J&J Innovative Medicine

Statistical Analysis Plan

A Phase 3 Multicenter, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Participants with Plaque Psoriasis involving Special Areas

(Protocol 77242113PSO3003; Phase 3)
AMENDMENT 1

JNJ-77242113

Status:	Approved
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Compliance: The study described in this report was performed according to the principles of Good Clinical Practice (GCP).

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LIST OF ABBREVIATIONS

ADA	anti-drug antibody
AE	adverse event
ALT	alanine aminotransferase
AMER	North America and South America region
APAC	Asia-Pacific region
ANCOVA	analysis of covariance
AST	aspartate aminotransferase
ATC	anatomic and therapeutic class
EQ-VAS	EuroQol visual analogue scale
EQ-5D	EuroQol-5 Dimension
EQ-5D-5L	EuroQol-5 Dimension 5-level
BMI	body mass index
BSA	body surface area
CDLQI	Children's Dermatology Life Quality Index
CI	confidence interval
CMH	Cochran-Mantel-Haenszel
CRF	case report form
CSR	clinical study report
C-SSRS	Columbia-Suicide Severity Rating Scale
CTCAE	Common Terminology Criteria for Adverse Events
CV	coefficient of variation
DBL	Database lock
DMC	Data Monitoring Committee
ECG	electrocardiogram
eCRF	electronic case report form
EU	European Union region
FAS	full analysis set
FCS	fully conditional specification
hf-PGA	Physician's Global Assessment of hands and/or feet
GenPs-SFQ	Genital Psoriasis Sexual Frequency Questionnaire
ICH	International Conference on Harmonisation
IQ	interquartile
IWRS	interactive web response system
LLOQ	lower limit of quantification
LS	least square
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed-effect Model Repeated Measure
mNAPSI	modified Nail Psoriasis Severity Index
NAb	neutralizing antibodies
NRS	Numerical Rating Scale
PASI	Psoriasis Area Severity Index
PD	pharmacodynamic(s)
PGA	Physician Global Assessment
PHQ-9	Patient Health Questionnaire-9
PK	pharmacokinetic(s)
PP	per protocol
PRO	patient reported outcome(s)
PROMIS-25	Patient-Reported Outcomes Measurement Information System-25
PROMIS-29	Patient-Reported Outcomes Measurement Information System-29

PsA	psoriatic arthritis
ppQLI	palmoplantar Quality of Life Instrument
PSSD	Psoriasis Symptom and Sign Diary
QTL	quality tolerance limit
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
sPGA-G	static Physician's Global Assessment of Genitalia
ss-IGA	scalp-specific Investigator Global Assessment
TEAE	treatment-emergent adverse event
US NCI	United States National Cancer Institute
TSQM-E	Treatment Satisfaction Questionnaire for Medication-Effectiveness
VAS	visual analog scale
WHO	World Health Organization
WHO-DD	World Health Organization Drug Dictionary

SUMMARY OF CHANGES IN AMENDMENT 1

The statistical analysis plan (SAP) was amended to implement the following modifications to the original SAP:

The following modifications were made based on the regulatory comments:

- Removed hypothetical estimand for the primary endpoint and key secondary endpoints.
- Added two sensitivity analyses (one using multiple imputation and the other one using tipping point analysis) to the primary estimand for the primary endpoint and main estimands for select key secondary endpoints.
- Added subgroup analysis based on ethnicity (Hispanic/Latino or Not Hispanic/Latino, Not Reported, and Unknown).

In addition, the following modifications were also made:

- Clarified the definition of baseline.
- Removed the geographic region (AMER, EU, APAC) as a stratification factor in CMH tests and the calculation of treatment difference (95% CI) for the primary endpoint. This was also done for analyses of some key secondary endpoints. These changes were due to small sample sizes for some strata with 3 stratification variables (geographic region, special area involvement and weight).
- Added the per protocol analyses for select key secondary endpoints.
- Clarified when an adverse event is considered treatment emergent by adding a 4-week window after last dose or treatment discontinuation.
- Clarified the calculations for PSSD symptom score and sign score.
- Clarified ECG analyses.
- Added subgroup analyses for IGA (overall) responses (IGA 0, IGA 0 or 1 and at least a 2-grade improvement from baseline) at Week 16 based on baseline special area severity.
- Noted that multiplicity adjusted p-values will be provided.
- Minor grammatical, formatting, or spelling changes were made.

1. INTRODUCTION

77242113PSO3003 is a randomized, double-blind, and placebo-controlled, parallel-group, multicenter, interventional study in participants with plaque psoriasis involving special areas (scalp, genital, and/or palmoplantar).

This Statistical Analysis Plan (SAP) contains definitions of analysis sets, derived variables, and statistical methods for all planned analyses for 77242113PSO3003 study.

1.1. Objectives, Endpoints and Estimands

Objectives and Endpoints

Objectives	Endpoints
Primary	
• To evaluate the efficacy of JNJ-77242113 in participants with plaque psoriasis involving special areas	• IGA (overall) score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16.
Secondary	
Key Secondary • To evaluate the general psoriasis and special area psoriasis efficacy of JNJ-77242113 in participants with plaque psoriasis involving special areas	• ss-IGA score 0 or 1 at Week 16. • PSSI 90 at Week 16. • sPGA-G score of 0 or 1 at Week 16. • hf-PGA score of 0 or 1 at Week 16. • IGA (overall) score of 0 at Week 16.
• To evaluate the effect of JNJ-77242113 on PROs in participants with plaque psoriasis involving special areas	• PSSD symptom score of 0 at Week 16. • ≥4-point improvement from baseline in PSSD Itch score at Week 16. • GenPs-SFQ item 2 score of 0 or 1 at Week 16. • ≥4-point improvement from baseline in Scalp Itch NRS score at Week 16. • ≥4-point improvement from baseline in GPSS Genital Itch NRS score (Item 1 from the GPSS) at Week 16.
Other Secondary • To assess the safety and tolerability of JNJ-77242113 in participants with plaque psoriasis involving special areas	• Frequency and type of AEs and SAEs.
• To further evaluate the effect of JNJ-77242113 in participants with plaque psoriasis involving special areas	• PASI 90 at Week 16. • PASI 75 at Week 16. • Change from baseline in PASI at Week 16.

