3 inhibitors. Potent inhibition of IL-12/23 and Type I/III IFN-driven responses in mouse models of autoimmunity (psoriasis, colitis, and systemic lupus erythematosus [SLE]) and in healthy humans have been demonstrated with deucravacitinib. It has been shown to be effective in treatment of chronic plaque psoriasis in Phase 2 and Phase 3 studies and is currently being evaluated in psoriatic arthritis, SLE, lupus nephritis, Crohn's disease, and ulcerative colitis.

The rationale for evaluating the efficacy and safety of deucravacitinib for the treatment of AA is:

- A major pathway in the TYK2 signaling cascade (IL-12-mediated T1 cell induction and IFNγ production) has been implicated in AA disease pathogenesis, as noted above
- Targeting the IL-12/23 pathway with biologic agents has been shown to be efficacious in case studies and Phase 2 studies in AA

Objectives and Endpoints:

Objectives	Endpoints
Primary: Efficacy	
To evaluate the efficacy of deucravacitinib versus placebo at Week 24	• Change from baseline in SALT score at Week 24
Primary: Safety	
To evaluate the safety and tolerability of deucravacitinib versus placebo	• Incidence of AEs, SAEs, AEs leading to study discontinuation, and AEIs • Change in laboratory, ECG, physical examination, and vital sign parameters over time
Secondary: Efficacy	
To evaluate the efficacy of deucravacitinib versus placebo on additional endpoints at Week 24	• Proportion of participants achieving a ≥ 50% reduction in SALT score (SALT50 response) from baseline at Week 24 • Proportion of participants achieving a SALT score ≤ 20 at Week 24 • Proportion of participants achieving an AA-IGA score of 0 or 1 at Week 24 with at least a 2-point change from baseline

Abbreviations: AA-IGA, Alopecia Areata Investigator Global Assessment; AE, adverse event; AEI, adverse event of interest; ECG, electrocardiogram; SAE, serious adverse event; SALT, Severity of Alopecia Tool.

Overall Design:

This is a randomized, placebo-controlled, double-blind, parallel group, multi-center Phase 2 study to evaluate the efficacy and safety of 2 dosages of deucravacitinib (6 mg once daily [QD] and 6 mg twice daily [BID]) in participants with AA.

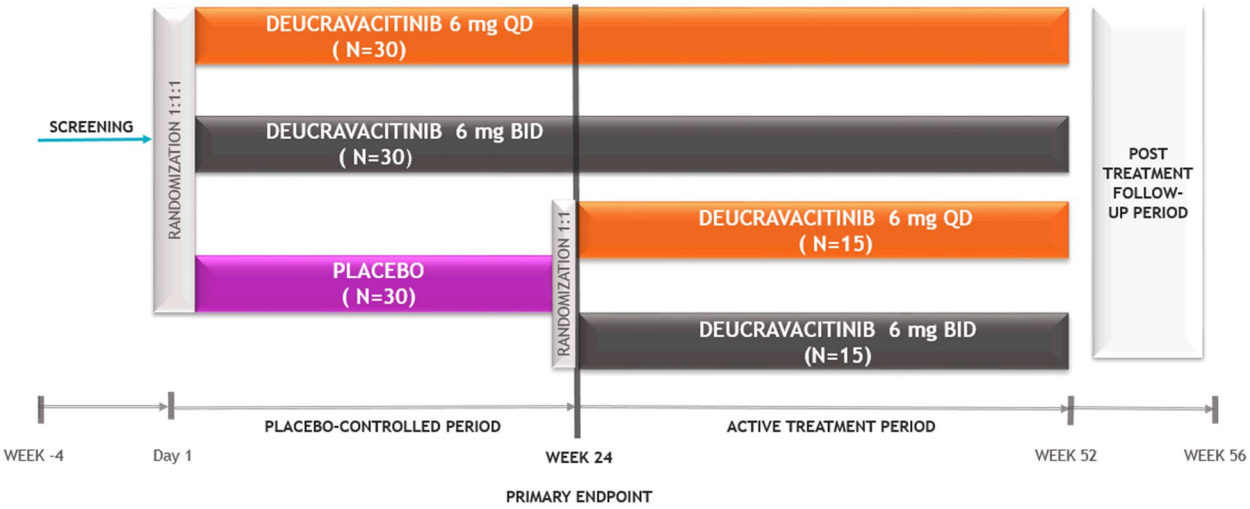
The primary endpoint of the study is the change from baseline in SALT score at Week 24.

The total duration of participation in the study will be approximately 60 weeks as follows:

- Screening Period: up to 4 weeks
- Placebo-controlled Treatment Period: 24 weeks (Day 1 to Week 24)
- Active Treatment Period: 28 weeks (Weeks 24 to 52)
- Post-treatment Follow-up Period: 4 weeks (Weeks 52 to 56)

The study design schematic is presented in Figure 1.

Figure 1: Study Design Schematic



Abbreviations: BID, twice daily; N, number; QD, once daily.

Eligible participants will be randomized on Day 1 in a blinded manner to receive deucravacitinib 6 mg QD, deucravacitinib 6 mg BID, or placebo in a 1:1:1 ratio. Randomization will be stratified by current duration of disease episode: < 4 years and ≥ 4 years. At the Week 24 study visit, the participants initially randomized to receive placebo will be re-randomized 1:1 in a blinded manner to receive deucravacitinib (6 mg QD or 6 mg BID) until Week 52. Participants initially randomized to deucravacitinib will continue on their assigned dosage in a blinded manner.

Number of Participants:

Approximately 90 participants will be randomized on Day 1 into 1 of 3 treatment arms in a 1:1:1 ratio, resulting in 30 participants in each of the 2 deucravacitinib treatment arms (6 mg QD and 6 mg BID) and 30 participants in the placebo arm.

Study Population:

Men and women ≥ 18 years to ≤ 65 years must meet the following criteria for entry into the study.

Key Inclusion Criteria:

- Signed Written Informed Consent
  - Participant must be willing and able to participate in the study and sign the informed consent form (ICF)
  - Participant must be willing and able to complete all study-specific procedures and visits
- Type of Participant and Target Disease Characteristics
  - Documented clinical diagnosis of AA for at least 6 months
  - Current episode of scalp hair loss (at Screening) must meet the following criteria:
    - Duration of at least 6 months

- ♦ Duration of current hair loss episode of AA affecting ≥ 50% of the scalp is not to exceed 8 years
- ♦ Scalp hair loss has been stable (ie, no significant spontaneous regrowth [> 10%] over the last 6 months)

– SALT score ≥ 50 at Screening and Day 1

Participant with complete scalp hair loss (SALT score of 100) with or without body hair involvement can be included

– Participant must have an Alopecia Areata Investigator Global Assessment (AA-IGA) grade ≥ 3 at Screening and Day 1
– Participant should not shave their scalp 7 days prior to the Screening visit, and agree to not shave their scalp 7 days prior to each study visit, to allow for SALT assessment of hair regrowth. If participant is using a hairpiece or wig, the participant must be willing and able to remove the hair prosthetic at each appointment. Participant should maintain a stable hair style to allow for reliable and consistent assessment of SALT throughout the study.
– Participant with current or a history of androgenetic alopecia can be included as long as, in the opinion of the investigator, the participant has either of the following classifications: Ludwig Scale ≤ II for women; Hamilton-Norwood Scale ≤ III for men.

Note: A male participant with Hamilton-Norwood III vertex or Hamilton-Norwood IIIa classification will be excluded.

Key Exclusion Criteria:

- Exclusionary Disease Characteristics
  - Participant with diffuse-type AA or other forms of hair loss, including traction alopecia, lichen planopilaris, central centrifugal cicatricial alopecia, frontal fibrosing alopecia, etc.
  - Other active skin diseases affecting the scalp that in the opinion of the investigator may interfere with accurate assessment of SALT score.
  - Extensive tattooing of the scalp that in the opinion of the investigator may interfere with the accurate assessment of SALT score.

Intervention Groups and Duration:

Participants will receive oral doses of the investigational product (IP) as tablets for 52 weeks.

- Deucravacitinib 6 mg QD: 52 weeks
- Deucravacitinib 6 mg BID: 52 weeks
- Placebo: 24 weeks of placebo followed by 28 weeks of deucravacitinib (6 mg QD or 6 mg BID)

Study Intervention:

Study Intervention for IM011134		
Medication	**Potency**	**IP/Non-IP**
Deucravacitinib	6 mg	IP
Placebo	N/A	IP

Abbreviations: IP, investigational product; mg, milligram, N/A, not applicable.

Statistical Methods

The primary efficacy analysis will be conducted on the randomized population. The randomized population consists of all participants who were randomized using Interactive Response Technology (IRT).

The analysis model for the primary efficacy endpoint will use the analysis of covariance (ANCOVA) to compare change from baseline of each active treatment group to placebo. The model will include treatment arm, the randomization stratification variable of alopecia episode duration (< 4 years and ≥ 4 years), and baseline SALT score. The primary methodology to impute the missing data will be multiple imputation with the assumption of missing at random. Additional sensitivity analyses will be further outlined in the statistical analysis plan (SAP).

The appropriate statistical models to each secondary [redacted] endpoints will be specified in detail in the SAP.

Data Monitoring Committee

A Data Monitoring Committee will be used in the study.

Other Committee: No

No other review committee will be used in the study.

2 SCHEDULE OF ACTIVITIES

Table 2-1: Screening Procedural Outline (IM011134)

Procedure	Screening Visit	Notes
Eligibility Assessments		
Informed Consent	X	
Enroll Participant	X	Enroll participant only after the protocol-specific informed consent has been signed. Obtain number from IRT. Participant who is not eligible should be screen-failed in IRT.
Review Inclusion/Exclusion Criteria	X	See full inclusion/exclusion criteria in Section 6.
Medical History	X	Record medical history, include current alcohol, illicit drug, tobacco, and nicotine product use. See Section 6 for eligibility criteria associated with medical history and surgical history.
AA-related History	X	Record age of first onset of AA and history of episodes.
Prior Alopecia-related Medications	X	Record prior treatments for AA and the responses to the therapies, including topical treatments.
Other (Non-Alopecia Related) Prior and Concomitant Medications	X	Record prior medications taken within 4 weeks of the first dose of study intervention on Day 1 and current medications.
SALT Assessment	X	To assess eligibility; see Section 6 and Appendix 5.
AA-IGA	X	To assess eligibility; see Section 6.
Hamilton-Norwood Scale/Ludwig Scale Classification	X	To assess eligibility; see Section 6.
Safety Assessments		
Complete Physical Examination	X	See Section 9.4.1.
Physical Measurements	X	Height and weight.
Vital Signs	X	Body temperature, respiratory rate, seated blood pressure, and heart rate. Blood pressure and heart rate should be measured after the participant has been resting quietly for at least 5 minutes; see Section 9.4.2.
12-lead ECG	X	Record ECGs after the participant has been supine for at least 5 minutes; see Section 9.4.3.

Table 2-1: Screening Procedural Outline (IM011134)

Procedure	Screening Visit	Notes
Chest Imaging (eg, X-ray, PA and Lateral)	X	Chest imaging is required if not performed within 6 months of Screening visit; a copy of the radiology report must be on file and reviewed by the investigator prior to dosing.
Monitor for Serious AEs	X	Record all SAEs from the date of participant's written consent.
Monitor for SARS CoV-2-related AEs	X	Record all AEs (SAEs and non-serious AEs) related to SARS-CoV-2 infection from time of consent.
Laboratory/Safety Assessments		
Clinical Safety Laboratory Assessments	X	Hematology, coagulation panel, chemistry panel, hemoglobin A1c, urinalysis, lipid panel (non-fasting); see Section 9.4.4.
TSH	X	If TSH is above the normal reference range, test free T4. If TSH is below normal range, test free T4 and T3; see Section 9.4.4.
Serology	X	HCV antibody with reflex to HCV RNA if positive; HBsAg, HBsAb, HBcAb with reflex HBV DNA if required; and HIV antibodies; see Section 9.4.4. For Japan-specific HBV serology requirements, see Appendix 9.
Tuberculosis Screening	X	QuantiFERON-TB Gold test; see Section 6.2. Exclusion Criterion #3.
Pregnancy Test (Serum)	X	WOCBP only; see Appendix 4.
FSH (Serum)	X	To confirm menopausal status; see Appendix 4.

Abbreviations: AA, alopecia areata; AA-IGA, Alopecia Areata Investigator Global Assessment; AE, adverse event; DNA, deoxyribonucleic acid; 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; IRT, Interactive Response Technology; PA, posteroanterior; RNA, ribonucleic acid; SAE, serious adverse event; SALT, Severity of Alopecia Tool; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; T3, triiodothyronine; T4, thyroxine; TB, tuberculosis; TSH, thyroid-stimulating hormone; WOCBP, women of childbearing potential.

Table 2-2: On Treatment Procedural Outline (IM011134): Week 0 through Week 24

Procedure	Week 0 (D1)[a]	Week 4 (D29 ± 3 d)	Week 8 (D57 ± 3 d)	Week 12 (D85 ± 3 d)	Week 16 (D113 ± 3 d)	Week 20 (D141 ± 3 d)	Week 24 (D169 ± 3 d)	Notes
Eligibility Assessments								
Review Inclusion/Exclusion Criteria	X							To confirm eligibility.
Randomize Participant[b]	X							
Safety Assessments								
Complete Physical Examination	X						X	See Section 9.4.1.
Targeted Physical Examination		X	X	X	X	X		As clinically indicated for reported AE/SAE. See Section 9.4.1.
Vital Signs	X	X	X	X	X	X	X	See Section 9.4.2.
Body Weight	X			X			X	
12-lead ECG	X						X	See Section 9.4.3.
AE and SAE Monitoring	X	X	X	X	X	X	X	See Section 9.2.
AEs of Suicidal Ideation and Behavior Monitoring	X	X	X	X	X	X	X	See Section 9.2.
Concomitant Medication Use Monitoring	X	X	X	X	X	X	X	
Clinical Efficacy/Health Outcomes Assessments								
SALT Assessment	X	X	X	X	X	X	X	See Appendix 5.
AA-IGA	X	X	X	X	X	X	X	See Section 9.1.
[redacted]								

Table 2-2: On Treatment Procedural Outline (IM011134): Week 0 through Week 24

Procedure	Week 0 (D1)[a]	Week 4 (D29 ± 3 d)	Week 8 (D57 ± 3 d)	Week 12 (D85 ± 3 d)	Week 16 (D113 ± 3 d)	Week 20 (D141 ± 3 d)	Week 24 (D169 ± 3 d)	Notes
Hamilton-Norwood Scale/Ludwig Scale Classification	X						X	
Medical Photography (Scalp)[c]	X						X	See Section 9.1.2.
Medical Photography (Eyelashes and Eyebrows)[d]	X						X	See Section 9.1.2.
[redacted]								
Laboratory Tests								
Hematology	X	X	X	X	X	X	X	See Section 9.4.4.
Chemistry Panel	X	X	X	X	X	X	X	See Section 9.4.4.
Fasting Lipid Panel	X			X			X	After at least a 10-hour fast. See Section 9.4.4.
Fasting Glucose	X			X			X	After at least a 10-hour fast. See Section 9.4.4.
Urinalysis	X						X	See Section 9.4.4.
Hemoglobin A1c	X						X	
Pregnancy Test (Urine)[e]	X	X	X	X	X	X	X	For WOCBP only. See Appendix 4.
HBV DNA Test (Japan only)	X	X	X	X	X	X	X	For participants with a negative HBsAg, but a positive HBcAb

Table 2-2: On Treatment Procedural Outline (IM011134): Week 0 through Week 24

Procedure	Week 0 (D1)[a]	Week 4 (D29 ± 3 d)	Week 8 (D57 ± 3 d)	Week 12 (D85 ± 3 d)	Week 16 (D113 ± 3 d)	Week 20 (D141 ± 3 d)	Week 24 (D169 ± 3 d)	Notes
								and/or HBsAb result at Screening. See Appendix 9.
Study Intervention								
Dispense Study Intervention	X	X	X	X	X	X	X	Dispense study intervention after all visit procedures have been performed.
Assess Study Intervention Compliance/Perform Study Intervention Accountability		X	X	X	X	X	X	
[redacted]								

Abbreviations: AA-IGA, Alopecia Areata Investigator Global Assessment; [redacted] AE, adverse event; BID, twice daily; [redacted] D, Day; d, days; DNA, deoxyribonucleic acid; ECG, electrocardiogram; ED, early discontinuation; HBcAb, hepatitis B core antibody; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IRT, Interactive Response Technology; [redacted] QD, once daily; SAE, serious adverse event; SALT, Severity of Alopecia Tool; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WOCBP, women of childbearing potential.

[a] All assessments and sample collections (laboratory test, [redacted]) should occur before study intervention administration.

[b] Participants will be randomized on Day 1 to either deucravacitinib (6 mg QD or 6 mg BID) or placebo; participants initially assigned to the placebo arm will be re-randomized in a blinded manner by IRT to deucravacitinib (6 mg QD or 6 mg BID) at Week 24.

[c] Photography of the scalp is required.

[d] Photography of eyebrows and eyelashes is optional and will only be performed on participants who provide consent. In those who consent, if new onset of eyebrows and/or eyelashes involvement (that is not involved at baseline) is observed after Day 1, a photograph should be taken at the visit when first observed, in addition to Week 24.

[e] If the urine pregnancy test is positive, a serum pregnancy test should be performed to confirm urine test results prior to initiation of study intervention on Day 1 and prior to discontinuing the participant. Study intervention is not to be administered until the results of the confirmatory test are known and negative.