Objectives	Endpoints
	• Percent change from baseline in PASI at Week 16. • Change from baseline in BSA at Week 16. • Percent change from baseline in mNAPSI score at Week 16. • f-PGA score of 0 or 1 at Week 16.
• To further evaluate the effect of JNJ-77242113 on PROs in participants with plaque psoriasis involving special areas	• PSSD symptom score of 0 at Week 8. • Change from baseline in PSSD symptom score at Week 16. • ≥4-point improvement from baseline in PSSD Itch score at Week 4. • Change from baseline in PSSD sign score at Week 16. • PSSD sign score of 0 at Week 16. • DLQI score of 0 or 1 at Week 16. • CDLQI score of 0 or 1 at Week 16. • Change from baseline in the domain scores of the PROMIS-29 score at Week 16. • Change from baseline in the domain scores of the PROMIS-25 pediatric score at Week 16. • Change from baseline in ppQLI score at Week 16. • Change from baseline in GPSS total score at Week 16.
Exploratory	
• To further assess the safety and tolerability of JNJ-77242113 in participants with plaque psoriasis involving special areas	• Frequency and type of related AEs and AEs leading to discontinuation of study intervention. • Laboratory parameters and change from baseline in laboratory parameters (hematology and chemistry).
• To further evaluate special areas psoriasis efficacy of JNJ-77242113	Endpoints will be based on the following assessments: • IGA, PASI, BSA, ss-IGA, PSSI, sPGA-G, hf-PGA, f-PGA, mNAPSI,
• To further evaluate the effect of JNJ-77242113 on PROs in participants with plaque psoriasis involving special areas	Endpoints will be based on the following assessments: • PSSD, DLQI/CDLQI, Scalp Itch NRS, GPSS, GenPs-SFQ, ppQLI, PROMIS-29/

Objectives	Endpoints
	PROMIS-25, TSQME, EQ-5D-5L, PsA Pain assessment, PsA Disease assessment,
• To evaluate the PK and immunogenicity of JNJ-77242113 and to explore the E-R relationship of JNJ-77242113 in participants with plaque psoriasis involving special areas	• JNJ-77242113 PK parameters. • The relationship between PK parameters and efficacy. • The incidence of ADAs to JNJ-77242113.
• To explore biomarkers in participants with plaque psoriasis involving special areas	• Change from baseline in cellular and molecular biomarkers in skin and blood.

1.2. Study Design

This is a randomized, double-blind, and placebo-controlled, parallel-group, multicenter, interventional study in participants with plaque psoriasis involving special areas (scalp, genital, and/or palmoplantar).

A target of 300 participants will be enrolled in this study in a 2:1 randomization ratio to JNJ-77242113 200 mg once daily or placebo. Treatment groups will be stratified by special area involvement reported in IWRS (with the order of baseline hf-PGA ≥3, sPGA-G ≥3, or ss-IGA ≥3), geographic region (AMER, EU, and APAC), and BSA category reported in IWRS (<10%, ≥10%).

- JNJ77242113 200 mg once daily
  - Week 0 to Week 156: Participants will receive JNJ-77242113 200 mg once daily through Week 156.
- Placebo to JNJ77242113 200 mg once daily
  - Week 0 to Week 16: Participants will receive placebo once daily through Week 16.
  - Week 16 to Week 156: Participants will cross-over to receive JNJ77242113 200 mg once daily through Week 156.

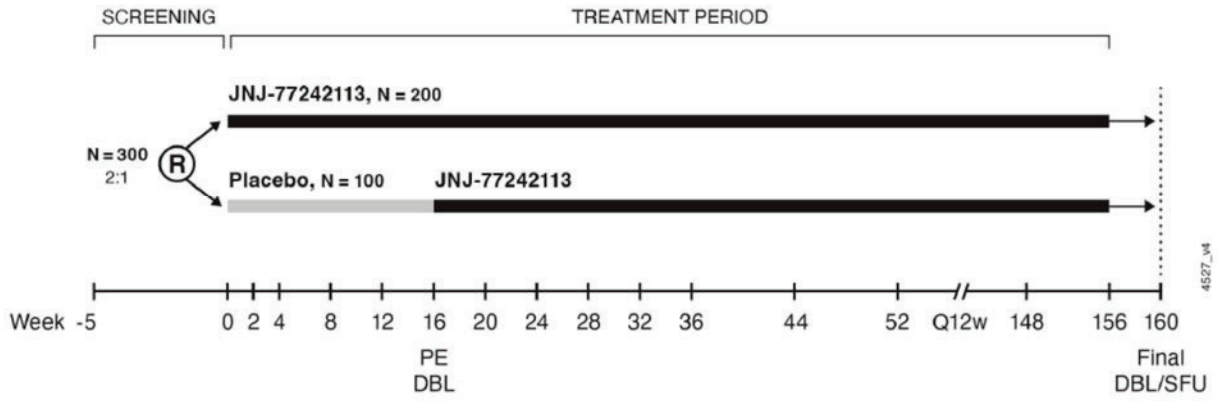
This study includes a 5-week screening period, a 16-week placebo-controlled period, and a 140-week active treatment period. All participants will have a 4-week safety follow-up period after discontinuation of study intervention or after the end of the treatment period. The total duration of this study for each participant is approximately 165 weeks.

The first DBL will occur when all participants (adults and adolescents) complete Week 16 of placebo-controlled period of the study. An additional DBL will occur when all participants (adults and adolescents) complete Week 52 of the study. The final DBL will occur when all participants complete the study. Additional DBLs may occur between Week 52 DBL and the final DBL to support publications or regulatory submissions.

An independent DMC will be commissioned for this study to review the safety data at an ongoing basis.

A diagram of the study design is provided in Figure 1.

Figure 1: Schematic Overview of the Study



DBL=database lock; PE=primary endpoint; Q12w = every 12 weeks; R=randomization; SFU=safety follow-up visit.

2. STATISTICAL HYPOTHESIS

The primary hypothesis is that JNJ-77242113 is superior to placebo in treatment of participants with plaque psoriasis involving special areas (scalp, genital, and/or palmoplantar) as assessed by the proportion of participants achieving an IGA (overall) score of cleared (0) or minimal (1) and a ≥2-grade improvement from baseline at Week 16. If superiority of JNJ-77242113 for the endpoint versus placebo is achieved, the study will be considered positive.