[redacted]

Table 2-3: On Treatment (Week 28 through Week 52) and Post-Treatment Follow-Up (Week 56) Procedural Outline (IM011134)

Procedure	Week 28 (D197 ± 3 d)	Week 32 (D225 ± 3 d)	Week 40 (D281± 7 d)	Week 48 (D337 ± 7 d)	Week 52/ED[a] (D365 ± 3 d)	Week 56/Post-Treatment Follow-Up (D393 ± 3 d)	Notes
Safety Assessments							
Complete Physical Examination					X		See Section 9.4.1.
Targeted Physical Examination	X	X	X	X		X	As clinically indicated for reported AE/SAE. See Section 9.4.1.
Vital Signs	X	X	X	X	X	X	See Section 9.4.2.
Body Weight			X		X		
12-lead ECG					X		See Section 9.4.3
AE and SAE Monitoring	X	X	X	X	X	X	See Section 9.2.
AEs of Suicidal Ideation and Behavior Monitoring	X	X	X	X	X	X	See Section 9.2.
Concomitant Medication Use Monitoring	X	X	X	X	X	X	See Section 7.7.
Clinical Efficacy/Health Outcomes Assessments							
SALT Assessment	X	X	X	X	X	X	See Appendix 5.
AA-IGA	X	X	X	X	X	X	See Section 9.1.
[redacted]							
Hamilton-Norwood Scale/Ludwig Scale Classification			X		X		
Medical Photography (Scalp)[b]			X		X		See Section 9.1.2.

Table 2-3: On Treatment (Week 28 through Week 52) and Post-Treatment Follow-Up (Week 56) Procedural Outline (IM011134)

Procedure	Week 28 (D197 ± 3 d)	Week 32 (D225 ± 3 d)	Week 40 (D281± 7 d)	Week 48 (D337 ± 7 d)	Week 52/ED[a] (D365 ± 3 d)	Week 56/Post-Treatment Follow-Up (D393 ± 3 d)	Notes
Medical Photography (Eyelashes and Eyebrows)[c]			X		X		See Section 9.1.2.
[redacted]							
Laboratory Tests							
Hematology	X	X	X	X	X	X	See Section 9.4.4.
Chemistry Panel	X	X	X	X	X	X	See Section 9.4.4.
Urinalysis	X		X		X		See Section 9.4.4.
Fasting Lipid Panel	X		X		X		After at least a 10-hour fast. See Section 9.4.4.
Fasting Glucose	X		X		X		After at least a 10-hour fast. See Section 9.4.4.
Hemoglobin A1c			X		X		
Pregnancy Test (Urine)[d]	X	X	X	X	X	X	WOCBP only. See Appendix 4.
HBV DNA Test (Japan only)	X	X	Testing will occur every 4 or 8 weeks (frequency of testing is at the discretion of the investigator).				For participants with a negative HBsAg, but a positive HBcAb and/or HBsAb result at Screening. See Appendix 9.

Table 2-3: On Treatment (Week 28 through Week 52) and Post-Treatment Follow-Up (Week 56) Procedural Outline (IM011134)

Procedure	Week 28 (D197 ± 3 d)	Week 32 (D225 ± 3 d)	Week 40 (D281± 7 d)	Week 48 (D337 ± 7 d)	Week 52/ED[a] (D365 ± 3 d)	Week 56/Post-Treatment Follow-Up (D393 ± 3 d)	Notes
Study Intervention							
Dispense Study Intervention	X	X	X	X			Dispense study intervention after all visit procedures have been performed.
Assess Study Intervention Compliance/ Perform Study Intervention Reconciliation	X	X	X	X	X		
[redacted]							

Abbreviations: AA-IGA, Alopecia Areata Investigator Global Assessment; [redacted] AE, adverse event; [redacted] D, Day; d, days; DNA, deoxyribonucleic acid; ECG, electrocardiogram; ED, early discontinuation; HBcAb, hepatitis B core antibody; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; [redacted] SAE, serious adverse event; SALT, Severity of Alopecia Tool; WOCBP, women of childbearing potential.

[a] ED: For participants who discontinue from the study prior to Week 52, all assessments scheduled for Week 52 are to be performed.

[b] Photography of the scalp is required.

[c] Photography of eyebrows and eyelashes is optional and will only be performed on participants who provide consent. In those who consent, if new onset of eyebrows and/or eyelashes involvement (that is not involved at baseline) is observed after Week 24, a photograph should be taken at the visit when first observed, in addition to Weeks 40 and 52.

d If the urine pregnancy is positive, a serum pregnancy test should be performed to confirm urine test results prior to discontinuing the participant. Study intervention is not to be administered until the results of the confirmatory test are known and negative.

3 INTRODUCTION

Alopecia areata (AA) is a chronic, relapsing, immune-mediated inflammatory disorder affecting hair follicles (HFs), causing nonscarring hair loss. AA can range from small patches of smooth, sharply demarcated, round patches of alopecia on any hair-bearing area to the complete loss of scalp hair (alopecia totalis) eyebrow, eyelash, and even complete total body hair loss (alopecia universalis).

The cardinal pathophysiology of AA is the collapse of the intrinsic immune privilege of healthy HFs. Normal hair growth is a life-long cyclic transformation involving anagen (active growth), catagen (involution), and telogen (quiescence) phases. AA is a chronic inflammatory disease of the HF that leads to premature and accelerated progression to catagen.[1,2] In healthy individuals, the HF is one of the immune-privileged sites of the body, similar to the anterior chamber of the eye, characterized by low levels of major histocompatibility complex (MHC) class I/II expression, suppressed natural killer (NK) cell activity, and the presence of immune-suppressant proteins.[3] The immune privilege in AA patients is effectively collapsed by perifollicular inflammation directed at the anagen phase HF bulb.[4] AA lesional skin is manifested by infiltration of mast cells, Langerhans cells, dendritic cells, cluster of differentiation (CD) 4+ and CD8+ T cells[5,6] and a potential establishment of tissue-resident memory CD8+ T cells.[7] While autoreactive CD8+ T cell-mediated cytotoxicity of bulb melanocytes is an important pathogenic mechanism of hair loss, the T_H1 effector cytokine IFNγ is a principal mediator of immune privilege collapse and anagen HF damage.[8,9] In addition to T1 cells, natural killer group 2D+ (NKG2D+) cells and NK-T cells are significant sources of IFNγ that also participate in AA pathogenesis.[10] In response to IFNγ, AA lesional HFs secrete CXC motif chemokine ligand (CXCL) 10, a chemokine that recruits more T1 cells (T_H1 [CD4+] and Tc1 [CD8+] T cells) from the periphery to ongoing lesions, thus effectively amplifying the loop. Therefore, targeted blockade of the IFNγ signaling pathway is a therapeutic concept currently being explored with other pharmacologic agents. Several case studies of off-label treatment of AA participants with tofacitinib, which is known to inhibit IFNγ signaling, further support such a therapeutic concept. IL-12 is known to promote the generation of IFNγ-secreting TH1 cells as well as to stimulate NK cells for IFNγ secretion. Apart from the dominant T_H1 signature, transcriptome analyses in lesional skin of AA patients have revealed that IL-23 is also upregulated.[11,12,13] Targeting the IL-12/23 pathway with biologic agents has been shown to be efficacious in Phase 2 studies in AA; case studies on blockade of IL-12 and IL-23 with ustekinumab have shown varying degrees of efficacy in AA participants.[14,15]

A variety of topical, intralesional, and systemic agents are used as treatment options, but the response to treatment varies widely, and none is Food and Drug Administration (FDA) approved.[16,17] Corticosteroids, either administered as an injection intradermally into the skin or applied topically as a cream, ointment, or gel, are the preferred initial treatment for participants with limited patchy AA. Second-line treatment options include contact immunotherapies, calcineurin inhibitors, and hair growth-stimulating solutions. However, while treatments can

induce hair growth in some participants, not only are results variable but none has been shown to alter the long-term course of the disease.[16,17] There are several compounds currently in Phase 2 and Phase 3 development, the majority being JAK inhibitors (eg, baricitinib, ruxolitinib, and ritlecitinib), which have demonstrated potential benefit in the treatment of AA. Baricitinib (JAK1/2 inhibitor) Phase 3 studies showed positive results in the treatment of AA.[18,19,20] The primary endpoint was met in both studies (proportion of participants achieving SALT score ≤ 20 at Week 36) and no deaths, thromboembolic events, opportunistic infections, or gastrointestinal (GI) perforations occurred.

Managing AA involves addressing the psychological needs of the patients. Many describe it as a chronic disease that touches multiple aspects of their daily lives and for many this can lead to anxiety and depression.[21] Patients with AA consistently demonstrate poor health-related quality of life similar to that seen in other chronic skin diseases including atopic dermatitis and psoriasis.[22] The lack of long-term effective treatments and the impact of AA on quality of life represent a significant unmet medical need.

3.1 Study Rationale

Tyrosine Kinase 2 (TYK2) is a nonreceptor tyrosine kinase associated with receptors for the p40-containing cytokines interleukin (IL)-12 and IL-23, as well as the Type I interferon (IFN) receptor, and is required for the activation of their downstream signaling pathways. TYK2 catalyzes the phosphorylation of the intracellular receptor domains and signal transducer and activator of transcription (STAT) proteins, resulting in the activation of STAT-dependent transcription and functional responses specific for these cytokines.[23,24,25] TYK2-dependent pathways and the cytokine networks they modulate have been implicated in the pathophysiology of multiple immune-mediated diseases.

Deucravacitinib (Bristol-Myers Squibb Company [BMS]-986165) is a potent, highly selective, oral small molecule inhibitor of TYK2 that binds to the regulatory domain of TYK2 and stabilizes the inhibitory interactions between the pseudokinase and the catalytic domains of the enzyme. The binding mode of deucravacitinib takes advantage of unique structural features of the TYK2 pseudokinase domain compared to other kinases and pseudokinases to provide high biochemical, cellular, and functional selectivity. This approach differentiates deucravacitinib from nonselective inhibitors of the Janus kinase (JAK) family of kinases that target the highly conserved adenosine triphosphate-binding site within the active site of the catalytic domain. As a result, deucravacitinib selectively blocks the IL-23, IL-12, and Type I IFN pathways involved in inflammatory diseases, without inhibiting -pathways mediated by JAK1/JAK3 (eg, IL2, IL-15, IL-7), -JAK2/JAK2 (eg, erythropoietin, thrombopoietin, granulocyte macrophage colony-stimulating factor), or JAK1/JAK2 (eg, IFNγ, IL-6). Therefore, deucravacitinib demonstrates a highly differentiated profile from inhibitors of closely related JAKs 1-3. Deucravacitinib could potentially interfere with the pathophysiology of AA. By blocking IL-12 receptor signaling, which is a critical upstream event of T_H1 development, deucravacitinib may reduce local IFNγ production at newly developing lesions.[26,27] In addition, deucravacitinib may minimize the spread of lesions since the emerging data suggest that T1 clonal expansion and maintenance of memory cell

population depends on IL-12 receptor signaling. In support of this, a pre-clinical animal study employing a xenograft model of AA demonstrated that immune-mediated hair loss was reversed by therapeutic treatment with BMS-986202, an analogue of deucravacitinib. Clinical data from a Phase 1 study in healthy volunteers (IM011002) showed that deucravacitinib reduced IL-12-induced IFNγ production from whole blood cells in a dose dependent manner. Further, deucravacitinib has been shown to be effective in the treatment of psoriasis (see below), an IL-23-mediated disease. Thus, these data support the clinical development of deucravacitinib for the treatment of AA.

This Phase 2 study is intended to determine whether inhibition of TYK2 is associated with clinical improvement of AA disease activity and modulation of related [redacted] as well as to assess the [redacted] safety, and tolerability of deucravacitinib in participants with AA in order to determine the dosage that provides the optimal benefit/risk assessment in this population.

3.2 Background

A comprehensive in vitro and in vivo characterization of deucravacitinib has been established and supports the development of this compound in humans. Furthermore, clinical data available from multiple Phase 1 studies in healthy participants, Phase 2 (IM011011) and Phase 3 (IM011046 and IM011047) studies in adult participants with moderate-to-severe plaque psoriasis (PsO), and a Phase 2 (IM011084) study in adult participants with psoriatic arthritis (PsA) helped to establish the safety of deucravacitinib and to characterize the PK and pharmacodynamic (PD) properties of deucravacitinib.

The 2 Phase 3 studies (IM011046 and IM011047) demonstrated the efficacy and safety of deucravacitinib in participants with moderate-to-severe PsO. In both studies, statistical significance was achieved for the deucravacitinib group compared with placebo for the co-primary endpoints at Week 16 (Static Physicians Global Assessment [sPGA] 0/1 response, Psoriasis Area Severity Index [PASI] 75 response). Deucravacitinib also demonstrated an acceptable safety and tolerability profile compared with placebo and apremilast (a positive control). The overall frequency of adverse events (AEs) in the 16-week placebo-controlled period in the deucravacitinib group was comparable to the apremilast group and higher than the placebo group. The most common AEs (> 5%) in the deucravacitinib group were nasopharyngitis and upper respiratory tract infection. There is no evidence of an increased risk of major adverse cardiac events (MACE) or extended MACE associated with deucravacitinib. The overall incidence of SAEs was low and comparable across treatment groups. Serious or systemic opportunistic or fungal infections were not observed.[28]

Deucravacitinib is also being developed for oral treatment of other immune-mediated diseases such as PsA, systemic lupus erythematosus (SLE), Crohn's disease, and ulcerative colitis (UC).

3.3 Benefit/Risk Assessment

At this early stage in the development of deucravacitinib for the treatment of participants with AA, assessments of benefit and risk rely on nonclinical data and the experience of participants in clinical trials for other indications. The dosages administered in this study are within the range

tested in the first-in-human (FIH) study that had been shown to be safe and well tolerated; the 6 mg once daily (QD) dosage has also been extensively characterized in patients with psoriasis. Deucravacitinib is being studied at various doses in other programs, including 6 mg QD and 12 mg QD in PsA; 6 mg BID and 12 mg BID in UC; and 3 mg BID, 6 mg BID, and 12 mg QD in Crohn's disease and SLE.

Findings in toxicology studies were consistent with expectations based on the pharmacology of deucravacitinib. Please refer to current version Investigator's Brochure (IB).

The risk for PK drug-drug interactions (DDIs) with deucravacitinib was assessed based on in vitro studies, clinical DDI studies, and relevant regulatory guidance. At the maximum concentrations expected in this study, the potential for DDIs involving drug- metabolizing enzymes and transporters is low. A thorough QT study (IM011048) indicated no effect on corrected QT and other relevant electrocardiographic parameters, even at a supratherapeutic dose of 36 mg.

Nonclinical data and clinical experience, indicate an overall favorable risk/benefit assessment for investigating deucravacitinib at dosages of 6 mg QD and 6 mg BID in the current Phase 2 study in AA. Detailed information about the known and expected benefits and risks and anticipated adverse events (AEs) of deucravacitinib is provided in the IB.

The global coronavirus disease 2019 (COVID-19) pandemic has been identified as a potential risk to clinical trial participants in general, and it may particularly affect individuals who are on immunosuppressive therapies for underlying chronic diseases. At this time, the Sponsor is tracking and accumulating data on COVID-19 and its potential effects on participants taking deucravacitinib. The data are analyzed on a regular basis. The risk of COVID-19 for participants taking deucravacitinib is still unknown due to insufficient clinical data. Deucravacitinib is an immunomodulator; therefore, participants taking deucravacitinib may have a higher chance of infections. Accordingly, this study has exclusion criteria aimed at minimizing the risk for serious infection and a study visit schedule that allows for monitoring of participants' safety.

In addition, the Sponsor has developed a guidance for investigators on how to manage a participant with a clinical suspicion of, or a diagnosis of, COVID-19. This includes criteria for temporarily interrupting or permanently discontinuing the investigational product (IP; Section 8.1 and Section 8.1.1), and criteria for reinitiating IP on resolution of a COVID-19 infection (Section 8.1.1). Investigators should apply clinical judgment and consider the risks and benefits of interruption versus continuation of deucravacitinib therapy in participants who are enrolled in this study. In order to facilitate reporting of COVID-19 events that occur during the study, all AEs and SAEs associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection or COVID-19 must be reported, regardless of relatedness or causality (Section 9.2.2). COVID-19-related AEs or SAEs reported after randomization will also trigger additional data collection through specialized electronic Case Report Form (eCRF) pages, which will allow the Sponsor to further evaluate these events. Testing to exclude participants with COVID-19 infection prior to enrollment and to inform decisions about participant care during the study should follow local standard practice and requirements.

4 OBJECTIVES AND ENDPOINTS

Table 4-1: Objectives and Endpoints

Objectives	Endpoints
Primary	
Efficacy	
To evaluate the efficacy of deucravacitinib versus placebo at Week 24	• Change from baseline in SALT score at Week 24
Safety	
To evaluate the safety and tolerability of deucravacitinib versus placebo	• Incidence of SAEs, AEs, AEs leading to study discontinuation, and AEIs • Change in laboratory, ECG, physical examination, and vital sign parameters over time
Secondary	
Efficacy	
To evaluate the efficacy of deucravacitinib versus placebo on additional endpoints at Week 24	• Proportion of participants achieving a ≥ 50% reduction in SALT score (SALT50 response) from baseline at Week 24 • Proportion of participants achieving a SALT score ≤ 20 at Week 24 • Proportion of participants achieving an AA-IGA score of 0 or 1 at Week 24 with at least a 2-point change from baseline
[redacted]	

Table 4-1: Objectives and Endpoints

Objectives	Endpoints
[redacted]	[redacted]

Abbreviations: AA, alopecia areata; AA-IGA, Alopecia Areata Investigator Global Assessment; [redacted] ECG, electrocardiogram; AE, adverse event; [redacted] ECG, electrocardiogram; [redacted] SAE, serious adverse event; SALT, Severity of Alopecia Tool; [redacted].

[redacted]

5 STUDY DESIGN

5.1 Overall Design

This is a randomized, placebo-controlled, double-blind, parallel group, multi-center Phase 2 study to evaluate the efficacy and safety of 2 dosages of deucravacitinib (6 mg QD and 6 mg BID) in participants with AA.

The primary endpoint of the study is the change from baseline in Severity of Alopecia Tool (SALT) score at Week 24.

The total duration of participation in the study will be approximately 60 weeks as follows:

- Screening Period: up to 4 weeks
- Placebo-controlled Treatment Period: 24 weeks (Day 1 to Week 24)
- Active Treatment Period: 28 weeks (Weeks 24 to 52)
- Post-Treatment Follow-up Period: 4 weeks (Weeks 52 to 56)

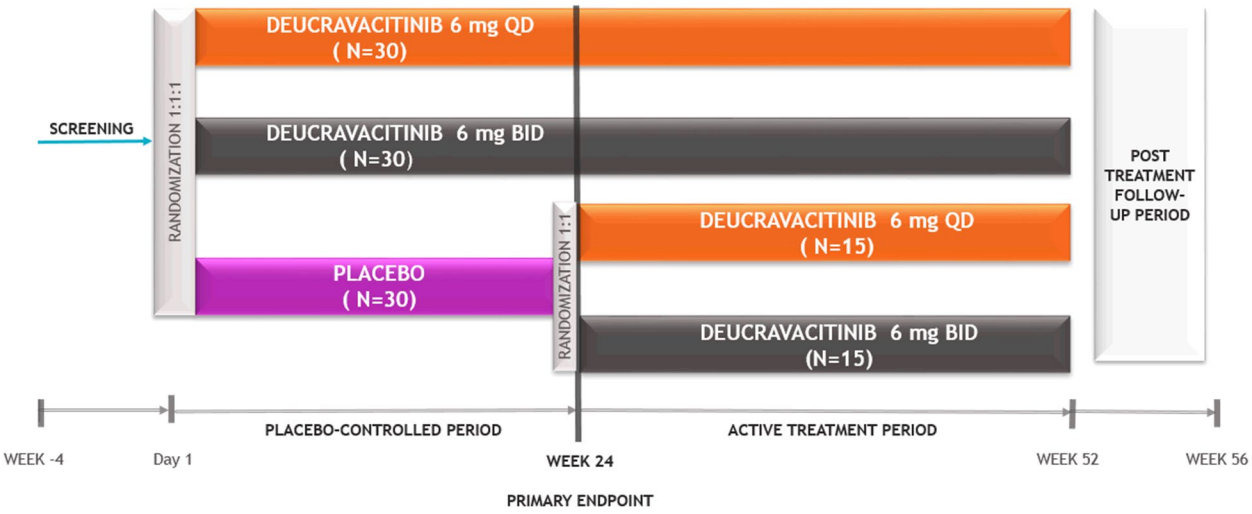
The study design schematic is presented in Figure 5.1-1.

Eligible participants will be randomized on Day 1, in a blinded manner, to receive deucravacitinib 6 mg QD, deucravacitinib 6 mg BID, or placebo in a 1:1:1 ratio. Randomization will be stratified by current duration of disease episode: < 4 years and ≥ 4 years. At the Week 24 study visit, the participants initially randomized to receive placebo will be re-randomized 1:1 in a blinded manner to receive deucravacitinib (6 mg QD or 6 mg BID) until Week 52. Participants initially randomized to deucravacitinib will continue on their assigned dosage in a blinded manner.

Efficacy and safety will be assessed throughout the study; samples will be collected for [redacted] assessments and to characterize the [redacted] properties of deucravacitinib, as per the Schedule of Activities (Section 2).

A database lock will be performed after all randomized participants have reached Week 24 or have discontinued prior to Week 24.

Figure 5.1-1: Study Design Schematic



Abbreviations: BID, twice daily; N, number; QD, once daily.

5.1.1 Data Monitoring Committee and Other External Committees

An independent external Data Monitoring Committee (DMC) will be charged with monitoring accumulating data from the trial, as well as general aspects of trial conduct. The committee will meet periodically during the study to review aggregate summaries of the efficacy and safety data from the trial. All members are selected with consideration for their respective expertise in the subject matter and/or in their experience in convening or participating in a DMC. Based on their overall benefit/risk evaluation, the DMC recommendations may include proceeding with the study per protocol, proceeding with the study with modification, or study suspension. The scope, conduct, membership, processes, and accountabilities of the DMC are specified in the DMC charter.

5.2 Number of Participants

Approximately 90 participants will be randomized on Day 1 into 1 of 3 treatment arms in a 1:1:1 ratio, resulting in 30 participants in each deucravacitinib treatment arm (6 mg QD and 6 mg BID) and 30 participants in the placebo arm.

Further details on sample size calculations are provided in Section 10.1.

5.3 End of Study Definition

The start of the trial is defined as the first visit for first participant screened.

End of trial is defined as the last visit or scheduled procedure shown in the Schedule of Activities for the last participant.

Primary completion is defined as the final date on which data for the primary endpoint were or are expected to be collected, if this is not the same.

A participant is considered to have completed the study if he/she has completed the last visit.

5.4 Scientific Rationale for Study Design

The purpose of the study is to gain a preliminary understanding of the efficacy and safety of deucravacitinib administered for up to 52 weeks in participants with AA.

The primary efficacy endpoint assessment, change from baseline in SALT score, at Week 24 accounts for the period required to demonstrate improvement in an accurate and reliable manner in this condition and is consistent with the design of AA clinical trials with other agents. A placebo control arm is included for the first 24 weeks to allow the effects of treatment to be appropriately attributed to study interventions received. At Week 24, participants in the placebo arm will be re-randomized 1:1 in a blinded manner to receive deucravacitinib (6 mg QD or 6 mg BID) for the remainder of the study; this will allow all study participants to receive deucravacitinib. Participants initially randomized to active study intervention will continue to receive their assigned dosage of deucravacitinib in a blinded manner for an additional 28 weeks, which will allow for an assessment of long- term safety and efficacy.

Randomization on Day 1 will be stratified by the duration of the current disease episode as this may impact potential responsiveness to study intervention for AA.

[redacted] assessments will be performed to characterize the biological activity of deucravacitinib and [redacted] properties, respectively, of the 2 dosages in participants with AA.

[redacted]

6 STUDY POPULATION

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.

For entry into the study, the following criteria MUST be met.

6.1 Inclusion Criteria

1) Signed Written Informed Consent
   a) Participant must be willing and able to participate in the study and sign the ICF
   b) Participant must be willing and able to complete all study-specific procedures and visits

2) Type of Participant and Target Disease Characteristics

   a) Documented clinical diagnosis of AA for at least 6 months
   b) Current episode of scalp hair loss (at Screening) must meet the following criteria:
      i) Duration at least 6 months
      ii) Duration of current hair loss episode of AA affecting ≥ 50% of the scalp not exceeding 8 years
      iii) Scalp hair loss has been stable (ie, no significant spontaneous regrowth [> 10%] over the last 6 months)
   c) SALT score ≥ 50 at Screening and Day 1 (see Appendix 5)

      Participant with complete scalp hair loss (SALT score of 100) with or without body hair involvement can be included.

   d) Participant must have an Alopecia Areata Investigator Global Assessment (AA-IGA) grade ≥ 3 at Screening and Day 1.
   e) Participant should not shave their scalp from 7 days prior to the Screening visit and agree to not shave their scalp 7 days prior to each study visit, to allow for SALT assessment of hair regrowth. If participant is using a hairpiece or wig, the participant must be willing and able to remove the hair prosthetic at each appointment. Participant should maintain a stable hair style to allow for reliable and consistent assessment of SALT throughout the study.
   f) Participant with current or a history of androgenetic alopecia can be included as long as, in the opinion of the investigator, the participant has either of the following classifications: Ludwig Scale[30] ≤ II for women; Hamilton-Norwood Scale[31] ≤ III for men.

Note: A male participant with Hamilton-Norwood III vertex or Hamilton-Norwood IIIa classification will be excluded.

3) Age of Participant

a) Men and women aged ≥ 18 years to ≤ 65 years at the time of Screening visit.

4) Reproductive Status

- Investigators shall counsel women of childbearing potential (WOCBP) participants, and male participants who are sexually active with WOCBP, on the importance of pregnancy prevention and the implications of an unexpected pregnancy.
- The investigator shall evaluate the effectiveness of the contraceptive method in relationship to the first dose of study intervention.
- Local laws and regulations may require the use of alternative and/or additional contraception methods.

a) Female Participants:

i) Women who are not of childbearing potential (as defined in Appendix 4) are exempt from contraceptive requirements.

ii) Woman of childbearing potential (WOCBP) must have a negative highly sensitive serum pregnancy test at Screening Visit, and a negative 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.

- If a urine test cannot be confirmed as negative (eg, an ambiguous result), a serum pregnancy test is required. In such cases, the participant must be excluded from participation if the serum pregnancy result is positive.
- Additional requirements for pregnancy testing during and after study intervention are located in the Schedule of Activities.
- The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy.

iii) WOCBP must agree to follow instructions for method(s) of contraception defined in Appendix 4 and as described below and included in the ICF.

- WOCBP is permitted to use hormonal contraception methods (as described in Appendix 4).

iv) A female participant is eligible to participate if she is not pregnant or breastfeeding, and at least one of the following conditions applies:

(1) Is not a WOCP

OR

(2) Is a WOCBP and using a contraceptive method that is highly effective (with a failure rate of < 1% per year), preferably with low user dependency, as described in Appendix 4, during the study period until the end of the study.

b) Male participants:

i) A male participant should maintain his usual practice with regard to contraception (if any); however, no specific contraceptive measures are required.

6.2 Exclusion Criteria

1) Exclusionary Disease Characteristics

a) Participant with diffuse-type AA or other forms of hair loss, including traction alopecia, lichen planopilaris, central centrifugal cicatricial alopecia, frontal fibrosing alopecia, etc

b) Other active skin diseases affecting the scalp that in the opinion of the investigator may interfere with accurate assessment of SALT score

c) Extensive tattooing of the scalp that, in the opinion of the investigator, may interfere with the accurate assessment of SALT score

2) Infectious/Immune-related Exclusions

a) In the event of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection within 4 weeks prior to Screening:

i) Symptoms must have completely resolved and, based on investigator assessment in consultation with the Medical Monitor, there are no sequelae that would place the participant at a higher risk of receiving investigational study intervention. See Section 6.4.1.

b) History or evidence of active infection and/or febrile illness within 14 days prior to Day 1

c) History of serious bacterial, fungal, or viral infection requiring hospitalization and intravenous (IV) antimicrobial treatment within 60 days prior to Day 1

d) Received live vaccines within 60 days prior to Day 1, or plans to receive a live vaccine during the study

e) Presence of herpes zoster lesions at Screening or Day 1, or history of serious herpes zoster or serious 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

f) Evidence of, or positive test for, hepatitis C virus (HCV) or hepatitis B virus (HBV) at Screening. The hepatitis screen includes testing for hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), hepatitis B core antibody (HBcAb) immunoglobulin G/M (IgG/IgM), followed by HBV deoxyribonucleic acid (DNA) testing if required, and antibodies to hepatitis C, confirmed by an HCV ribonucleic acid (RNA) testing if required. See Section 9.4.4 and Appendix 9.

For Japan: Participants who are HBsAg positive will be excluded from the study. Participants who are HBsAg negative but positive for HBsAb and/or HBcAb may be eligible and must also be tested for quantitative HBV DNA. Participants with detectable levels as specified by local guidelines at Screening will be excluded; see Appendix 9. Participants with HBV DNA < 2.1 Log copy/mL (20 IU/mL) can be enrolled in the study but must undergo periodic monitoring of HBV DNA and liver enzymes, such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Monitoring should be performed every 4 weeks, up to and including the Week 32 study visit. Starting with Week 40, testing should occur every 4 or 8 weeks, at the discretion of the investigator, through the end of the study.

g) Positive test for human immunodeficiency virus by antibody testing at Screening

h) Any history of known or suspected congenital or acquired immunodeficiency state or condition that would compromise the participant's immune status (eg, history of

opportunistic infections [eg, *Pneumocystis jirovecii* pneumonia, histoplasmosis, or coccidioidomycosis], history of splenectomy, primary immunodeficiency)

3) **Any of the following tuberculosis (TB) criteria**:
   a) History of active TB prior to Screening visit, regardless of completion of adequate intervention
   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 scan) obtained during the Screening period or anytime within 6 months prior to the Screening visit with documentation, showing evidence of current active or history of active pulmonary TB
   d) Latent TB infection (LTBI) defined as a positive IFN gamma release assay (IGRA), by QuantiFERON-TB Gold test at Screening, in the absence of clinical manifestations
   e) Participant may be eligible if there are no current signs or symptoms of active TB AND participant has received adequate documented treatment for LTBI within 5 years of Screening OR has initiated prophylactic treatment for LTBI per local guidelines.
      i) For participant that is not currently on prophylactic treatment for LTBI per local guidelines, including participant that has documented completed treatment for LTBI within 5 years of Screening, results of initial IGRA test that is indeterminate with no signs or symptoms of active TB must be retested for confirmation. If the second test is again indeterminate, the participant will be excluded from the study. If the retest is positive, the participant must be treated as having LTBI. If the retest is negative, the participant may be eligible provided no other exclusion criteria for TB are met.
      ii) For participant on prophylactic treatment for LTBI per local guidelines, and there are no current signs or symptoms of active TB, retesting of an initial positive or indeterminate result is not required and participant may be eligible provided no other exclusion criteria for TB are met, and participant continues to complete treatment for LTBI per local guidelines.

4) Medical History and Concurrent Diseases
   a) Any major illness/condition or evidence of an unstable clinical condition (eg, renal, hepatic, hematologic, gastrointestinal (GI), endocrine, pulmonary, psychiatric, neurologic, 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 participant if he or she participates in the study.
   b) Any major surgery within 4 weeks prior to study intervention administration (Day 1).
   c) Drug or alcohol abuse, as determined by the investigator, within 6 months prior to Day 1.
   d) Unstable coronary heart disease or other cardiovascular disease, defined as a recent clinical cardiovascular event (eg, cardiac arrhythmias, unstable angina, unstable ischemic heart disease, myocardial infarction, stroke, rapid atrial fibrillation) in the 3 months prior to Screening, or a cardiac hospitalization (eg, revascularization procedure, pacemaker implantation) within 3 months prior to Screening.
   e) Uncontrolled arterial hypertension characterized by a systolic blood pressure (BP) > 160 mm Hg or diastolic BP > 100 mm Hg at Screening.

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

f) Class III or IV congestive heart failure by New York Heart Association criteria

g) Participant has cancer or history of cancer (solid organ or hematologic including myelodysplastic syndrome) or lymphoproliferative disease within the previous 5 years (other than resected cutaneous basal cell or squamous cell carcinoma, or carcinoma of cervix in situ that has been treated with no evidence of recurrence)

h) Any sound medical, psychiatric, and/or social reason as determined by the investigator during Screening or at Day 1

5) Previous/Concomitant Therapy

a) Prior exposure to deucravacitinib

b) History of lack of response to ustekinumab, in the opinion of the investigator, (or any other therapeutic agent targeted to IL-12, IL-17, or IL-23) after at least 3 months of therapy

c) History of lack of response to a JAK inhibitor (eg, tofacitinib, ruxolitinib), in the opinion of the investigator

d) Thyroid medication or thyroid replacement therapies, if used, must be stable for 2 months and be maintained as such throughout the study.

e) Any ongoing treatment known to affect hair growth including, but not limited to, topical steroids (applied to the scalp), intralesional steroids, systemic steroids, anthralin, squaric acid, diphenylcyclopropenone, topical calcineurin inhibitors (applied to the scalp), cyclosporine, finasteride/minoxidil (oral or topical) or other medication that cannot be discontinued at least 4 weeks prior to study intervention initiation (Day 1) and throughout the study.

f) Ongoing treatment with an immune system modulator or suppressant that cannot be discontinued at least 4 weeks or 5 times the elimination half-life prior to study intervention initiation (Day 1) and throughout the study.

g) Treatment with an experimental antibody or experimental biologic therapy within 6 months prior to Day 1, OR received any other experimental therapy or new investigational agent within 4 weeks or 5 half-lives (whichever is longer) prior to study intervention initiation (Day 1) and throughout the study, OR is currently enrolled in an investigational study.

6) Physical and Laboratory Evaluations

a) At Screening

i) Absolute white blood cell count < 3,000/mm^3

ii) Absolute lymphocyte count < 500/mm^3

iii) Absolute neutrophil count < 1,000/mm^3

iv) Platelet count < 100,000/mm^3

v) Hemoglobin < 9 g/dL

vi) Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) > 3 × upper limit of normal (ULN)

vii) Total unconjugated and/or conjugated bilirubin >2 × ULN

b) Electrocardiogram (ECG) abnormalities that are considered clinically significant and would pose an unacceptable risk to the participant if participating in the study at Screening and Day 1.

c) Clinically significant abnormalities in laboratory testing including (but not limited to):

i) Serum creatinine > 2 × ULN or renal impairment based on an estimated glomerular filtration rate (eGFR) < 45 mL/min/1.73 m^2 (calculated using the Modification of Diet in Renal Disease [MDRD] equation) at Screening

d) Inability to have venipuncture performed and/or tolerate venous access

e) Any other significant laboratory abnormalities that, in the opinion of the investigator, might place the participant at unacceptable risk for participation in this study

7) Allergies and adverse drug reactions which, in the opinion of the investigator, could affect the safety of the participant

8) Hypersensitivity to any component of the study medication formulation; if there is a significant drug allergy or anaphylaxis consult with the Medical Monitor.

9) Other Exclusion Criteria

a) Prisoner or participant who is involuntarily incarcerated. (Note: Under certain specific circumstances, and only in countries where local regulations permit, a person who has been imprisoned may be included or permitted to continue as a participant. Strict conditions apply, and BMS approval is required.)

b) Participant who is 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 the study protocol

d) Site personnel or their immediate family

e) Inability to tolerate oral medication.

6.3 Lifestyle Restrictions

No restrictions are required.

6.3.1 Meals and Dietary Restrictions

Study intervention may be taken without regard to meals. However, blood samples for laboratory assessments are to be collected in a fasted state at specified visits. Refer to Schedule of Activities (Section 2).