The null hypothesis is that there is no difference between JNJ-77242113 and placebo in the primary endpoint.

2.1. Multiplicity Adjustment

A multiplicity adjustment procedure will be used to control the overall Type I error rate of α=0.05 (2-sided) for the primary and 10 key secondary endpoints. The testing procedure begins with the test of superiority of the JNJ-77242113 group compared with the placebo group in the primary endpoint. Key secondary endpoints will only be tested if the primary endpoint is significant. The testing strategy is devised based on the expected power and relative importance of the endpoints. If the primary endpoint is not significant (ie, p >0.05), all subsequent p-values in the testing hierarchy will be considered nominal. After testing of the primary endpoint, and if p-value is ≤0.05, the testing procedure will continue with superiority tests for the key secondary endpoints.

When the primary endpoint is positive, a truncated Bonferroni-Holm procedure (Holm, 1979) as shown in Figure 2 will be applied to the key secondary endpoints at Week 16 in Tier 1. In this truncated version, if ss-IGA 0/1 or sPGA-G 0/1 is significant at their assigned alpha levels, 1/3 of the assigned alpha level will be passed down to the endpoints in Tier 2.

The Bonferroni-Holm procedure will be used to test endpoints in Tier 2 at an alpha level propagated from Tier 1. If any test within this tier is not significant, the other tests in the same tier

could still be declared significant if they meet the Bonferroni-Holm's thresholds, but the formal testing will stop and all p-values from the endpoints in subsequent tiers will be considered nominal. If all tests in Tier 2 are significant based on Bonferroni-Holm's procedure, then testing will continue to the remaining endpoints in a fixed sequence ordered below. If GenPs-SFQ is significant at its assigned alpha level, its assigned alpha level will be passed back with equal weights to the Tier 1 endpoints.

The endpoints within each tier are listed below; see Figure 2 below for an illustration of the full testing procedure.

Tier 1: truncated Bonferroni-Holm procedure

- ss-IGA score of 0 or 1 at Week 16
- hf-PGA score of 0 or 1 at Week 16
- sPGA-G of score of 0 or 1 at Week 16

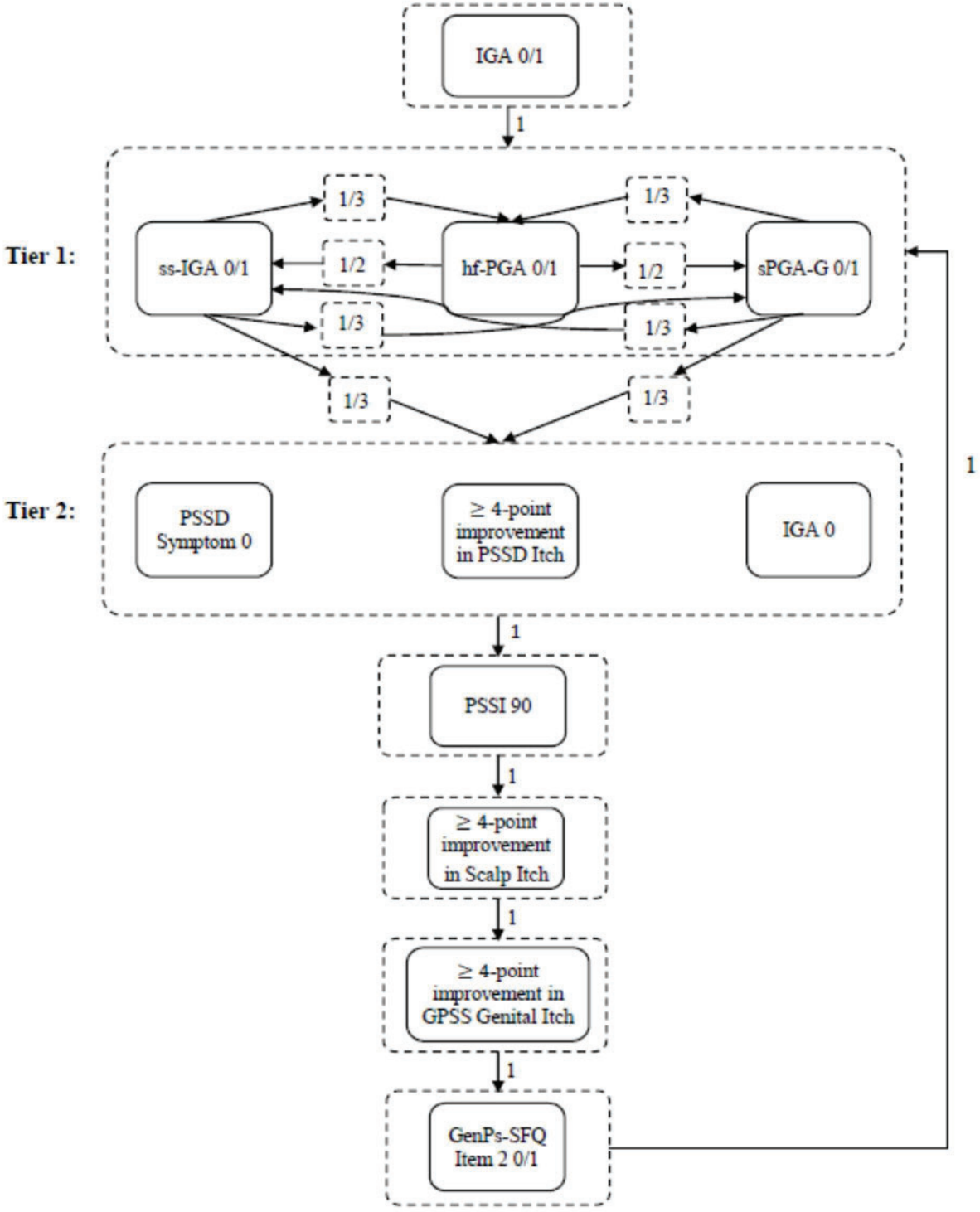
Tier 2: Bonferroni-Holm procedure

- PSSD symptom score of 0 at Week 16
- ≥4-point improvement from baseline in PSSD Itch score at Week 16
- IGA (overall) score of 0 at Week 16

Remaining endpoints will be tested in a fixed sequential order as follows:

- PSSI 90 at Week 16
- ≥4-point improvement from baseline in Scalp Itch NRS score at Week 16
- ≥4-point improvement from baseline in GPSS Genital Itch NRS score (Item 1 from the GPSS) at Week 16
- GenPs-SFQ item 2 score of 0 or 1 at Week 16

Figure 2: Testing procedure for the primary endpoint and key secondary endpoints



The study will be considered successful if the test for the primary endpoint is positive. For all key secondary endpoints specified above, both multiplicity-adjusted and nominal p-values will be provided. Statistical significance will be claimed if the adjusted p-value is ≤0.05. No multiplicity adjustments will be made for the other secondary endpoints and exploratory endpoints. These statistical tests will be performed at the 2-sided 0.05 significance level. Nominal p-values will be presented.