6.3.2 Caffeine, Alcohol and Tobacco

No restrictions are required; however, excessive use of caffeine, alcohol, and tobacco or other nicotine-containing products should be avoided.

6.3.3 Activity

Participants are to refrain from strenuous physical activity (activity that is more strenuous than the participant's usual daily activity) 1 day prior to blood draw for chemistry panel, which includes creatine kinase.

6.4 Screen Failures

Screen failures are defined as participants who consent to participate in the clinical study but who are not subsequently randomized in the study/included in the analysis population.

A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants, 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).

6.4.1 Retesting During Screening or Lead-In Period

Laboratory and/or clinical assessments that are included in Table 2-1, the Schedule of Activities, Screening Procedural Outline, may be repeated in an effort to find all possible well-qualified participants. Consultation with the Medical Monitor may be needed to identify whether repeat testing of any particular parameter is clinically relevant.

The study permits the re-screening (after the end of the initial 4-week Screening period) of a participant who discontinues the study as a pretreatment failure (ie, the participant fails Screening and has not been treated). The participant must be re-consented and will be assigned a new identification number, and a full Screening visit must be performed again. A participant can only be rescreened once. Depending on the timing of re-screening, repetition of some assessments may not be required. Duration of existing treatments and required discontinuation periods shall be considered relative to the start of study intervention (Day 1). The most current result prior to randomization is the value by which study inclusion will be assessed, because it represents the participant's most current clinical state.

Testing for asymptomatic COVID-19 infection via molecular testing is not required. However, some participants may develop suspected or confirmed symptomatic COVID-19 infection, or be discovered to have asymptomatic COVID-19 infection during the Screening period. In such cases, participants may be considered eligible for the study after meeting all inclusion/exclusion criteria related to active infection, and after meeting the following criteria:

- At least 10 days (20 days for severe/critical illness) have passed since symptoms first appeared or positive test result, and
- At least 24 hours have passed since last fever without the use of fever-reducing medications, and
- Symptoms (eg, cough, shortness of breath) have resolved, and
- In the opinion of the investigator, there are no COVID-19 sequelae that may place the participant at a higher risk of receiving investigational study intervention, and

- Negative follow-up molecular test for COVID-19 based on institutional, local or regional guidelines

7 STUDY INTERVENTION(S) AND CONCOMITANT THERAPY

Study intervention is defined as any investigational intervention(s), marketed product(s), placebo, procedure(s) or medical device intended to be administered to a study participant according to the study protocol.

Study intervention includes both Investigational (Medicinal) Product (IP/IMP) and Non-investigational/Auxiliary (Medicinal) Product (Non-IP/Non-IMP/AxMP) as indicated in Table 7.1-1.

An IP, also known as IMP in some regions, is defined 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 from 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 Non–IPs/AxMPs.

Table 7.1-1 shows the study interventions for this study.

7.1 Study Interventions Administered

Study intervention will be administered BID as tablets for 52 weeks. Study intervention will be supplied in blister cards. The tablets will be arranged into sets with 1 tablet to be taken in the morning and 1 tablet to be taken in the evening, approximately 12 hours apart. Study intervention may be taken with or without food. If the participant forgets a dose but remembers within 4 hours of the planned dose time, the dose should be taken. If the missed dose is remembered more than 4 hours after it should have been taken, that dose should not be taken and the next scheduled dose should be taken at the usual time.

On Day 1 and at study visits when pre-dose [redacted] samples will be collected, study intervention should be administered at the site.

The selection and timing of dose for each participant is as follows:

Table 7.1-1: Study Interventions

Intervention Name	Deucravacitinib (BMS–986165) QD	Deucravacitinib (BMS–986165) BID	Placebo (BID)
Type	drug	drug	N/A
Dose Formulation	tablet	tablet	tablet
Unit Dose Strength	6 mg	6 mg	N/A

Table 7.1-1: Study Interventions

Intervention Name	Deucravacitinib (BMS–986165) QD	Deucravacitinib (BMS–986165) BID	Placebo (BID)
Dosage Level and Frequency	6 mg QD (1 active tablet in morning and 1 placebo tablet in evening)	6 mg BID (1 active tablet in morning and 1 active tablet in evening)	BID (1 placebo tablet in morning and 1 placebo tablet in evening)
Route of Administration	oral	oral	oral
Use	experimental	experimental	placebo
IMP and Non-IMP/AxMP	IMP	IMP	IMP
Sourcing	Provided centrally by the Sponsor	Provided centrally by the Sponsor	Provided centrally by the Sponsor
Packaging and Labeling	Study intervention will be provided in blister cards. Each blister card will be labeled as required per country requirement	Study intervention will be provided in blister cards. Each blister card will be labeled as required per country requirement	Study intervention will be provided in blister cards. Each blister card will be labeled as required per country requirement

Abbreviations: AxMP, Auxiliary Medicinal Product; BID, twice daily; IMP, Investigational Medicinal Product; mg, milligram; N/A, not applicable; PO, per os; QD, once daily.

7.2 Method of Study Intervention Assignment

At the time of the Screening visit, immediately after informed consent is obtained and before any study-related procedures are performed, the investigative site will access the enrollment option utilizing Interactive Response Technology (IRT) for assignment of a participant number (including a participant not subsequently randomized or treated). This number will be unique across all sites. Enrolled participants, including those not dosed, will be assigned sequential participant numbers. The participant number may not be used for any other participant. If a potential participant is rescreened, they will be given a new identification number.

Eligible participants will be centrally randomized on Day 1/Week 0, using IRT, to receive oral treatment with deucravacitinib (6 mg QD or 6 mg BID) or placebo BID in accordance with the stratification criteria. Randomization numbers will be assigned prior to dosing. At the Week 24 study visit, the participants initially randomized to receive placebo will be automatically re-randomized by the IRT to receive deucravacitinib (6 mg QD or 6 mg BID) in a blinded manner until Week 52; participants initially randomized to receive deucravacitinib (6 mg QD or 6 mg BID) will remain on their assigned study intervention, in a blinded manner, until Week 52.

7.3 Blinding

Study intervention will be blinded to study personnel and participants prior to final database lock. BMS personnel will also be blinded to study intervention during the first 24 weeks of placebo-controlled intervention. However, following the Week 24 database lock, designated BMS personnel may have access to the unblinded data. The study team members who are responsible

for managing the study and are site-facing, will remain blinded to treatment assignment and the results of this analysis. Additionally, a bioanalytical scientist (or a designee in the external central bioanalytical laboratory) may be unblinded (obtain the randomization codes) prior to database lock to facilitate the bioanalytical analysis of [redacted] samples in order to minimize unnecessary bioanalytical analysis of samples. Of note, for operational considerations, the managers of drug supply and IRT will be unblinded to study intervention throughout the study.

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

Before breaking the blind of an individual participant's treatment, the investigator should determine that the unblinded information is necessary (ie, that it will alter the participant'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 participant is receiving the IP.

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 actual task of unblinding can be delegated by the investigator to a designee assigned the task on the Delegation of Authority. The Principal Investigator or appointed designee should only perform the emergency unblinding after the decision to unblind the participant has been documented.

For this study, the method of unblinding for emergency purposes is through the IRT system. For information on how to unblind in an emergency, consult the IRT manual.

In cases of accidental unblinding, contact the Medical Monitor and ensure every attempt is made to minimize additional disclosure and the impact of unblinding.

Any request to unblind a participant for nonemergency purposes should be discussed with the Medical Monitor.

In case of an emergency, the investigator(s) has unrestricted access to randomization information via the IRT and is capable of breaking the blind through the IRT system without prior approval from the Sponsor. Following the unblinding, the investigator shall notify the Medical Monitor or designee that the unblinding took place.

7.4 Dose Modification

Dose modification is not allowed.

7.5 Preparation/Handling/Storage/Accountability

The IP/AxMP must be stored in a secure area according to local regulations. It is the responsibility of the investigator, or designee where permitted, to ensure that IP/AxMP is only

dispensed to study participants. The IP/AxMP must be dispensed only from official study sites by authorized personnel according to local regulations.

The product storage manager should ensure that the study intervention 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 intervention arise, the study intervention should not be dispensed, and BMS should be contacted immediately.

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

IP/AxMP documentation (whether supplied by BMS or not) must be maintained that includes all processes required to ensure the 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).

IP for this study should be stored at 15°C to 25°C and protected from light. Store in original container.

- The investigator or designee must confirm appropriate temperature conditions have been maintained during transit for all study intervention received and any discrepancies are reported and resolved before use of the study intervention.
- The investigator, institution, or the head of the medical institution (where applicable) is responsible for study intervention accountability, reconciliation, and record maintenance (ie, receipt, reconciliation, and final disposition records).
- Further guidance and information for final disposition of unused study interventions are provided in Appendix 2.

7.6 Treatment Compliance

Study intervention compliance will be monitored as indicated in the Schedule of Activities using standard study intervention accountability procedures (comparing the number of tablets returned to number dispensed, considering the expected regimen, and reported missed doses). Study intervention accountability will be reviewed by the investigative site staff at each visit to assess treatment compliance. Site staff will discuss any discrepancies with the participant and remind the participant of the importance of compliance with the assigned regimen.

7.7 Concomitant Therapy

All prior treatments for AA should be recorded on the electronic Case Report Form (eCRF).

All medications taken within 4 weeks of the first dose of study intervention on Day 1 through the Post-Treatment Follow-up visit should be recorded on the eCRF.

Concomitant medications (prescription, over the counter, or herbal) should be administered during the study only if they are to be used for treatment of specific medical reasons.

A non-live vaccine may be administered during the study, but the effect on immune responses with study intervention is unknown and could be blunted (see Section 7.7.2).

Use of systemic corticosteroid medications (< 7 days in duration) to treat non-AA medical conditions is allowed but should be discussed with the Medical Monitor to determine if the intercurrent condition affects the safety of the participant, or if the corticosteroid treatment is likely to confound efficacy assessments.

Note: Topical corticosteroids and topical calcineurin inhibitors are permitted but cannot be applied on the eyelids, eyebrows, or scalp. Otic, ophthalmic, nasal, and inhaled corticosteroids within recommended doses and with no systemic effects are permitted.

7.7.1 Prohibited and/or Restricted Treatments

Prohibited and/or restricted medications during the study are described below. Refer to Section 6.2 Exclusion Criteria-Previous/Concomitant Therapy for medical restrictions affecting eligibility.

- Use of any medications/therapy that would affect hair regrowth
- Any use of biologic medications (eg, adalimumab, etanercept, infliximab, ustekinumab)
- Any use of JAK inhibitors (eg, tofacitinib, baricitinib, ritlecitinib).
- Live vaccination (including, but not limited to, any live attenuated COVID-19 vaccines) should not be used during the study, including the safety follow-up period of 30 days following last dose of IP (see Section 7.7.2 for permitted vaccines).
- Exposure to any investigational drug, investigational vaccine, or placebo outside of the current study. Specifically, participants currently in other interventional trials for COVID-19, including investigational COVID-19 vaccination trials that are not authorized or approved by relevant health authorities, should not participate in BMS clinical trials.

7.7.2 Permitted Vaccines (Including COVID-19 Vaccine)

Administration of a non-live vaccine is allowed during the study. However, the efficacy and safety of non-live vaccines (including non-live COVID-19 vaccines) in participants receiving deucravacitinib is unknown. The following are examples of non-live vaccines: inactivated vaccines (eg, heat-killed and formalin-killed vaccines); subunit vaccines (eg, influenza and pneumococcal vaccines); toxoid vaccines; nucleic acid vaccines that do not encode potentially infectious virus: messenger mRNA vaccines (eg, Comirnaty, Pfizer/BioNTech; Spikevax, Moderna COVID-19 vaccines), and replication-incompetent recombinant adenovirus vector DNA vaccines (eg, Vaxzevria, AstraZeneca/University of Oxford COVID-19 vaccine).

For COVID-19 vaccines, the full series per local guidance should be completed prior to enrollment when feasible and when a delay in enrollment would not put the study participant at risk. Ideally, AEs attributable to a vaccine should have resolved prior to enrollment.

If a participant has received a specific COVID-19 vaccination, details such as type and date of vaccine received should be recorded on the COVID-19 Vaccination Form.

Please contact the Medical Monitor with any questions related to COVID-19 vaccines.

7.8 Continued Access to Study Intervention After the End of the Study

At the end of the study, BMS will not continue to provide BMS-supplied study intervention to participants/investigators unless BMS chooses to extend the study. The investigator should ensure that participants continue to receive appropriate standard of care to treat AA.

BMS reserves the right to terminate access to BMS-supplied study intervention if for example but not limited to the following: a) the study is terminated due to safety concerns; b) the development of deucravacitinib for AA is terminated for other reasons, including but not limited to, lack of efficacy and/or not meeting the study objectives; c) the participant can obtain medication from a government-sponsored or private health program. In all cases, BMS will follow local regulations.

8 DISCONTINUATION CRITERIA

8.1 Discontinuation from Study Intervention

Participants MUST discontinue IP (and Non-IP/AxMP at the discretion of the investigator) for any of the following reasons:

- Participant's request to stop study intervention. Participants who request to discontinue study intervention 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 participant specifically withdraws consent for any further contact with him/her or persons previously authorized by the participant 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 participant
- 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. (Note: Under specific circumstances and only in countries where local regulations permit, a participant who has been imprisoned may be permitted to continue as a participant. Strict conditions apply, and BMS approval is required)
- Participant reports suicidal ideation, suicidal behavior, or suicide attempts at any time after randomization. The participant should then be immediately referred to a mental health professional for evaluation of suicide risk
- Abnormal liver tests suggestive of drug-induced liver injury (DILI), or if the investigator believes that it is in the best interest of the participant
- Malignancy; however, a participant who develops non-melanoma skin cancer may continue in the study at the discretion of the investigator
- Pregnancy, positive pregnancy test, or participant expresses an interest in becoming pregnant
- Participant develops active TB during the study or prematurely discontinues treatment for LTBI, or participant is noncompliant with LTBI therapy
- Japan only: Participant with positive HBsAb at Screening or positive HBcAb with negative or undetectable HBV DNA (< 1.3 Log IU/mL [20 IU/mL]) at Screening, for whom quantitative

HBV DNA becomes detectable (≥ 1.3 Log IU/mL ([20 IU/mL]) at any time during treatment with the IP

- Inability or failure to comply with protocol requirements, in the opinion of the investigator
- Unblinding of a participant's study intervention assignment, to investigator or participant, for any reason (emergency or nonemergency)

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.

All participants who discontinue study intervention should comply with protocol-specified follow-up procedures as outlined in Section 2 (Table 2-3). The only exceptions to this requirement is when a participant withdraws consent for all study procedures, including post-treatment study follow-up, or loses the ability to consent freely (eg, is imprisoned or involuntarily incarcerated for the treatment of either a psychiatric or physical illness).

If study intervention is discontinued prior to the participant's completion of the study, the reason for the discontinuation must be documented in the participant's medical records per local regulatory requirements in each region/country and entered on the appropriate Case Report Form (CRF) page.

8.1.1 Temporary Interruption

Temporary study intervention interruption is only allowed if the participant develops an AE that, in the opinion of the investigator, indicates that it is in the participant's best interest that the study intervention be interrupted.

Study intervention in this situation should be stopped until the AE has resolved per investigator judgment.

Temporary interruption of study intervention should be implemented in the context of clinical suspicion for SARS-CoV-2 infection or a positive diagnostic test for SARS-CoV-2. When study intervention is interrupted in a confirmed case of SARS-CoV-2 infection, the investigator should determine whether the resolution of symptoms alone (ie, without repeat diagnostic testing for SARS-CoV-2) is sufficient to resume study intervention. The investigator may consult with the Medical Monitor.

Temporary interruption of study intervention may be considered in the event of SARS-CoV-2 vaccination according to local guidelines.

Any temporary study intervention interruption, as well as restart, must be documented on the appropriate CRF page.

8.1.2 Post-study Intervention Study Follow-up

Participants who discontinue study intervention may continue to be followed.

Participants who discontinue study intervention should complete all assessments indicated for the Week 52/Early Discontinuation (ED) visit and the Post-treatment Follow-up visit as outlined in the Schedule of Activities (Table 2-3).

8.2 Discontinuation from the Study

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

- Participants should notify the investigator of the decision to withdraw consent from future follow-up.
- The withdrawal of consent should be explained in detail in the medical records by the investigator, as to whether the withdrawal is from further treatment with study intervention only or also from study procedures and/or post-treatment study follow-up, and entered on the appropriate CRF page.
- In the event that vital status (whether the participant 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 participant withdraws consent for disclosure of future information, the Sponsor may retain and continue to use any data collected before such a withdrawal of consent.

8.2.1 Individual Discontinuation Criteria

- A participant may withdraw completely from the study at any time at his/her own request, or may be withdrawn at any time at the discretion of the investigator for safety, behavioral, compliance, or administrative reasons. This is expected to be uncommon. Stopping study intervention is not considered withdrawal from the study.
- At the time of discontinuing from the study, if possible, an early termination visit should be conducted, as shown in the Schedule of Activities. See the Schedule of Activities for data to be collected at the time of study discontinuation and follow-up and for any further evaluations that need to be completed.
- The participant will be permanently discontinued both from the study intervention and from the study at that time.
- If the participant withdraws consent for disclosure of future information, the Sponsor may retain and continue to use any data collected before such a withdrawal of consent.

8.3 Lost to Follow-up

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- All reasonable efforts must be made to locate participants to determine and report their ongoing status. This includes follow-up with persons authorized by the participant.
- Lost to follow-up is defined by the inability to reach the participant after a minimum of **three (3)** documented phone calls, faxes, or emails, as well as lack of response by participant to one (1) registered mail letter. All attempts should be documented in the participant's medical records.

- If it is determined that the participant has died, the site will use permissible local methods to obtain date and cause of death.
- If the investigator's use of a third-party representative to assist in the follow-up portion of the study has been included in the participant's informed consent, then the investigator may use a Sponsor-retained third-party representative to assist site staff with obtaining the participant'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 participant remains lost to follow-up, then the last known alive date as determined by the investigator should be reported and documented in the participant's medical records.

9 STUDY ASSESSMENTS AND PROCEDURES

All Screening evaluations must be completed and reviewed to confirm that potential participants meet all eligibility criteria before randomization. The investigator will maintain a Screening Log to record details of all participants screened and to confirm eligibility or record reasons for Screening failure, as applicable.

Procedures conducted as part of the participant's routine clinical management (eg, blood count) performed before signing the informed consent may be utilized for screening purposes, provided the procedure meets the protocol-defined criteria and has been performed within the timeframe defined in Section 6.

Below is the suggested order in which to perform the evaluations at each applicable visit:

[redacted]

- Concomitant medications
- Adverse event monitoring
- 12-lead ECG
- Vital signs
- Body weight and height
- Physical examination and efficacy assessments. Assessments should be completed in the following order:
  - Hamilton-Norwood/Ludwig Classification
  - SALT Assessment
  - [redacted]
  - AA-IGA
  - Medical photography of scalp and eyebrows/eyelashes (if consent obtained)

  - [redacted] (if consent obtained)
- Urine pregnancy test (WOCBP) and urinalysis
- Blood sampling for [redacted] laboratory assessments. Please refer to [redacted] regarding requirement for pre-and post-dose sample collection times
- Study intervention accountability and study intervention compliance
- Dispensing of study intervention

9.1 Efficacy Assessments

The efficacy assessments listed below are commonly used tools to characterize disease severity in patients with AA and are established endpoints in clinical practice for assessing treatment efficacy in AA

All investigator-administered assessments should be performed by a dermatologist or appropriately trained licensed health care provider who is experienced in the assessment of patients with AA. All efficacy evaluators must receive and document protocol-specific efficacy assessment training prior to performing the evaluations.

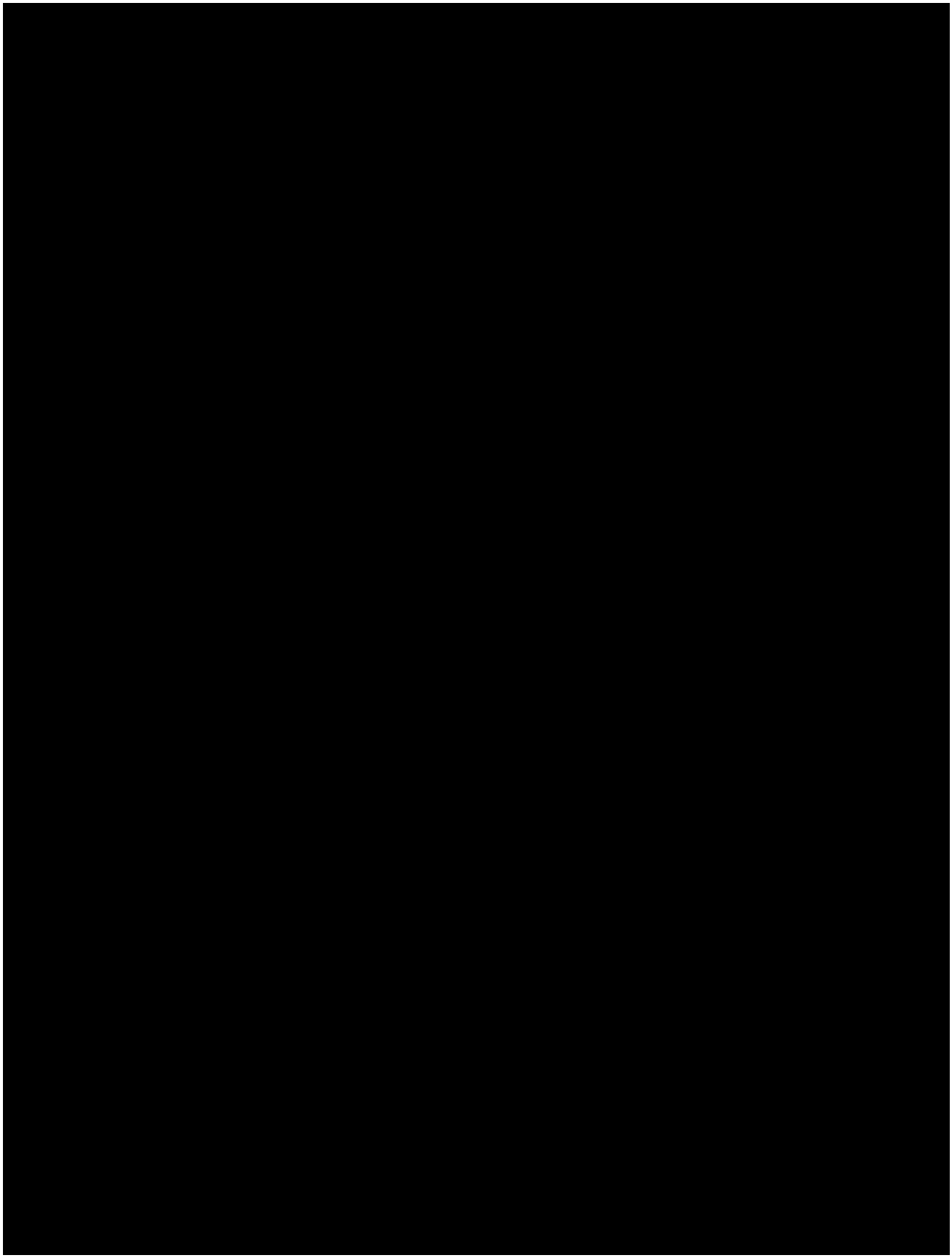
To ensure consistency and reduce variability, the same evaluator must assess all dermatological clinical evaluations for any individual participant throughout the study whenever possible; a back-up experienced, qualified, and protocol-trained evaluator will only be allowed on rare occurrences, when the designated evaluator is unable to perform the evaluation.

- SALT Assessment (Appendix 5[32,33]) This is a quantitative rating scale for measuring the severity of terminal hair loss in each of the 4 quadrants of the scalp: posterior (back), vertex (top), left, and right profile. To obtain a SALT score, the degree of scalp hair loss is assessed as a percentage of each scalp region affected and is multiplied by its respective weighting factor (the scalp surface area) for each of the 4 sections in order to provide a subtotal for each region. The SALT score is the sum of these subtotals. SALT scores can range from 0 (no hair loss) to 100 (total scalp hair loss).

  SALT50 indicates at least a 50% improvement from baseline in the SALT score at a particular time point, indicating 50% hair regrowth. [redacted] The proportion of participants achieving these responses will be assessed at all visits. [redacted]

- AA-IGA: The AA-IGA utilizes a 5-point scale, in which the investigator assesses scalp hair loss based on the SALT assessment. The AA-IGA measures AA severity at a single point in time (without taking into account the baseline disease condition). The participant's scalp hair loss, as it looks at the time of evaluation, is scored as none (0) (0% scalp hair loss), limited (1) (1%-20% scalp hair loss), moderate (2) (21%-49% scalp hair loss), severe (3) (50%-94% scalp hair loss), or very severe (4) (95%-100% scalp hair loss).

[redacted]



9.1.2 Medical Photography

Medical photography of the scalp is required at the visits indicated in the Schedule of Activities. A separate consent will be required to allow for photography of a participant's face for eyelash and eyebrow evaluation at Day 1, Week 24, Week 40, and Week 52. In participants who provide optional consent, if new onset involvement of eyelashes and/or eyebrows (not present at baseline) is observed after Day 1, a photograph of the eyelashes and or eyebrows should be taken at the visit first observed, in addition to Weeks 24, 40, and 52.

An external reviewer will assess for regrowth of eyebrows and eyelashes.

Sites will be equipped with clinical photography supplies. Any photographs may be used as supplemental documentation for publications and to increase understanding of effect of study intervention on hair regrowth.

Detailed instructions on the collection and transmission of digital images will be provided to the investigator in a separate manual at or before the time of study initiation.

9.2 Adverse Events

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

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

The investigator and any qualified 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 intervention or the study, or that caused the participant to discontinue before completing the study.

Refer to Appendix 3 for SAE reporting.

9.2.1 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 more carefully. AEIs may be serious or nonserious and may require further investigation to better characterize and understand them. In the deucravacitinib clinical development program, select infections (opportunistic, TB, herpes zoster) and malignancies have been identified as AEIs based on the mechanism of action of deucravacitinib. Therefore, in order to better characterize and understand these AEIs, information may be collected on supplemental CRFs. Additionally, information on potential AEIs based on the disease or population under study may be collected on supplemental CRFs.

9.2.2 Time Period and Frequency for Collecting AE and SAE Information

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 following discontinuation of dosing.

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

- Medical occurrences that begin before the start of study intervention but after obtaining informed consent will be recorded on the appropriate section of the CRF 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 participants. However, if the investigator learns of any SAE, including a death, at any time after a participant has been discontinued from the study, and he/she considers the event reasonably related to the study intervention 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.

In order to facilitate enhanced reporting of COVID-19 events that occur during the study, all AEs and SAEs reported after the time of consent that are related to SARS-CoV-2 or COVID-19 infection must be reported (Section 9.2).

9.2.3 Method of Detecting AEs and SAEs

AEs can be spontaneously reported or elicited during open-ended questioning, examination, or evaluation of a participant. Care should be taken not to introduce bias when collecting AE and/or SAEs. Inquiry about specific AEs, should be guided by clinical judgment in the context of known AEs, when appropriate for the program or protocol.

9.2.4 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 intervention and for those present at the end of study intervention as appropriate.
- All identified nonserious AEs must be recorded and described on the nonserious AE page of the CRF (paper or electronic). Completion of supplemental CRFs may be requested for AEs and/or laboratory abnormalities that are reported/identified during the course of the study.

After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs, and nonserious AEs of special interest (as defined in Section 9.2.1) will be followed until resolution, until the condition stabilizes, until the event is otherwise explained, or until the participant is lost to follow-up (as defined in Section 8.3).

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

9.2.5 Regulatory Reporting Requirements for SAEs

- Prompt notification by the investigator to the Sponsor of SAEs is essential so that legal obligations and ethical responsibilities toward the safety of participants 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 Investigator's Brochure and will notify the IRB/ IEC, if appropriate according to local requirements.

The Sponsor or designee must report AEs to regulatory authorities and ethics committees according to local applicable laws and regulations. A SUSAR (suspected, unexpected serious adverse reaction) is a subset of SAEs and must be reported to the appropriate regulatory authorities and investigators in accordance with local and global guidelines and requirements.

9.2.6 Pregnancy

If, following initiation of the study intervention, it is subsequently discovered that a participant is pregnant or may have been pregnant at the time of study exposure and through the end of the safety follow-up period the investigator must immediately notify the BMS Medical Monitor/designee of this event and complete and forward a Pregnancy Surveillance Form to the BMS designee within 24 hours of awareness of the event and in accordance with SAE reporting procedures described in Appendix 3.

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

Any pregnancy that occurs in a female partner of a male study participant should be reported to the Sponsor or designee. In order for the 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.

9.2.7 Laboratory Test Result Abnormalities

The following laboratory test result abnormalities should be captured on the nonserious AE CRF page or SAE eCRF, as appropriate. Paper forms are only intended as a back-up option when the electronic system is not functioning.

- Any laboratory test result that is clinically significant or meets the definition of an SAE
- Any laboratory test result abnormality that required the participant to have study intervention discontinued or interrupted
- Any laboratory test result abnormality that required the participant to receive specific corrective therapy

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

9.2.8 Potential Drug Induced Liver Injury (DILI)

All occurrences of potential DILIs, meeting the defined criteria, must be reported as SAEs (see Section 9.2.5 and Appendix 3 for reporting details).

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 9.2 and Appendix 3 for reporting details).

Potential DILI is defined as:

- AT (ALT or AST) elevation > 3 times upper limit of normal (ULN)
  AND
- Total bilirubin > 2 times ULN, without initial findings of cholestasis (elevated serum alkaline phosphatase)
  AND
- 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.

9.2.9 Other Safety Considerations

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

9.3 Overdose

For this study, any dose of deucravacitinib greater than 2 days' worth of study intervention within a 24-hour time period will be considered an overdose. Overdoses that meet the regulatory definition of SAE will be reported as an SAE (see Appendix 3).

The investigator should do the following in the event of an overdose:

1) Contact the Medical Monitor immediately.
2) Closely monitor the participant for AEs/SAEs and laboratory abnormalities until deucravacitinib can no longer be detected systemically (at least 3 days).
3) Document the quantity of the excess dose as well as the duration of the overdosing in the eCRF.

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 participant.

9.4 Safety

Planned time points for all safety assessments are listed in the Schedule of Activities.

All urgent safety concerns must be discussed with the Sponsor immediately upon occurrence or awareness to determine if the participant should continue or discontinue study intervention.

Safety evaluations that will be performed in addition to AE monitoring are physical examinations, vital signs, ECGs, concomitant medication use, and laboratory tests.

9.4.1 Physical Examinations

A complete physical examination will include general appearance, head, eyes, ears, nose, mouth, throat, neck, extremities, cardiovascular, respiratory, GI/abdomen, lymphatic, musculoskeletal, skin, and psychiatric and neurologic examinations. A targeted physical examination will include any organ system associated with an AE or a laboratory abnormality.

9.4.2 Vital signs

Vital sign assessments include body temperature, respiratory rate, seated blood pressure, and heart rate. Blood pressure and heart rate should be measured after the participant has been resting quietly for at least 5 minutes.

9.4.3 Electrocardiograms

A 12-lead ECG should be performed after the participant has remained supine for at least 5 minutes prior to the ECG; blood samples for laboratory, [redacted] assessments should be collected after the tracing so that the ECG results remain as accurate as possible. The ECG results will be read by the principal study investigator or a qualified and delegated designee as per local requirements.

9.4.4 Clinical Safety Laboratory Assessments

- Investigators must document their review of each laboratory safety report.
- The assessments to be performed at specified visits are indicated below.

Hematology	
Hemoglobin	
Hematocrit	
White Blood Count, including differential	
Platelet count	
Coagulation Panel[c]	
International Normalized Ratio	
Prothrombin Time	
Partial Thromboplastin Time or Activated Thromboplastin Time	
Chemistry Panel	
Aspartate aminotransferase (AST)	Total Protein
Alanine aminotransferase (ALT)	Albumin
Total bilirubin	Sodium
Direct bilirubin (if total bilirubin > ULN)	Potassium

Alkaline phosphatase Lactate dehydrogenase Creatinine Blood Urea Nitrogen (BUN) Uric acid Glucose (fasting[b]), at specified visits Hemoglobin A1c, at specified visits	Chloride Calcium Phosphorus Creatine Kinase[a] Estimated Glomerular Filtration Rate
Urinalysis	
Protein Glucose Blood Leukocyte Esterase Specific Gravity pH Microscopic examination (reflex if abnormal)	
Lipid Panel[b]	
Cholesterol (total) High Density Lipoprotein Low Density Lipoprotein	
Triglycerides	
Infectious Serology[c]	
Hepatitis C Antibody confirmed by HCV-RNA testing if required Hepatitis B Surface Antigen	
Hepatitis B Surface Antibody Hepatitis B Core Antibody Hepatitis B DNA as required with confirmed HBV infection; see Appendix 9 (Japan only). Human Immunodeficiency Virus -1 and -2 Antibody	
Other Analyses	
Pregnancy test (WOCBP only: serum HCG test at Screening, urine HCG test all other visits) Follicle-stimulating Hormone (to confirm menopausal status)[c] Thyroid-stimulating Hormone[c,d]	

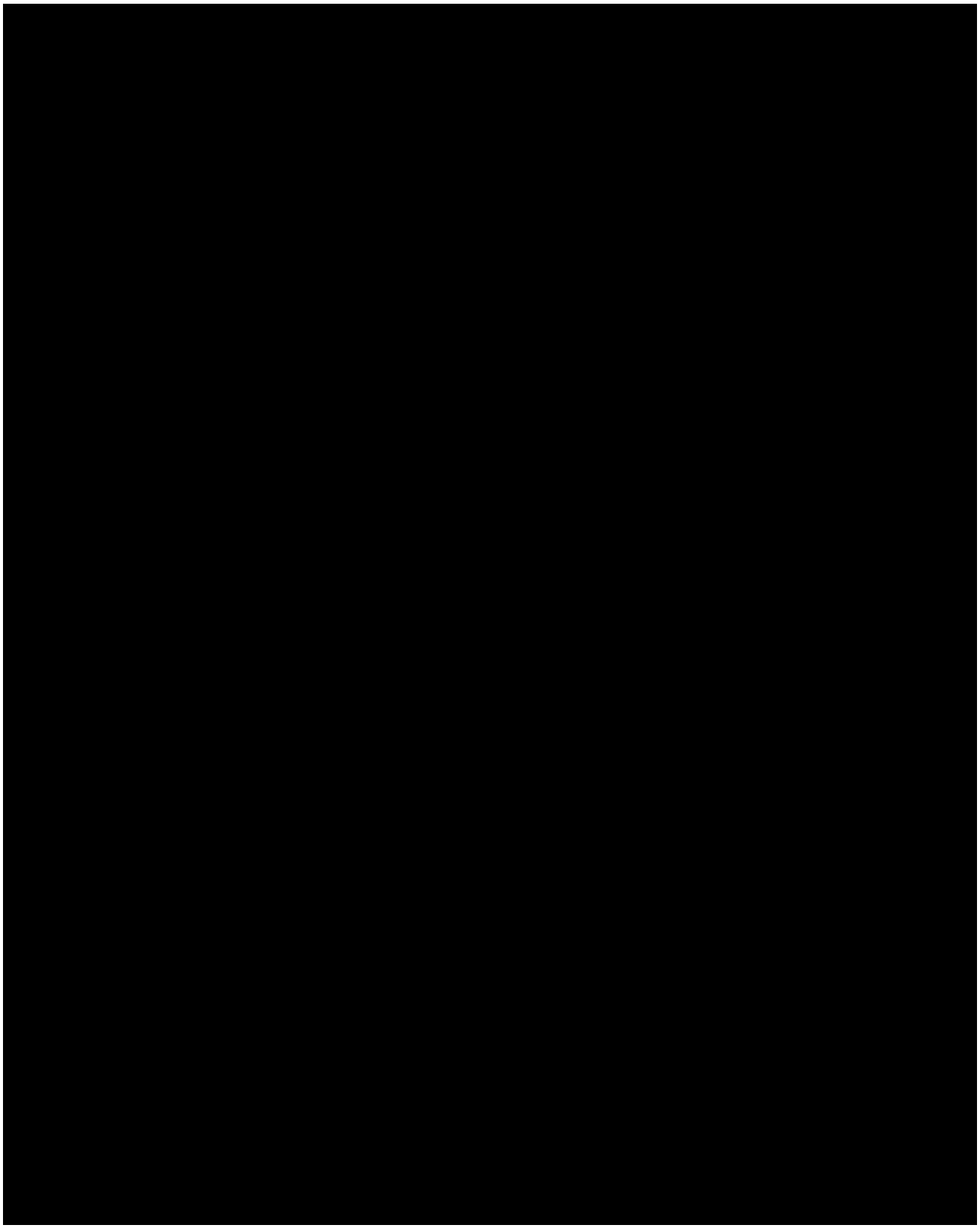
Abbreviations: CK, creatine kinase; DNA, deoxyribonucleic acid; HBV, hepatitis B virus; HCV, hepatitis C virus; RNA, ribonucleic acid; TSH, thyroid-stimulating hormone; ULN, upper limit of normal; WOCBP, women of childbearing potential.