3. ANALYSIS SETS

For purposes of analysis, the following analysis sets are defined in Table 1:

Table 1: Definition of Analysis Sets

Analysis Sets	Description
Enrolled	All participants who signed the ICF
Randomized	All participants who were randomized at Week 0 in the study
Full Analysis Set (FAS)	All participants who were randomized at Week 0 in the study
Per Protocol (PP)	The per protocol analysis set (PP) includes a subset of participants in the full analysis set (FAS) who were in general compliance with the protocol. Compliance is defined as participants in FAS and meet the following criteria: • Had a total BSA ≥1% at the screening and baseline visit, and had an IGA (overall) score ≥2 at the screening and baseline visit And at least one of the following: o ss-IGA score ≥3 at screening and baseline, and/or o sPGA-G ≥3 at screening and baseline, and/or o hf-PGA score ≥3 at screening and baseline. • Had an overall compliance of study treatment at least 80% and ≤120% prior to Week 16. Participants with intercurrent events 1 and 2 (Section 4.2.2.1) will be included in the per protocol analysis set.
Safety Analysis Set	All randomized participants who took at least 1 dose of study intervention
PK Analysis Set	All randomized participants who received at least 1 dose of JNJ-77242113 and had at least 1 valid blood sample drawn for PK analysis after their first dose of JNJ77242113
Immunogenicity Analysis Set	All randomized participants who received at least 1 dose of JNJ-77242113 and who had at least 1 sample obtained after the first dose of JNJ-77242113 for the detection of antibodies to JNJ-77242113

4. STATISTICAL ANALYSES

4.1. General Considerations

Unless specified otherwise, efficacy data summaries will be provided by intervention group for the FAS. Data primarily will be summarized using descriptive statistics. Continuous variables will be summarized using the number of observations, mean, SD, median, interquartile range, minimum and maximum, as appropriate. Categorical values will be summarized using the number of observations and percentages as appropriate. In addition, graphical data displays (eg, line plots) and participant listings may also be used to summarize/present the data.

For binary endpoints, treatment comparisons will be performed using a CMH test stratified by special area involvement (baseline hf-PGA ≥3, sPGA-G ≥3, or ss-IGA ≥3), geographic region (AMER, EU, and APAC), and BSA category (<10%, ≥10%), if applicable. For endpoints related to special area, special area involvement will not be included in the CMH test as a stratification factor. In case of rare events for binary endpoints, Fisher's exact test will be used. For repeated measure continuous endpoints, treatment comparisons will be performed using a MMRM model. The MMRM will include treatment, special area involvement, geographic region (AMER, EU, APAC), BSA category and baseline value, as explanatory factors. The MMRM model will also

include visit, treatment group by visit interaction, and baseline value by visit interaction as additional explanatory factors. An unrestricted (UN) variance-covariance matrix for repeated measures within a participant will be used. If the model with unstructured covariance structure does not converge, alternative covariance structures will be tried in the following order, with the first structure that converges being used in the analysis: heterogeneous Toeplitz, standard Toeplitz, and autoregressive of order 1. For endpoints related to special areas, the MMRM will not include special area involvement as an explanatory factor.

The LS mean estimates and their corresponding 95% CI will be provided at each timepoint. In addition, the estimates of LS mean difference and 95% CIs between treatment groups will be provided. Analysis of covariance will be used to analyze some continuous endpoints when appropriate. The ANCOVA will include treatment group, baseline value, special area involvement, geographic region, and BSA category. The LS mean estimates and their corresponding 95% CI will be provided. In addition, LS mean difference and 95% CIs between treatment groups will be provided.

In general, all statistical tests will be performed at a significance level of 0.05 (2-sided) unless otherwise specified. Multiplicity adjustment procedure will be used to control the overall Type I error rate for the primary and key secondary endpoints (section 2.1). No adjustments for multiple comparisons will be made for other secondary endpoints and exploratory endpoints. Nominal p-values for other secondary endpoints and exploratory endpoints will be reported but should not be used to infer statistical significance.

The baseline measurement for efficacy endpoints is defined as the closest measurement taken prior to or on the first study agent administration date. The baseline measurement for other endpoints including safety, PK and immunogenicity is defined as the closest measurement taken prior to the time of the first study agent administration.

4.1.1. Analysis Visit Windows

Unless otherwise specified, nominal visits will be used for all by visit analyses. The study visits scheduled after randomization should occur at the time delineated in the Schedule of Activities of the protocol.

4.1.2. Reference Date, Study Day and Relative Day

The Reference Date is the date of the first study agent administration. If the date of the first study agent administration is missing or the first study agent administration is not done, then the Reference Date equals the corresponding visit date (eg, Week 0 visit date). If the corresponding visit date is also missing, then the Reference Date equals the randomization date. Study day is defined as the number of days from the study reference date to the event/visit date. It will be calculated as follows:

- If the event/assessment occurs on or after the reference date, then study day = event/assessment date – reference date + 1.

- If the event/assessment occurs before the reference date, then study day = event/assessment date – reference date.

Hence, the day of reference date is Study Day 1; the previous day is Study Day -1.

4.1.3. Change and Percent Change from Baseline

The change from baseline is calculated as the post baseline value minus the baseline value.

Change from Baseline = Post Baseline Value – Baseline Value

Percent Change from Baseline = $\frac{(Post\ Baseline\ Value - Baseline\ Value)}{Baseline\ Value} X\ 100$

If a higher score indicates more severe disease in efficacy assessments, then a negative change indicates an improvement, and a positive change indicates worsening.