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

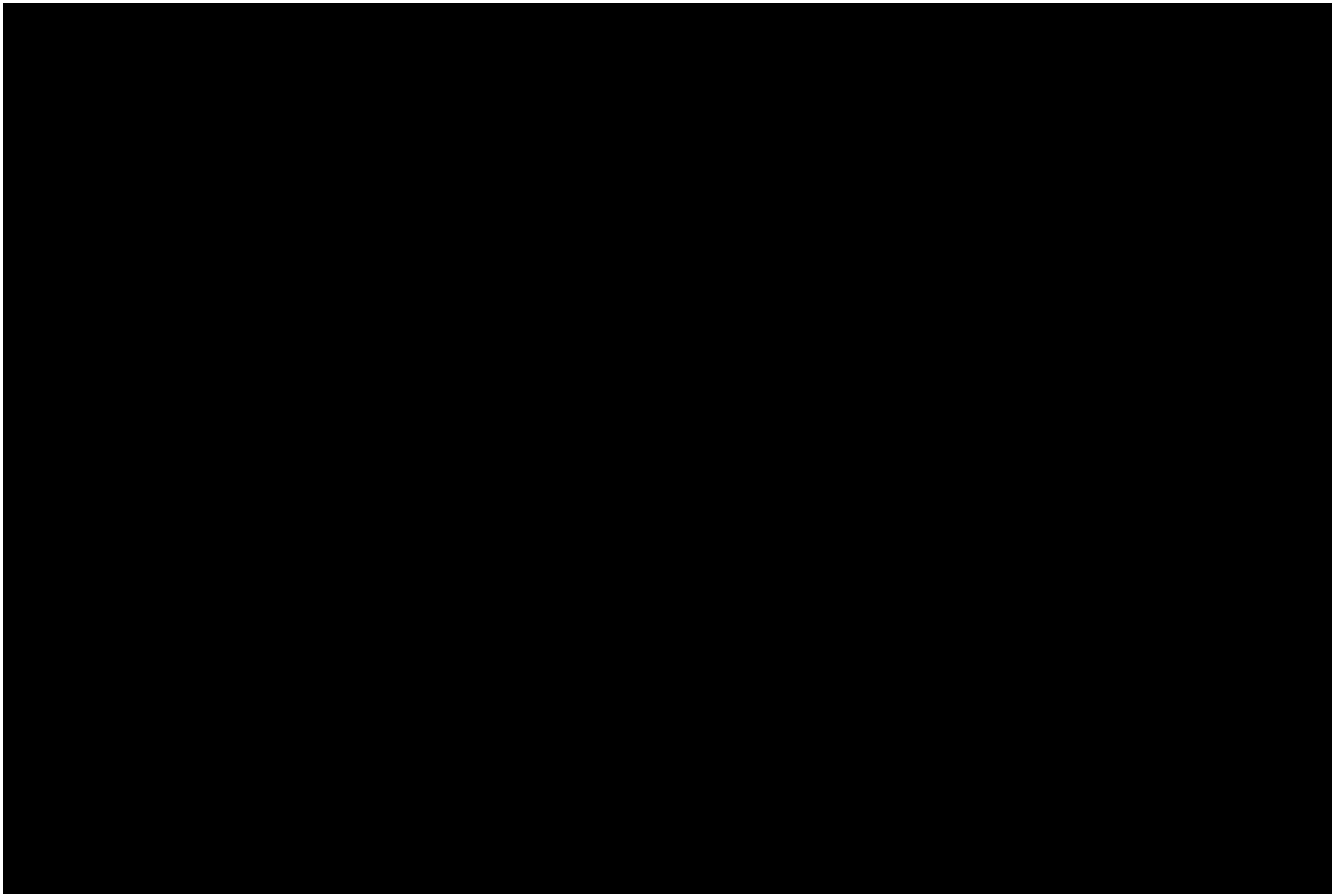
[b] Samples will be collected after the participant has fasted for ≥ 10 hours; fasting not required for samples collected at the Screening visit.

[c] Performed at Screening.

[d] If TSH is above the normal reference range, test free T4; if TSH is below the normal range, test free T4 and T3.



[redacted]



[redacted]

[redacted]

[redacted]

9.9 Other Assessments

[redacted] It may also be used to support health authority requests for further analysis (refer to [redacted]

9.10 Health Economics OR Medical Resource Utilization and Health Economics

Health Economics/Medical Resource Utilization and Health Economics parameters will not be evaluated in this study.

10 STATISTICAL CONSIDERATIONS

10.1 Statistical Hypothesis

Let μ_1 and μ_2 be the population means of change from baseline at Week 24 in SALT for 6 mg QD and 6 mg BID dosages of deucravacitinib, respectively, and μ_0 be the population mean of change from baseline at Week 24 in SALT for placebo; the 2 primary hypotheses for this study are:

1) $H0_1$: $\mu_1 = \mu_0$ versus $H1_1$: $\mu_1 \neq \mu_0$
2) $H0_2$: $\mu_2 = \mu_0$ versus $H1_2$: $\mu_2 \neq \mu_0$

10.2 Sample Size Determination

Approximately 90 participants will be randomized on Day 1 in a 1:1:1 ratio, resulting in 30 participants in each deucravacitinib dose arm (6 mg QD and 6 mg BID) and 30 participants in the placebo arm.

Assuming a 39-point difference in change in SALT score from baseline to Week 24 between both deucravacitinib doses and placebo, and a common standard deviation (SD) of 43 points, the following table presents 2 scenarios on sample size and overall power of the study.

Type I error	Sample Size	Overall Power
0.10	25	93%
0.05	25	88%

Assuming a 15% drop out rate and an overall type I error of 0.10 level:

1) Without multiplicity adjustment for 2 doses to be compared with the placebo, the study overall power with a sample size of 30 in each arm is 93%
2) With Bonferroni adjustment for 2 doses to be compared with the placebo, the study overall power with a sample size of 30 in each arm is 88%

The expected difference (39 points) between deucravacitinib dose and placebo and common SD (43 points) in the change from baseline in the SALT score are based on an average of recently reported data from clinical trials with oral compounds in participants with moderate to severe AA treated with an oral TYK2/JAK1 inhibitor, PF-06700841 (placebo-adjusted mean 49.5 points, 95% confidence interval [CI] [37.1, 61.8]), and with an oral JAK 3 inhibitor, PF-06651600 (placebo-adjusted mean 33.6 points, 95% CI [21.4, 45.7]) compared to placebo.[18]

10.3 Analysis Sets

For the purposes of analyses, the following populations are defined:

Population	Description
Enrolled	All participants who signed the informed consent.
Randomized	All participants who were in the enrolled population and were randomized using IRT.
Safety	All participants who were in the randomized population and received at least 1 dose of study intervention.
[redacted]	

Abbreviations: IRT, Interactive Response Technology.

10.4 Statistical Analysis

10.4.1 General Considerations

All efficacy analyses will be carried out on the randomized population and will be analyzed according to the treatment assigned at randomization.

All safety analyses will be carried out on the safety population and will be analyzed by the actual treatment received.

The statistical analysis plan (SAP) will be developed and finalized before database lock and will describe the selection of participants to be included in the analyses and procedures for accounting for missing, unused, and spurious data. Below is a summary of planned statistical analyses of the primary and secondary endpoints.

The SAP will include a more technical and detailed description of the statistical analyses described in this section. This section is a summary of the planned statistical analyses of the most important endpoints.

A description of the participant population will be included in the clinical study report, including subgroups of age, gender, race, and other study specific populations and demographic characteristics. A description of participant disposition will also be included in the clinical study report.

A database lock will occur once all randomized participants have completed the Week 24 assessments or have discontinued prior to Week 24. Analyses of the collected efficacy and safety results during the 24-week placebo-controlled period will be performed in order to aid in planning for subsequent clinical development. Details of these analyses will be described in the SAP.

10.4.2 Primary Efficacy Endpoints

The 2 primary hypotheses, as specified in Section 10.1, will be tested on the overall significance level of 10%. To strongly control the overall type I error at 10% level, the Bonferroni adjustment will be used to adjust multiplicity due to 2 deucravacitinib dose arms to be compared with the placebo arm.

The primary efficacy endpoint (change in SALT score from baseline to Week 24 [Day 169]) will be analyzed on the randomized population using an analysis of covariance (ANCOVA). The ANCOVA model will include treatment arm, the randomization stratification variable of alopecia episode duration (< 4 years and ≥ 4 years), as factors, and baseline SALT score as a covariate.

The primary methodology to impute the missing data will be multiple imputation with the assumption of missing at random.

Additional sensitivity analyses will be further outlined in the SAP.

10.4.3 Secondary Efficacy Endpoint(s)

The analyses and summary statistics for all secondary efficacy endpoints, as specified in Table 4-1, will be presented in appropriate tables. The 90% confidence intervals and p values will be provided, as needed, by applying appropriate statistical models to each endpoint that will be specified in detail in the SAP.

[redacted]

10.4.5 Other Safety Analyses

All safety analyses will be carried out on the safety population.

Adverse events will be monitored during the trial and the data analyzed with respect to incidence within each treatment arm as well as severity and potential relationship of the AEs to study intervention. Adverse events will be summarized for the safety population by System Organ Class

and Preferred Term and presented in descending order of frequency within each System Organ Class. Serious AEs and AEs leading to discontinuation will be summarized similarly.

Associated laboratory parameters such as hepatic profile, renal function, and hematology values will be grouped and presented together. Changes from baseline to each visit for each laboratory parameter will also be summarized.

The change from baseline to each visit for each of the vital sign variables will be summarized. Abnormal vital sign values will be flagged and listed.

The change from baseline to each visit for each of the ECG parameters will be summarized.

10.4.6 Other Analyses

Not applicable.

10.5 Interim Analysis

Not applicable.

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12 APPENDICES

APPENDIX 1 ABBREVIATIONS

Term	Definition
AA	alopecia areata
AA-IGA	Alopecia Areata Investigator Global Assessment
[redacted]	
AE	adverse event
AEI	adverse event of interest
ALT	alanine aminotransferase
ANCOVA	analysis of covariance
APTT	activated partial thromboplastin time
[redacted]	
AT	aminotransaminase
AST	aspartate aminotransferase
AxMP	auxiliary medicinal product
BID	twice daily
BMS	Bristol-Myers Squibb Company
BP	blood pressure
BUN	blood urea nitrogen
Cavg	average concentration
CBC	complete blood count
CD	cluster of differentiation
CFR	Code of Federal Regulations
CI	confidence interval
CK	creatine kinase
Cmin	minimum observed concentration
COVID-19	coronavirus disease 2019
CRF	Case Report Form, paper or electronic
CRO	Contract Research Organization
[redacted]	
CXCL	CXC motif chemokine ligand
D	Day
d	days
DDI	drug-drug interaction
DILI	drug-induced liver injury

Term	Definition
DMC	Data Monitoring Committee
DNA	deoxyribonucleic acid
ECG	electrocardiogram
eCRF	electronic Case Report Form
ED	early discontinuation
eGFR	estimated glomerular filtration rate
[redacted]	
E-R	exposure-response
FAS	Full Analysis Set
FDA	Food and Drug Administration
FIH	first-in-human
FSH	follicle stimulating hormone
GI	gastrointestinal
HbA1c	hemoglobin A1c
HBcAb	hepatitis B core antibody
HBsAb	hepatitis B surface antibody
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCG	human chorionic gonadotropin
Hct	hematocrit
HCV	hepatitis C virus
HDL	high density lipoprotein
HF	hair follicle
Hgb	hemoglobin
HIV	human immunodeficiency virus
hr	hour
hs-CRP	high-sensitivity C-reactive protein
IB	Investigator Brochure
ICF	informed consent form
IFN	interferon

Term	Definition
Ig	immunoglobulin
IGRA	IFN gamma release assay
IL	interleukin
IMP	Investigational Medicinal Product
INR	international normalized ratio
IP	investigational product
IRB	Institutional Review Board
IRT	Interactive Response Technology
IU	international unit
IV	intravenous
JAK	Janus kinase
LDH	lactate dehydrogenase
LDL	low density lipoprotein
LTBI	latent TB infection
MACE	major adverse cardiovascular events
MHC	major histocompatibility complex
min	minute
N/A	not applicable
NA	nucleoside/nucleotide analogues
NK	natural killer
NKG2D+	natural killer group 2D+
PA	posteroanterior
PASI	psoriasis area severity index
PD	pharmacodynamics
PE	physical examination
[redacted]	
PK	pharmacokinetics
PO	per os

Term	Definition
PsA	psoriatic arthritis
PsO	plaque psoriasis
PT	prothrombin time
PTT	partial thromboplastin time
QD	once daily
RNA	ribonucleic acid
SAE	serious adverse event
SALT	Severity of Alopecia Tool
SAP	statistical analysis plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SD	standard deviation
SLE	systemic lupus erythematosus
SOA	Schedule of Activities
STAT	signal transducer and activator of transcription
T3	triiodothyronine
T4	thyroxine
TB	tuberculosis
[redacted]	
TE	target engagement
TSH	thyroid-stimulating hormone
TYK2	tyrosine kinase 2
UC	ulcerative colitis
ULN	upper limit of normal
WOCBP	women of childbearing potential

APPENDIX 2 STUDY GOVERNANCE CONSIDERATIONS

The terms "participant" and "subject" refer to a person who has consented to participate in the clinical research study. Typically, the term "participant" is used in the protocol and the term "subject" is used in the Case Report Form (CRF).

REGULATORY AND ETHICAL CONSIDERATIONS

This study will be conducted in accordance with:

- Consensus ethical principles derived from international guidelines, including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines
- Applicable International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines
- Applicable laws, regulations, and requirements

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

All potential serious breaches must be reported to the Sponsor or designee immediately. A potential serious breach is defined as a Quality Issue (eg, protocol deviation) that is likely to affect, to a significant degree, one or more of the following: (1) the rights, physical safety or mental integrity of one or more participants; (2) the scientific value of the clinical trial (eg, reliability and robustness of generated data). Items (1) or (2) can be associated with either GCP regulation(s) or trial protocol(s).

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, Investigator's Brochure, product labeling information, ICF, participant recruitment materials (eg, advertisements), and any other written information to be provided to participants.

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

The investigator is responsible for providing oversight of the conduct of the study at the site and adherence to requirements of the following where applicable:

- ICH guidelines,
- United States Code of Federal Regulations, Title 21, Part 50 (21CFR50)
- European Union Directive 2001/20/EC; or
- European Regulation 536/2014 for clinical studies (if applicable),
- European Medical Device Regulation 2017/745 for clinical device research (if applicable),
- the IRB/IEC
- and all other applicable local regulations.

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 the local Health Authority), except where necessary to eliminate an immediate hazard(s) to study participants.

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
- 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 the local Health Authority, must be sent to Bristol-Myers Squibb (BMS).

If an amendment substantially alters the study design or increases the potential risk to the participant: (1) the ICF 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 participants 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 participants prior to enrollment.

FINANCIAL DISCLOSURE

Investigators and sub-investigators will provide the Sponsor with sufficient, accurate financial information, in accordance with 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 participants are clearly and fully informed about the purpose, potential risks, and other critical issues regarding clinical studies in which they volunteer to participate.

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

The investigator or his/her representative must:

- Obtain IRB/IEC written approval/favorable opinion of the written ICF and any other information to be provided to the participant prior to the beginning of the study and after any revisions are completed for new information.
- Provide a copy of the ICF and written information about the study in the language in which the participant is proficient prior to clinical study participation. The language must be nontechnical and easily understood.
- Explain the nature of the study to the participant or his/her legally acceptable representative and answer all questions regarding the study.
- Inform participant that his/her participation is voluntary. Participant or his/her legally acceptable representative will be required to sign a statement of informed consent that meets the requirements of 21 CFR 50, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act (HIPAA) requirements, where applicable, and the IRB/IEC or study center.
- Allow time necessary for participant or his/her legally acceptable representative to inquire about the details of the study.

Obtain an ICF signed and personally dated by participant or his/her legally acceptable representative and by the person who conducted the informed consent discussion.

- Include a statement in participant's medical record that written informed consent was obtained before participant was enrolled in the study and the date the written consent was obtained. The authorized person obtaining the informed consent must also sign the ICF.
- Re-consent participant to the most current version of the ICF(s) during his/her participation in the study, as applicable.

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

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

The ICF must also include a statement that BMS and local and foreign regulatory authorities have direct access to participant records.

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

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

Participant unable to give their written informed consent (eg, stroke or participants with severe dementia) may only be enrolled in the study with the consent of a legally acceptable representative. The participant must also be informed about the nature of the study to the extent compatible with his or her understanding, and should this participant become capable, he or she should personally sign and date the ICF as soon as possible. The explicit wish of a participant 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 participants are the most important considerations and should prevail over interests of science and society.

BMS COMMITMENT TO DIVERSITY IN CLINICAL TRIALS

The mission of BMS is to transform patients' lives through science by discovering, developing, and delivering innovative medicines that help them prevail over serious diseases.

BMS is committed to doing its part to ensure that patients have a fair and just opportunity to achieve optimal health outcomes.

BMS is working to improve the recruitment of a diverse participant population with the goal that the clinical trial becomes more reflective of the real-world population and the people impacted by the diseases studied.

DATA PROTECTION, DATA PRIVACY, AND DATA SECURITY

BMS collects and processes personal data of study participants, patients, health care providers, and researchers for biopharmaceutical research and development to advance innovative, high-quality medicines that address the medical needs of patients. BMS ensures the privacy, protection, and confidentiality of such personal data to comply with applicable laws. To achieve these goals, BMS has internal policies that indicate measures and controls for processing personal data. BMS adheres to these standards to ensure that collection and processing of personal data are limited and proportionate to the purpose for which BMS collects such personal data. This purpose is clearly and unambiguously notified to the individual at the time of collection of personal data. In the true

spirit of science, BMS is dedicated to sharing clinical trial information and data with participants, medical/research communities, the media, policy makers, and the general public. This is done in a manner that safeguards participant privacy and informed consent while respecting the integrity of national regulatory systems. Clinical trial data, health-related research, and pharmacovigilance activities on key-coded health data transferred by BMS across national borders is done in compliance with the relevant data protection laws in the country and GCP requirements.

BMS protects Personal Information with adequate and appropriate security controls as indicated under the data protection laws. To align with the recommended security standards, BMS has adopted internal security standards and policies to protect personal data at every stage of its processing.

To supplement these standards, BMS enters into Clinical Trial Agreements (CTAgs) with confidentiality obligations to ensure proper handling and protection of personal data by third parties accessing and handling personal data.

BMS takes unauthorized access and disclosure of Personal Information very seriously. BMS has adopted the security standards that include National Institute of Standards and Technology Cybersecurity Framework for studies in the US. BMS aligns with these standards to continuously assess and improve its ability to protect, detect, and respond to cyber attacks and other unauthorized attempts to access personal data. These standards also aid in mitigating possible adverse effects. Furthermore, BMS Information Technology has defined 6 principles to protect our digital resources and information:

1) Responsibilities of IT Personnel
2) Securing the BMS Digital Infrastructure
3) Identity and Access Management
4) External Partner Connections
5) Cyber Threat Detection and Response
6) Internal Cyber Incident Investigation

SOURCE DOCUMENTS

Source documents provide evidence for the existence of the participant and substantiate the integrity of the data collected. Source documents are filed at the investigator's site.

Data reported on the CRF or entered in the electronic CRF (eCRF) that are transcribed from source documents must be consistent with the source documents or the discrepancies must be explained.

- The investigator may need to request previous medical records or transfer records, depending on the study. Also, current medical records must be available.
- Definitions of what constitutes source data can be found in systems that 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).

The investigator is responsible for ensuring that the source data are accurate, legible, contemporaneous, original, and attributable, whether the data are handwritten 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 records/electronic health records, adverse event (AE) tracking/reporting, protocol-required assessments, and/or drug accountability records.

When paper records from such systems are used in place of an 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 INTERVENTION RECORDS

Records for study intervention (whether supplied by BMS, its vendors, or the site) must substantiate study intervention 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: • amount received and placed in storage area • amount currently in storage area • label identification number or batch number • amount dispensed to and returned by each participant, including unique participant identifiers • amount transferred to another area/site for dispensing or storage • nonstudy disposition (eg, lost, wasted) • amount destroyed at study site, if applicable • amount returned to BMS • retain samples for bioavailability/bioequivalence/biocomparability, if applicable • 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 standard operating procedures/standards of the sourcing pharmacy

BMS or its 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 (EDC) tool, eCRFs 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 Pregnancy Surveillance Form, respectively. If the

electronic SAE form is not available, a paper SAE form can be used. Spaces may be left blank only in those circumstances permitted by study-specific CRF completion guidelines provided by the Sponsor or designee.

The confidentiality of records that could identify participants 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 and SAE/pregnancy CRFs must be promptly reviewed, signed, and dated by the investigator or qualified physician who is a sub-investigator and who is delegated this task on the Delegation of Authority Form. Sub-investigators in Japan may not be delegated the CRF approval task. For eCRFs, review and approval/signature is completed electronically through the BMS EDC tool. The investigator must retain a copy of the CRFs, including records of the changes and corrections.

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

MONITORING

Monitoring details describing strategy, including definition of study critical data items and processes (eg, risk-based initiatives in operations and quality such as risk management and mitigation strategies and analytical risk-based monitoring), methods, responsibilities, and requirements, including handling of noncompliance issues and monitoring techniques (central, remote, or on-site monitoring) are provided in the monitoring plan.

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 the 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 the 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 its 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 its 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 its designee.

RETURN OF STUDY TREATMENT

For this study, study treatments (those supplied by BMS or 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 interventions 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). Partially used study interventions and/or empty containers may be destroyed after proper reconciliation and documentation. But unused IMP must be reconciled by site monitor/Clinical Research Associate prior to destruction. 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; eg, study treatments sourced from the site's 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 of study interventions, 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 standard operating procedures 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 (eg, 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 Study 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.

STUDY AND SITE START AND CLOSURE

The Sponsor/designee reserves the right to close the study site or to terminate the study at any time for any reason at the sole discretion of the Sponsor. Study sites will be closed upon study completion. A study site is considered closed when all required documents and study supplies have been collected and a study-site closure visit has been performed.

The investigator may initiate study-site closure at any time, provided there is reasonable cause and sufficient notice is given in advance of the intended termination.

Reasons for the early closure of a study site by the Sponsor or investigator may include, but are not limited to:

- Failure of the investigator to comply with the protocol, the requirements of the IRB/IEC or local Health Authorities, the Sponsor's procedures, or GCP guidelines
- Inadequate recruitment of participants by the investigator
- Discontinuation of further study intervention development

If the study is prematurely terminated or suspended, the Sponsor shall promptly inform the investigators, the IECs/IRBs, the regulatory authorities, and any contract research organization(s) used in the study of the reason for termination or suspension, as specified by the applicable regulatory requirements. The investigator shall promptly inform the participant and should assure appropriate participant therapy and/or follow-up.

DISSEMINATION OF CLINICAL STUDY DATA

In order to benefit potential study participants, patients, healthcare providers and researchers, and to help BMS honor its commitments to study participants, BMS will make information about clinical research studies and a summary of their results available to the public as per regulatory and BMS requirements. BMS will post study information on local, national or regional databases

in compliance with national and international standards for disclosure. BMS may also voluntarily disclose information to applicable databases.

CLINICAL STUDY REPORT

A Signatory Investigator must be selected to sign the Clinical Study Report (CSR).

For each CSR related to this protocol, the following criteria will be used to select the Signatory Investigator:

- External Principal Investigator designated at protocol development
- National Coordinating Investigator
- Study Steering Committee chair or their designee
- Participant recruitment (eg, among the top quartile of enrollers)
- Involvement in trial design
- Regionalrepresentation (eg, among top quartile of enrollers from a specified region or country)

SCIENTIFIC PUBLICATIONS

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

Scientific publications (such as abstracts, congress podium presentations and posters, and manuscripts) of the study results will be a collaborative effort between the study Sponsor and the external authors. No public presentation or publication of any interim results may be made by any Principal Investigator, sub-investigator, or any other member of the study staff without the prior written consent of the Sponsor.

Authorship of publications at BMS is aligned with the criteria of the International Committee of Medical Journal Editors (ICMJE, www.icmje.org). Authorship selection is based upon significant contributions to the study (ie, ICMJE criterion #1). Authors must meet all 4 ICMJE criteria for authorship:

1) Substantial intellectual contribution to the conception or design of the work; or the acquisition of data (ie, evaluable participants with quality data), analysis, or interpretation of data for the work (eg, problem solving, advice, evaluation, insights and conclusion); AND
2) Drafting the work or revising it critically for important intellectual content; AND
3) Final approval of the version to be published; AND
4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Those who make the most significant contributions, as defined above, will be considered by BMS for authorship of the primary publication. Sub-investigators will generally not be considered for authorship in the primary publication. Geographic representation will also be considered.

Authors will be listed by order of significant contributions (highest to lowest), with the exception of the last author. Authors in first and last position have provided the most significant contributions to the work.

For secondary analyses and related publications, author list and author order may vary from primary to reflect additional contributions.

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 pre-existing medical condition in a clinical investigation participant administered study treatment 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 treatment, whether or not considered related to the study treatment.

Events Meeting the AE Definition

- Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or results from other safety assessments (eg, electrocardiograms, 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/serious adverse event (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 NOT 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

A serious adverse event (SAE) is defined as any untoward medical occurrence that, at any dose:
Results in death.
Is life-threatening (defined as an event in which the participant 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). NOTE: The following hospitalizations are not considered SAEs in Bristol-Myers Squibb (BMS) clinical studies: • 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). • Elective surgery, planned prior to signing consent. • Admissions as per protocol for a planned medical/surgical procedure. • Routine health assessment requiring admission for baseline/trending of health status (eg, routine colonoscopy). • Medical/surgical admission other than to remedy ill health and planned prior to entry into the study. Appropriate documentation is required in these cases. • 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). • Admission for administration of anticancer therapy in the absence of any other SAEs (applies to oncology protocols).
Results in persistent or significant disability/incapacity.
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 participant 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 and 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 9.2.7 for the definition of potential DILI.)

Pregnancy and DILI must follow the same transmission timing and processes to BMS as used for SAEs. (See Section 9.2.5 for reporting pregnancies.)

EVALUATING AES AND SAES

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, evidence, 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 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 the 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 the Sponsor.
- The investigator may change his/her opinion of causality in light of follow-up information and send an SAE follow-up report with the updated causality assessment.
- The causality assessment is one of the criteria used when determining regulatory reporting requirements.

Assessment of Intensity

The investigator will make an assessment of intensity for each AE and SAE reported during the study and assign it to 1 of the following categories:

- Mild: An event that is easily tolerated by the participant, 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.

An event is defined as "serious" when it meets at least 1 of the predefined outcomes as described in the definition of an SAE, NOT when it is rated as severe.

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 treatment 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 treatment, and pregnancies must be reported to BMS (or designee) immediately within 24 hours of awareness of the event.
- SAEs must be recorded on the SAE Report Form.

  The required method for SAE data reporting is through the electronic case report form (eCRF).

  The paper SAE Report Form is intended only as a back-up option when the electronic data capture system is unavailable/not functioning for transmission of the eCRF to BMS (or designee).

  In this case, the paper form is transmitted via email or confirmed facsimile transmission.

  When paper forms are used, the original paper forms are to remain on site.
- Pregnancies must be recorded on paper Pregnancy Surveillance Forms and transmitted via email or confirmed facsimile transmission.

SAE Email Address: [redacted]

SAE Facsimile Number: *Will be provided by local site monitor.*

SAE Telephone Contact (required for SAE and pregnancy reporting): *Will be provided by local site monitor.*

APPENDIX 4 WOMEN OF CHILDBEARING POTENTIAL DEFINITIONS AND METHODS OF CONTRACEPTION

Appendix 4 provides general information and definitions related to Woman of Childbearing Potential and methods of contraception that can be applied to most clinical trials. For information specific to this study regarding acceptable contraception requirements for female and male participants, refer to Section 6.1 of the protocol. Only the contraception methods as described in Section 6.1 are acceptable for this study.

DEFINITIONS

Woman of Childbearing Potential (WOCBP)

A woman is considered fertile following menarche and until becoming postmenopausal 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 participant'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. Suggested guidelines for the duration of the washout periods for HRT types are presented below. 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.

End of Relevant Systemic Exposure

End of relevant systemic exposure is the timepoint where the Investigational Medicinal Product (IMP) or any active major metabolites have decreased to a concentration that is no longer considered to be relevant for human teratogenicity or fetotoxicity. This should be evaluated in context of safety margins from the no-observed-adverse-effect level or the time required for 5 half-lives of the IMP to pass.

METHODS OF CONTRACEPTION

Note: Intravaginal and transdermal combined hormonal contraceptives are not approved by the Health Authority in Japan. Also, progestogen-only hormonal contraceptives are not approved by the Health Authority in Japan.

Local laws and regulations may require use of alternative and/or additional contraception methods.

Highly Effective Contraceptive Methods That Are <u>User Dependent</u> *Failure rate of < 1% per year when used consistently and correctly.*[a]
• Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation and/or implantation. (This method of contraception can only be used by WOCBP participants in studies where hormonal contraception is permitted by the study protocol.)[b] Oral (birth control pills) Intravaginal (rings) Transdermal • Combined (estrogen-and progestogen-containing) hormonal contraception must begin at least 30 days prior to initiation of study therapy.
• Progestogen-only hormonal contraception associated with inhibition of ovulation. (This method of contraception can only be used by WOCBP participants in studies where hormonal contraception is permitted by the study protocol.)[b] Oral Injectable • Progestogen-only hormonal contraception must begin at least 30 days prior to initiation of study therapy.
Highly Effective Methods That Are User Independent
• Implantable progestogen-only hormonal contraception associated with inhibition of ovulation and/or implantation. (This method of contraception can only be used by WOCBP participants in studies where hormonal contraception is permitted by the study protocol.)[b]

• Intrauterine device. • Intrauterine hormone-releasing system (IUS). (This method of contraception can only be used by WOCBP participants in studies where hormonal contraception is permitted by the study protocol.)[b,c] • Bilateral tubal occlusion.
• Vasectomized partner Having 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. A vasectomy is a highly effective contraception method provided that the participant 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. *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 participant.* • Continuous abstinence must begin at least 30 days prior to initiation of study therapy. • It is not necessary to use any other method of contraception when complete abstinence is elected. • WOCBP participants who choose complete abstinence must continue to have pregnancy tests, as specified in Section 2. • Acceptable alternate methods of highly effective contraception must be discussed in the event that the WOCBP participant chooses to forego complete abstinence. • Periodic abstinence (including, but not limited to, calendar, symptothermal, postovulation methods), withdrawal (coitus interruptus), spermicides only, and lactational amenorrhea method (LAM) are not acceptable methods of contraception for this study.
NOTES: [a] Typical use failure rates may differ from failure rates when contraceptive methods are used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for participants 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. For information specific to this study regarding permissibility of hormonal contraception, refer to .Sections 6.1 INCLUSION CRITERIA and 7.7.1 PROHIBITED AND/OR RESTRICTED TREATMENTS of the protocol. [c] IUSs are acceptable methods of contraception in the absence of definitive drug interaction studies when hormone exposures from intrauterine devices do not alter contraception effectiveness. For information specific to this

study regarding permissibility of hormonal contraception, refer to. Sections 6.1 INCLUSION CRITERIA and 7.7.1 PROHIBITED AND/OR RESTRICTED TREATMENTS of the protocol.

Less Than Highly Effective Contraceptive Methods That Are User Dependent *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. • Diaphragm with spermicide. • Cervical cap with spermicide. • Vaginal sponge with spermicide. • Progestogen-only oral hormonal contraception, where inhibition of ovulation is not the primary mechanism of action. (This method of contraception cannot be used by WOCBP participants in studies where hormonal contraception is prohibited.)
Unacceptable Methods of Contraception
• Periodic abstinence (calendar, symptothermal, postovulation methods). • Withdrawal (coitus interruptus). • Spermicide only. • LAM.

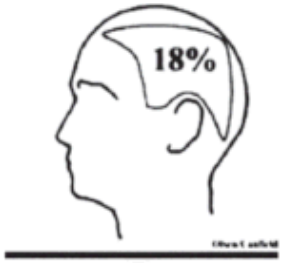
COLLECTION OF PREGNANCY INFORMATION

Guidance for collection of pregnancy information and outcome of pregnancy on the Pregnancy Surveillance Form is provided in Section 9.2.5 and Appendix 3.

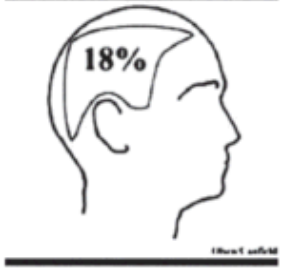
APPENDIX 5 SEVERITY OF ALOPECIA TOOL (SALT)

The Severity of Alopecia Tool (SALT) score is a quantitative rating scale for measuring the severity of AA based on the amount of terminal hair loss in each of the 4 quadrants of the scalp; back region, top region, left and right regions of the scalp (see Figure 1). To calculate a SALT score, the degree of scalp hair loss, as a percentage of each scalp region affected, is determined. Each region is multiplied by its respective weighting factor (percentage surface area of the scalp in that area), in order to achieve a subtotal for each region. The SALT score is the sum of the scalp hair loss in each area (sum of the subtotals).