4.2. Primary Endpoint/Estimands and Analysis

4.2.1. Definition of Endpoint

The primary endpoint in this study is achieving IGA (overall) 0 or 1 response at Week 16 as defined in the variable attribute of the primary estimand.

The IGA documents the physician's assessment of the participant's psoriasis status according to the following categories: induration, scaling, and erythema. The participant's psoriasis is assessed as cleared (0), minimal (1), mild (2), moderate (3), or severe (4).

An IGA (overall) 0 or 1 criteria: defined as a participant achieving an IGA (overall) score of cleared (0) or minimal (1), AND at least a 2-grade improvement from baseline.

4.2.2. Estimand

Primary Study Objective: To evaluate the efficacy of JNJ-77242113 compared to placebo at Week 16 in participants with plaque psoriasis involving special areas.

Clinical Question of Interest: For an adult or adolescent patient with plaque psoriasis involving special areas, what would be the expected effect of being assigned JNJ-77242113 on the likelihood of experiencing a treatment response at Week 16?

4.2.2.1. Primary Estimand

The primary estimand, aligned with the above primary objective and clinical question of interest, provides precise descriptions of the treatment effect of interest that are defined by the following 5 attributes.

Treatment condition of interest vs alternative treatment condition:

- Experimental: JNJ-77242113 200 mg QD
- Placebo

Population: Patients ≥12 years of age with plaque psoriasis involving special areas (scalp, genital, and/or palmoplantar).

Variable: Achieving an IGA (overall) score of 0 or 1 response at Week 16, where an IGA (overall) score of 0 or 1 responder is defined as a patient meeting an IGA (overall) 0 or 1 criteria at Week 16 and not experiencing either ICE 1 or ICE 2 (see Table 2).

Intercurrent Events and Corresponding Strategies (Refer to Table 2):

Table 2: Intercurrent Events (ICEs) and Their Corresponding Strategies:

ICEs	Strategy for Addressing Intercurrent Events
1. Discontinuation of treatment due to lack of efficacy, or due to an AE of worsening of psoriasis. 2. Initiation of other medication or therapy that could improve psoriasis (see Appendix 7).	**Composite Strategy:** The occurrence of these ICEs is captured in the variable definition as patients with these ICEs are considered non-responders
3. Discontinuation of treatment for other reasons than ICE 1	**Treatment Policy:** Strategy targeting the effect of treatment assignment, regardless of the occurrence of this ICE.

Note: For patients experiencing multiple ICEs, ICE 2 will override ICE 3 and the composite strategy will be applied.

Population Level Summary: Difference in the proportions between JNJ-77242113 and placebo.

4.2.2.2. Supplementary Estimand (Treatment Policy Estimand):

In this supplementary estimand, the components that change from the definition of the primary estimand are:

Variable: Achieving a response at Week 16 based on a scale will be the same as meeting the defined efficacy criteria, without accounting for ICEs 1 and 2 in the response definition of Primary Estimand's Variable attribute.

In this supplementary estimand, treatment policy strategy will be used to address ICEs 1-3.

Treatment Policy Strategy: Strategy targeting the effect of treatment assignment, regardless of the occurrence of ICEs.

4.2.3. Analysis Methods

4.2.3.1. Main Analytical Approach

Analysis for the primary endpoint will be based on FAS, including data from all randomized participants. Participants will be analyzed based on their assigned intervention group, regardless of the actual intervention received.

According to the primary estimand, participants with ICEs 1-2 before Week 16 will be considered as non-responders for the primary endpoint at Week 16. Participants with ICE 3, observed data after this ICE will be utilized in the analysis. For participants experiencing multiple ICEs, an ICE 2 will override an ICE 3. After accounting for the ICEs for the primary estimand, participants with missing data for the primary endpoint at Week 16 will be considered as non-responders.

In the primary analysis, the proportion of IGA (overall) score of 0 or 1 responders at Week 16 will be summarized by treatment group. To address the primary objective, a 2-sided (α=0.05) CMH chi-square test stratified by special area involvement (baseline hf-PGA ≥3, sPGA-G ≥3, and ss-IGA ≥3) and BSA category (i.e, <10%, ≥10%) will be used for the primary endpoint.

Difference in response rates between the JNJ-77242113 group and the placebo group at Week 16 and their corresponding 95% CIs (using Miettinen-Nurminen method [Miettinen and Nurminen, 1985]) will be calculated adjusting for special area involvement and BSA category using Mantel-Haenszel (MH) weights.

The study will be considered positive if the JNJ-77242113 group is significantly different from the placebo group for the primary endpoint at a 2-sided test with α level of 0.05.

In addition, the proportion of IGA (overall) score of 0 or 1 responders at Week 16 will be summarized by region, country, and investigator site. To evaluate the consistency of the efficacy, subgroup analyses of primary endpoints based on demographics, baseline disease characteristics and previous psoriasis medications and therapies will be performed. The detailed subgroup analyses for the primary endpoint are specified in Section 4.6.6

4.2.3.2. Sensitivity Analysis

To address the robustness of the primary endpoint analysis results, two sensitivity analyses will be performed to assess missing data assumptions.

4.2.3.2.1. Sensitivity Analysis 1

Under the primary estimand, a sensitivity analysis using multiple imputation will be performed. In this sensitivity analysis, after accounting for the ICEs, missing data will then be imputed using multiple imputations (MI) by fully conditional specification (FCS).

More specifically, the missing IGA (overall) score of 0 or 1 responses will be imputed with FCS logistic regression including treatment group, special area involvement, and BSA category, baseline IGA (overall) score, and IGA (overall) 0 or 1 response status through Week 16 in the model with seed = 789 and 500 imputations.

A CMH test stratified by special area involvement, and BSA category will be used to obtain the CMH statistic for each imputed dataset.

The general association test statistic from the CMH test for each imputed dataset will be transformed using the Wilson-Hilferty transformation (Wilson and Hilferty, 1931) to create a more normal distributed statistic:

$$Z = \frac{(CMH)^{(1/3)} - 7/9}{(2/9)^{(1/2)}}.$$

The resulting transformed values will be combined using SAS PROC MIANALYZE to obtain an overall p-value for the CMH test.