Percentage surface area of the scalp for each of the four regions.[1]



Left Region of Scalp



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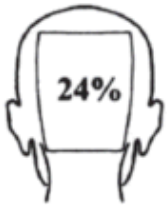
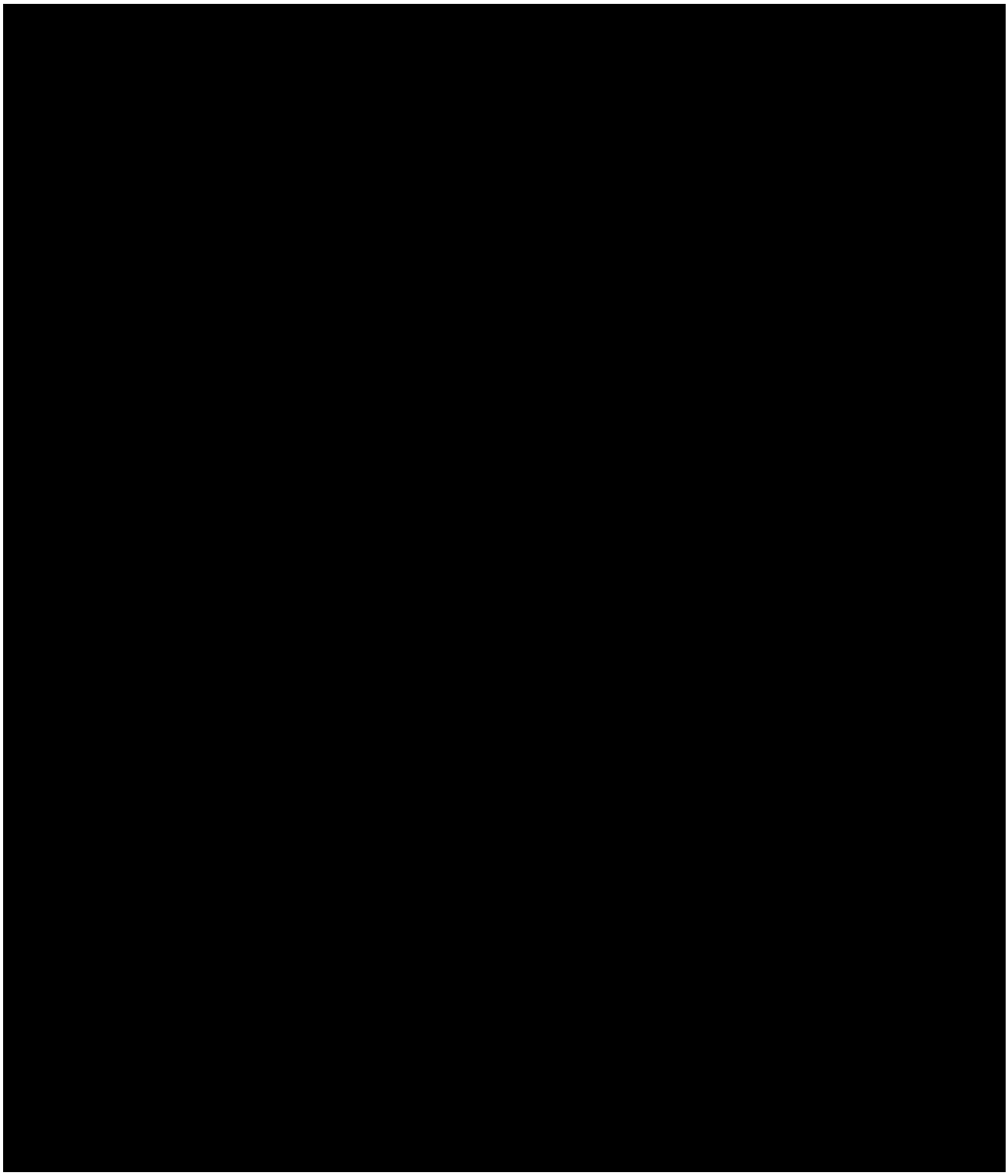


Back Region of Scalp

[1] J Am Acad Dermatol Sep 2004 Olsen et al



APPENDIX 9 INTERPRETATION OF HEPATITIS SEROLOGIC TEST RESULTS (JAPAN SPECIFIC)

Hepatitis C Virus

Testing for hepatitis C virus (HCV) is a 2-step process: (i) anti-HCV antibody and (ii) HCV ribonucleic acid (RNA).

Participants with a negative result for anti-HCV antibody may be eligible for the study.

Participants with a positive or indeterminate result for anti-HCV antibody require additional HCV RNA testing to determine eligibility. Participants with negative or undetectable HCV RNA may be eligible for the study. Participants with positive or detectable HCV RNA have HCV infection, will be excluded from the study, and should be referred for appropriate assessment and consideration for treatment.

Participants who were previously treated with an approved treatment regimen for HCV infection may be eligible to participate in the study provided they achieve a Week 24 sustained virologic response (undetectable HCV RNA 24 weeks after completion of a full course of an approved treatment regimen for HCV infection).

Hepatitis B Serologic Test Results

As study treatment in this study is expected to demonstrate immunosuppressive effects, it is imperative to carefully evaluate and exclude participants with potentially active hepatitis B virus (HBV) infection. For this reason, in order to fully evaluate a participant's eligibility for enrollment, the exclusion criterion 2) f) (see Section 6.2) requires interpretation of data from 3 standard tests for HBV (ie, measurement of hepatitis B surface antigen [HBsAg], hepatitis B core antibody [HBcAb], and hepatitis B surface antibody [HBsAb]).

Eligibility for enrollment should be assessed as follows:

- HBsAg positive participant is to be excluded from the study (acute or chronic infection).
- In a participant that is HBsAg negative and HBcAb positive and/or HBsAb positive (HBV DNA is required)
    - If HBV DNA is ≥20 IU/ml, participant is to be excluded from the study
    - If HBV DNA is <20 IU/ml, participant may be eligible; see below

Please refer to the below "Interpretation of Hepatitis B Serologic Test Results[1] provided by the Department of Health and Human Services, Centers for Disease Control and Prevention.

Interpretation of Hepatitis B Serologic Test Results

Hepatitis B serologic testing involves measurement of several hepatitis B virus (HBV)-specific antigens and antibodies. Different serologic "markers" or combinations of markers are used to identify different phases of HBV infection and to determine whether a patient has acute or chronic HBV infection, is immune to HBV as a result of prior infection or vaccination, or is susceptible to infection.

HBsAg **anti-HBc** **anti-HBs**	negative negative negative	Susceptible
HBsAg **anti-HBc** **anti-HBs**	negative positive positive	Immune due to natural infection
HBsAg **anti-HBc** **anti-HBs**	negative negative positive	Immune due to hepatitis B vaccination
HBsAg **anti-HBc** **IgM anti-HBc** **anti-HBs**	positive positive positive negative	Acutely infected
HBsAg **anti-HBc** **IgM anti-HBc** **anti-HBs**	positive positive negative negative	Chronically infected
HBsAg **anti-HBc** **anti-HBs**	negative positive negative	Interpretation unclear; four possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible 3. "Low level" chronic infection 4. Resolving acute infection

Adapted from: A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. Part I: Immunization of Infants, Children, and Adolescents. MMWR 2005;54(No. RR-16).

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Division of Viral Hepatitis

CDC

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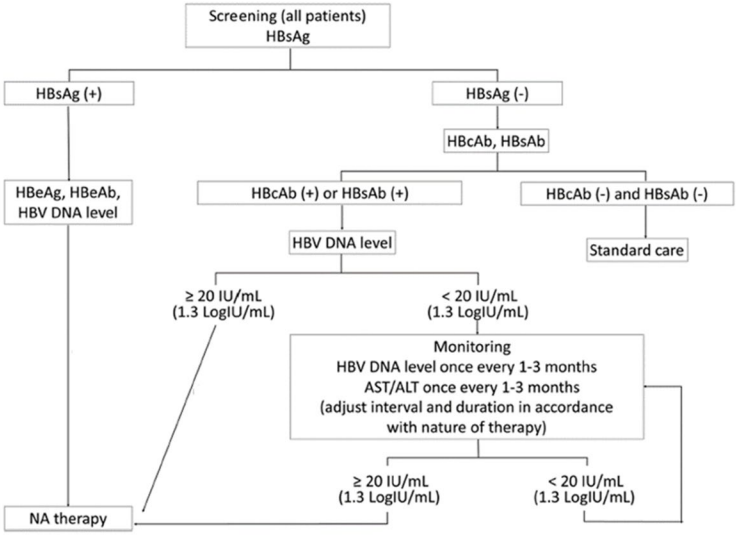
- **Hepatitis B surface antigen (HBsAg):** A protein on the surface of hepatitis B virus; it can be detected in high levels in serum during acute or chronic hepatitis B virus infection. The presence of HBsAg indicates that the person is infectious. The body normally produces antibodies to HBsAg as part of the normal immune response to infection. HBsAg is the antigen used to make hepatitis B vaccine.
- **Hepatitis B surface antibody (anti-HBs):** The presence of anti-HBs is generally interpreted as indicating recovery and immunity from hepatitis B virus infection. Anti-HBs also develops in a person who has been successfully vaccinated against hepatitis B.
- **Total hepatitis B core antibody (anti-HBc):** Appears at the onset of symptoms in acute hepatitis B and persists for life. The presence of anti-HBc indicates previous or ongoing infection with hepatitis B virus in an undefined time frame.
- **IgM antibody to hepatitis B core antigen (IgM anti-HBc):** Positivity indicates recent infection with hepatitis B virus (≤6 mos). Its presence indicates acute infection.

For Japan

Participants who are HBsAg positive will be excluded from the study. Participants who are HBsAg negative but positive for HBsAb and/or HBcAb will perform the quantitative HBV deoxyribonucleic acid (DNA) test to determine their eligibility to participate. Participants with detectable HBV DNA levels at screening, as defined per the local guidelines, are to be excluded. Participants with a negative HBsAg, but a positive HBcAb and/or HBsAb may be randomized if HBV DNA levels are undetectable during Screening (see chart below[2]). These participants will be followed with HBV DNA testing and review of liver chemistries throughout their participation in the study.

During the treatment and follow-up periods, participants in this subgroup will have HBV DNA tested every 4 weeks, up to and including the Week 32 study visit. Starting with Week 40, Testing should occur every 4 or 8 weeks, at the discretion of the investigator, through the end of the study.

If participants in this subgroup have detectable HBV DNA levels, which are defined per the local guidelines, at any time, they must permanently discontinue study treatment; the investigator should consider referring them for appropriate specialty care and follow-up. Participants should continue in the study as described in Section 8.1.



Adapted from Japan Society of Hepatology Guidelines for the Management of Hepatitis B Virus Infection: 2019 update.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; DNA, deoxyribonucleic acid; HBcAb, hepatitis B core antibody; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; NA, nucleoside/nucleotide analogues.

REFERENCES:

1. Interpretation of hepatitis B serologic test results. Centers for Disease Control and Prevention. Accessed 21-Jul-2022. https://www.cdc.gov/hepatitis/hbv/pdfs/serologicchartv8.pdf.

2. Drafting Committee for Hepatitis Management Guidelines, the Japan Society of Hepatology. Japan Society of Hepatology Guidelines for the Management of Hepatitis B Virus Infection: 2019 update. Hepatol Res 2020;50:892-923.

APPENDIX 10 PROTOCOL AMENDMENT SUMMARY OF CHANGE HISTORY

Overall Rationale for the Protocol Amendment 01, 24-Mar-2022

The primary reason for Protocol Amendment 01 is to refine the endpoints based on recently available external data.

Additional revisions include the addition of a summary of the completed Phase 3 psoriasis deucravacitinib trials; updates to the background section based on new compounds in development; update of the Protocol Summary to align with respective changes to the protocol; updated study contacts on the Title Page.

Minor formatting and typographical corrections as well as updates to align with the current BMS guidance have been made and have not been summarized.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01

Section Number & Title	Description of Change	Brief Rationale
Global	Changed BMS-986165 to deucravacitinib.	To update the protocol with the approved generic name.
Table 2-1: Screening Procedural Outline (IM011134)	Updated text in the Notes column.	To provide clarity and further guidance on screening procedures.
Table 2-1: Screening Procedural Outline (IM011134) [redacted]	[redacted]	[redacted]
Table 2-2: On Treatment Procedural Outline (IM011134): Week 0 through Week 24 Table 2-3: On Treatment (Week 28 through Week 52) and Post-Treatment Follow-Up (Week 56) Procedural Outline (IM011134) Table 4-1: Objectives and Endpoints Section 9: Study Assessments and Procedures Section 9.1: Efficacy Assessments [redacted]	[redacted]	

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
Table 2-2: On Treatment Procedural Outline (IM011134): Week 0 through Week 24 Table 2-3: On Treatment (Week 28 through Week 52) and Post-Treatment Follow-Up (Week 56) Procedural Outline (IM011134) Section 9: Study Assessments and Procedures	• Added note to Dispense Study Intervention row to dispense after all visit procedures have been performed. [redacted] • Added footnote "a" to Week 0 stating that all assessments and sample collections should occur before study intervention administration. • Removed Body Weight assessments from Week 28 and Week 56 and removed Urinalysis from Week 56. [redacted]	• To ensure that participants do not take study intervention prior to completion of assessments. [redacted] • To ensure baseline samples are collected and assessments are performed prior to dosing. • To reduce burden on site and participant. [redacted]
Section 3: Introduction	Added information on compounds currently in development which have demonstrated potential benefit in the treatment of alopecia areata.	To include information not available at the time of the final protocol.
Section 3.1: Study Rationale	Updated text with pre-clinical animal study of a deucravacitinib analogue, and most recent efficacy and safety data from Phase 3 studies.	To further support development of deucravacitinib for this indication.
Section 3.2: Background	Added efficacy and safety information from 2 Phase 3 trials of deucravacitinib in participants with moderate-to-severe plaque psoriasis.	At time of final protocol, the 2 Phase 3 studies were ongoing and data were not yet available.
Section 3.3: Benefit/Risk Assessment	• Added dosing information from first-in-human study for safety and tolerability of deucravacitinib daily dose of 6 mg. • Updated text to include coronavirus disease 2019 (COVID-19) as a potential risk and information related to guidance for investigators in relation to COVID-19.	• To support the benefit/risk assessment. • To provide a summary of benefit/risk information in the context of the COVID-19 pandemic.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
Table 4-1: Objectives and Endpoints	• Updated wording of objectives from assess to evaluate. • Moved assessment of safety from a secondary objective to a primary objective. 	• To refine primary and secondary endpoints. • Safety is a key assessment for this new deucravacitinib indication.  • To align language with other deucravacitinib protocols.
Section 5.1: Overall Design Section 10.4.2 Primary Efficacy Analyses	Updated the stratification for randomization of current disease duration from ≤ 3.5 years and > 3.5 years to < 4 years to ≥ 4 years.	To align with competitor trials on disease duration for stratification.
[redacted]		
Section 6.1: Inclusion Criteria	Added requirement of a negative highly sensitive serum pregnancy test at Screening Visit to criterion 4) a).	To clarify criterion for pregnancy testing at Screening.
Section 6.2: Exclusion Criteria	• Added note to criterion 5) e) that low-potency topical corticosteroids are permitted but cannot be applied to the scalp. • Added criterion 9) e) regarding inability to tolerate oral medication.	• To clarify guidance for topical steroid application. • To ensure participant is able to tolerate oral medication before participating in the study.
Section 6.3.3: Activity	Added that strenuous physical activity is activity that is more strenuous than the participant's usual daily activity.	To further clarify the restriction of strenuous physical activity.
Section 7.2: Method of Study Intervention Assignment	Added statement that participants initially randomized to receive deucravacitinib will remain on their assigned study intervention, in a blinded manner, until Week 52.	To clarify guidance on study intervention assignment and blinding until Week 52.
Section 7.3: Blinding	Modified text regarding blinding of study intervention, result of Week	To clarify when the unblinded analysis will occur and who will remain blinded.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
	24 database lock analysis, and unblinding.	
Section 7.7: Concomitant Therapy	Moved text from Section 7.7.1: Prohibited and/or Restricted Treatments related to systemic corticosteroid medication use when and discussions with the Medical Monitor should occur.	To clarify guidance on the use of systemic corticosteroid medications in the concomitant therapy section.
Section 7.7.1: Prohibited and/or Restricted Treatments	Added Janus kinase (JAK) inhibitors.	To clarify that any use of JAK inhibitors is prohibited.
Section 7.7.2: Permitted Vaccines (Including COVID-19 Vaccine)	Added information on COVID-19 vaccines and investigational vaccines.	To provide information for permitted vaccines on the study.
Section 8.1.1: Temporary Interruption	Added confirmed or suspected cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).	To provide guidance for temporary discontinuation of study intervention in the context of the COVID-19 pandemic.
Section 9.1: Efficacy Assessments	Added training requirement for evaluators.	To ensure consistency and reduce variability of assessments.
Section 9.1: Efficacy Assessments [redacted]	[redacted]	
[redacted]		
Section 9.2.1: Adverse Events of Interest	Added information on adverse events of interest (AEIs).	To better characterize and understand AEIs related to deucravacitinib.
Section 9.2.2: Time Period and Frequency for Collecting AE and SAE Information	Added statement regarding reporting of adverse events (AEs) and serious adverse events (SAEs) related to SARS-CoV-2 or COVID-19 infection.	To align with current guidance regarding reporting of AEs, SAEs, and those related to SARS-CoV-2 infection.
[redacted]		

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
Section 10.1: Statistical Hypothesis	Added section.	To articulate the primary study hypotheses to reflect there are 2 dosages to be compared with placebo.
Section 10.2: Sample Size Determination	• Updated text for sample size and overall power of the study. • Updated text for TYK2/JAK 1 and JAK 3 inhibitors.	• To restate power calculations to address multiplicity by Bonferroni procedure. • For clarification on JAK inhibitor analysis.
Section 10.3: Analysis Sets	• Updated description text for full analysis set and randomized populations. • Removed as treated population. • Added safety population.	For alignment across the protocol.
Section 10.4: Statistical Analysis	Updated section with information on general considerations, primary efficacy endpoints, secondary efficacy endpoints, [redacted] and other safety analyses.	To clarify statistical analyses for all efficacy endpoints (primary, secondary, [redacted]).