The common risk differences and 95% CIs in the primary endpoint will be calculated using Mantel-Haenszel stratum weights and Sato variance estimator (Sato, 1989) adjusting for special area involvement and BSA category for each imputed dataset. The resulting values will be combined to obtain an overall risk difference and 95% CI.

4.2.3.2.2. Sensitivity Analysis 2

Under the primary estimand, another sensitivity analysis will also be performed using a tipping point analysis with Bernoulli draws to impute missing IGA 0 or 1 response status at Week 16 after intercurrent events are accounted for. The tipping point analysis involves the following distinct steps:

1. Some p will be assumed for each treatment group's response rate, which could vary by treatment group, to impute the response status (Yes/No) for participants with a missing response based on a Bernoulli distribution. This will be repeated 200 times with seed = 20240719 to generate 200 multiple imputations.

2. The common risk difference between JNJ77242113 and placebo will be calculated using Mantel-Haenszel stratum weights adjusting for special area involvement and BSA category for each imputed dataset. The resulting values will be combined to obtain an overall risk difference..

3. The results (with a Wilson-Hilferty transformation) from the imputed data sets will then be combined to produce p-value based on Rubin's rule.

The analysis will be repeated for a range of values for p (for example, 0% to 100% in increments of 10%, for the placebo group and the JNJ-77242113 group independently). For this tipping point analysis, the analysis will allow for assumptions about the response rates in the two arms to vary independently; furthermore, it will include scenarios where imputed missing values on JNJ-77242113 group have worse outcomes than missing values on the placebo group.

4.2.3.3. Supplementary Analysis

The analysis specified below for supplementary estimand will be applied to the comparison for the primary endpoint.

4.2.3.3.1. Supplementary Analysis (Treatment Policy Estimand)

The primary endpoint will also be analyzed utilizing the treatment policy estimand. For participants who experienced ICEs 1-3 through Week 16, the analysis will be performed using observed data regardless of intercurrent events. Participants with missing data will be imputed as non-responders. The same CMH test as for the primary estimand will be performed.

4.2.3.4. Per Protocol Analysis

The primary efficacy endpoint will be evaluated for comparison between JNJ-77242113 group and placebo group in the PP population based on the primary estimand. The same data handling rule and analysis method specified in Section 4.2.3.1 will be applied.

4.3. Secondary Endpoints Analyses

4.3.1. Key Secondary Endpoints/Estimands

4.3.1.1. Definition of Endpoints

4.3.1.1.1. Scalp-specific Investigator Global Assessment (ss-IGA)

The ss-IGA instrument is used to evaluate the disease severity of scalp psoriasis. The lesions are assessed in terms of the clinical signs of redness, thickness, and scaliness which are scored as: absence of disease (0), very mild disease (1), mild disease (2), moderate disease (3), and severe disease (4).

Meeting ss-IGA score of 0 or 1 criteria: defined as having an ss-IGA score of absence of disease (0) or very mild disease (1) response.

4.3.1.1.2. Psoriasis Scalp Severity Index (PSSI)

The PSSI is the result of a modified area score with the severity score, which is equivalent to the PASI severity score. Involvement and severity of psoriasis on the PSSI is scored by physicians on a scale from 0 to 72, where 0 = no psoriasis and higher scores indicate more severe disease.

Assessment of extent of scalp psoriasis	
1	<10%
2	10 – 29%
3	30 – 49%
4	50 – 69%
5	70 – 89%
6	90 – 100%
Assessment of clinical symptoms (erythema, induration, and desquamation)	
0	Absent
1	Slight
2	Moderate
3	Severe
4	Severest possible
PSSI score = Sum of scores for erythema, induration, and desquamation × involved area (range 0 – 72)	

Thaçi D, Daiber W, Boehncke WH, Kaufmann R, 2001.

Meeting PSSI 90 criteria: defined as having at least a 90% reduction from baseline in PSSI total score.

4.3.1.1.3. Static Physician's Global Assessment of Genitalia (sPGA-G)

The sPGA-G is a 6-point scale to assess the severity of genital psoriasis at a given time point. The sPGA-G evaluates erythema, plaque elevation, and scale of genital psoriatic lesions. The severity of genital psoriasis is assessed as clear (0), minimal (1), mild (2), moderate (3), severe (4), and very severe (5).

Meeting sPGA-G score of 0 or 1 criteria: defined as having an sPGA-G score of clear (0) or minimal (1).

4.3.1.1.4. Physician's Global Assessment of Hands and/or Feet (hf-PGA)

The severity of hand and foot psoriasis has been assessed in various clinical studies using an hf-PGA instrument. The plaques are scored on a 5-point scale as: clear (0), almost clear (1), mild (2), moderate (3), and severe (4).

Meeting hf-PGA 0 or 1 criteria: defined as having an hf-PGA score of clear (0) or almost clear (1) among participants.

4.3.1.1.5. Investigator's Global Assessment (IGA)

Refer to section 4.2.1 for details.

Meeting IGA (overall) of cleared (0) criteria: defined as having an IGA score of cleared (0) response.

4.3.1.1.6. Psoriasis Symptom and Sign Diary (PSSD)

The PSSD will be utilized in the adult and adolescent populations and includes PRO questionnaires designed to measure the severity of psoriasis symptoms and signs for the assessment of treatment benefit. There are 2 versions of the PSSD: a 24-hour recall version that asks the participant to answer the questions thinking about the last 24 hours through Week 16 visit and a 7-day recall version asking the participant to answer the questions thinking about the last 7 days after Week 16. Both versions of the PSSD are self-administered PRO instruments and include 11 items in total, with 5 items covering symptoms (itch, pain, stinging, burning, and skin tightness) and 6 items covering participant-observable signs (skin dryness, cracking, scaling, shedding or flaking, redness, and bleeding). A 0 to 10 numerical rating scale for severity is used for each item. For both the 24-hour and 7-day recall versions, 2 subscores will be derived each ranging from 0 to 100: the PSSD symptom score and the PSSD sign score. For all scores, a higher score indicates more severe disease.

The calculations of PSSD symptom and sign scores are listed below.

PSSD Item Score (0-10)

a. PSSD 24-hr recall: for each individual item, the response over seven days is averaged into a weekly item score (i.e., 7 days [from day -7 to -1] prior to a visit).

b. PSSD 7-day recall: each individual item response is used as the score.

Symptom Score (0-100)

a. Symptom score includes the following items: itch (Q1), skin tightness (Q4), burning (Q9), stinging (Q10), and pain (Q11).

b. PSSD 24-hr recall: Compute the average of the 5 weekly symptom item scores when at least 3 items are available (≥50% of 5 items). Multiply the average by 10 to convert into 0-100 scoring (0-least severe, 100-most severe).
c. PSSD 7-day recall: Average symptom items when at least 3 items (≥50% of 5 items) on this scale are answered. Multiply the average by 10 to convert into 0-100 scoring (0-least severe, 100-most severe).

Sign Score (0-100)

a. Sign score includes the following items: skin dryness (Q2), cracking (Q3), scaling (Q5), shedding or flaking (Q6), redness (Q7) and bleeding (Q8).

b. PSSD 24-hr recall: Compute the average of the 6 weekly sign item scores when at least 3 items are available (≥50% of 6 items). Multiply the average by 10 to convert into 0-100 scoring (0-least severe, 100-most severe).

c. PSSD 7-day recall: Average sign items when at least 3 items (≥50% of 6 items) on this scale are answered. Multiply the average by 10 to convert into 0-100 scoring (0-least severe, 100-most severe).

For the PSSD 24-hr recall, at least four non-missing days of assessments out of 7 days (either consecutive or nonconsecutive) prior to a specific visit are necessary to derive a weekly score for that visit. For select time points (i.e., baseline and Week 16), if there are less than 4 non-missing days of assessments in the 7-day window, the most recent 4 non-missing days of assessments in the 10-day window prior to that specific visit will be used. If there are less than 4 non-missing days of assessments in the 10-day window for baseline and Week 16, or 7-day window for other visits (weeks 2, 4, 8, 12), data are considered missing for that visit.

Meeting PSSD symptom score of 0 criteria: defined as having a PSSD symptom score of 0.

Meeting PSSD Itch score ≥4-point improvement criteria: defined as having at least a 4-point improvement from baseline in PSSD Itch score.

4.3.1.1.7. Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ)

The GenPs-SFQ will be utilized in the adult population and is a 2-item participant-reported instrument used to assess the impact of genital psoriasis on the frequency of sexual activity in the

last 7 days. Item 1 assesses overall frequency of sexual activity in the last 7 days (none/zero, once, or 2 or more times), and item 2 assesses how frequently genital psoriasis symptoms have limited the frequency of sexual activity in the last 7 days (never [0], rarely [1], sometimes [2], often [3], or always [4]).

GenPs-SFQ data is collected only for adult participants with active genital psoriasis at Week 0, i.e. baseline sPGA-G score >0.

Meeting GenPs-SFQ item 2 score of 0 or 1 criteria: defined as having an GenPs-SFQ item 2 score of never (0) or rarely (1).

4.3.1.1.8. Scalp Itch Numeric Rating Scale (Scalp Itch NRS)

The Scalp Itch NRS is a single item instrument that evaluates the severity of scalp itch in adult and adolescent populations over the past 24 hours. The instrument uses an NRS score ranging from 0 (no scalp itch) to 10 (worst scalp itch imaginable).

Daily diary data through Week 16: For each individual item from daily diary, the response over seven days is averaged into a weekly score (i.e. 7 days [from day -7 to -1] prior to a visit).

For the Scalp Itch NRS 24-hr recall, at least four non-missing days of assessments out of 7 days (either consecutive or nonconsecutive) prior to a specific visit are necessary to derive a weekly score for that visit. For select time points (i.e., baseline and Week 16), if there are less than 4 non-missing days of assessments in the 7-day window, the most recent 4 non-missing days of assessments in the 10-day window prior to that specific visit will be used. If there are less than 4 non-missing days of assessments in 10-day window for baseline and Week 16, or 7-day window for other visits (weeks 2, 4, 8, 12), data are considered missing for that visit.

Data after Week 16: The item response is used as the score.

Meeting ≥4-point improvement in Scalp Itch NRS score criteria: defined as having at least a 4-point improvement from baseline in Scalp Itch NRS score.

4.3.1.1.9. Genital Psoriasis Symptoms Scale (GPSS)

The GPSS is a participant-administered assessment of 8 symptoms: itch, pain, discomfort, stinging, burning, redness, scaling, and cracking. Each respondent is asked to answer the questions based on the psoriasis symptoms in his or her genital area. The overall severity for each individual genital psoriasis symptom is indicated by selecting the number from an NRS of 0 to 10 that best describes the worst level of each symptom in the genital area in the past 24 hours, ranging from 0 (no severity) to 10 (worst imaginable severity).

Item Score (0-10)

Daily diary data through Week 16: For each individual item from daily diary, the response over seven days is averaged into a weekly item score (i.e. 7 days [from day -7 to -1] prior to a visit).

Data after Week 16: Each individual item response is used as the score.

Total Score (0-80)

Daily diary data through Week 16: Total score is derived by summing the weekly item scores**.** If any item score is missing, the GPSS total score will be missing.

Data after Week 16: Total score is derived by summing the item scores. If any item score is missing, the GPSS total score will be missing.

For the GPSS individual item from daily diary with 24-hr recall, at least four non-missing days of assessments out of 7 days (either consecutive or nonconsecutive) prior to a specific visit are necessary to derive a weekly score for that visit. For select time points (i.e., baseline and Week 16), if there are less than 4 non-missing days of assessments in the 7-day window, the most recent 4 non-missing days of assessments in the 10-day window prior to that specific visit will be used. If there are less than 4 non-missing days of assessments in the 10-day window for baseline and Week 16, or 7-day window for other visits (weeks 2, 4, 8, 12), data are considered missing for that visit.

Meeting ≥4-point improvement in GPSS Genital Itch NRS score criteria: defined as having at least a 4-point improvement from baseline in GPSS Genital Itch NRS score (Item 1 from the GPSS).

4.3.1.2. Estimands

4.3.1.2.1. Main Estimands for Key Secondary Endpoints (Sec 1-10)

The main estimands for key secondary endpoints at Week 16 have same attributes as primary estimand, except for attributes of variable and population defined in the below Table 3.

Table 3: List of Variables and Populations for Key Secondary Endpoints.

Estimands	**Variable** **Achieving a response based on:**	**Population**
General Psoriasis and Special Area Psoriasis		
Sec 1	ss-IGA score of 0 or 1 response at Week 16	Patients ≥12 years of age with plaque psoriasis involving special areas (scalp, genital, and/or palmoplantar) and with a baseline ss-IGA score ≥3
Sec 2	PSSI 90 response at Week 16	
Sec 3	sPGA-G score of 0 or 1 response at Week 16	Patients ≥12 years of age with plaque psoriasis involving special areas (scalp, genital, and/or palmoplantar) and with a baseline sPGA-G score ≥3

Sec 4	hf-PGA score of 0 or 1 response at Week 16	Patients ≥12 years of age with plaque psoriasis involving special areas (scalp, genital, and/or palmoplantar) and with a baseline hf-PGA score ≥3
Sec 5	IGA (overall) score of 0 response at Week 16	Same population as the primary estimand specified in Section 4.2.2.1
PROs		
Sec 6	PSSD symptom score of 0 response at Week 16	Patients ≥12 years of age with plaque psoriasis involving special areas (scalp, genital, and/or palmoplantar) and with a baseline PSSD symptom score >0
Sec 7	≥4-point improvement from baseline in PSSD Itch score at Week 16	Patients ≥12 years of age with plaque psoriasis involving special areas (scalp, genital, and/or palmoplantar) and with a baseline PSSD Itch score ≥4
Sec 8	GenPs-SFQ item 2 score of 0 or 1 response at Week 16	Adult patients with plaque psoriasis involving special areas (scalp, genital, and/or palmoplantar) and with a baseline GenPs-SFQ item 2 score ≥2 and a baseline sPGA-G score ≥3
Sec 9	≥4-point improvement from baseline in Scalp Itch NRS score at Week 16	Patients ≥12 years of age with plaque psoriasis involving special areas (scalp, genital, and/or palmoplantar) and with a baseline Scalp Itch NRS score ≥4 and a baseline ss-IGA score ≥3
Sec 10	≥4-point improvement from baseline in GPSS Genital Itch NRS score (Item 1 from the GPSS) at Week 16	Patients ≥12 years of age with plaque psoriasis involving special areas (scalp, genital, and/or palmoplantar) and with a baseline GPSS Genital Itch NRS score (Item 1 from the GPSS) ≥4 and a baseline sPGA-G score ≥3

As in the primary estimand, achieving a response based on a scale is defined as meeting the efficacy criteria based on that scale and not experiencing ICEs 1 and 2.

4.3.1.2.2. Supplementary Estimands for Key Secondary Endpoints

The supplementary estimands have the same components as the main estimand for all key secondary endpoints, except for the strategies used for ICEs and not counting ICEs as non-responders in the definition of Variable. The same Treatment Policy estimand (Section 4.2.2.2) for the primary endpoint will be used for the key secondary endpoints.

4.3.1.3. Analysis Methods

4.3.1.3.1. Analytical Approaches for Main Estimands

The efficacy analyses for key secondary endpoints will be based on the FAS by intervention group. In order to control the overall Type I error rate (α=0.05), multiplicity adjustment will be applied to the analyses of the primary endpoints and key secondary endpoints listed above. The detailed methods of analysis and approach to control the Type I error for multiplicity is specified in Section 2.1.

The binary key secondary endpoints at Week 16 will be analyzed using the main estimand described in section 4.3.1.2.1. The analysis strategy for ICEs and missing data will be handled in the same manner as the primary estimand (Section 4.2.3.1). Composite strategy will be used for ICEs 1 and 2 where participants with those ICEs will be considered as non-responders and treatment policy strategy will be used for ICE 3 where observed data will be used. After the application of ICEs, participants with missing data will be imputed as non-responders. The proportions of participants achieving an IGA score of 0, and ≥4-point improvement from baseline in PSSD Itch score response at Week 16 will be summarized and compared between intervention groups in the same manner as the primary endpoint. For special areas related endpoints, when sample size is large enough, a CMH test as well as difference in response rates between the JNJ-77242113 group and the placebo group at Week 16 and their corresponding 95% CIs (using Miettinen-Nurminen method) will be calculated adjusting for geographic region and BSA category using Mantel-Haenszel weights. For endpoints with smaller sample size (eg, ≥4-point improvement from baseline in GPSS Genital Itch NRS score [Item 1 from the GPSS] response at Week 16) for special areas related endpoints and PSSD symptom score of 0, a CMH test as well as difference in response rates between the JNJ-77242113 group and the placebo group at Week 16 and their corresponding 95% CIs (using Miettinen-Nurminen method) will be calculated adjusting for BSA category using Mantel-Haenszel weights.

4.3.1.3.2. Sensitivity Analyses for Select Key Secondary Endpoints

Under the main estimands, the similar two sensitivity analyses specified for the primary endpoint will also be performed for the following select key secondary endpoints:

- ss-IGA score of 0 or 1 at Week 16 among participants with a baseline ss-IGA score ≥3
- sPGA-G score of 0 or 1 at Week 16 among participants with a baseline sPGA-G score ≥3
- hf-PGA score of 0 or 1 at Week 16 among participants with a baseline hf-PGA score ≥3

4.3.1.3.3. Supplementary Analysis

Similar to the supplementary analyses for the primary endpoint, the analyses specified in Section 4.2.3.3.1 (Treatment Policy Estimand) for the primary endpoint will be applied to supplementary estimands for the key secondary endpoints. No adjustments for multiple comparisons will be made for the supplementary analysis of the key secondary endpoints.per

4.3.1.3.4. Per Protocol Analysis for Select Key Secondary Endpoints

The following select key secondary endpoints will be evaluated for comparisons between the JNJ-77242113 group and the placebo group in the PP population based on the corresponding main estimands.

- ss-IGA score of 0 or 1 at Week 16 among participants with a baseline ss-IGA score ≥3
- sPGA-G score of 0 or 1 at Week 16 among participants with a baseline sPGA-G score ≥3
- hf-PGA score of 0 or 1 at Week 16 among participants with a baseline hf-PGA score ≥3

4.3.1.3.5. Subgroup Analyses

To evaluate the consistency of the efficacy, subgroup analyses of the following select key secondary endpoints based on demographics, baseline disease characteristics, and previous psoriasis medications and therapies will be performed (Section 4.6.6).

- IGA 0 response at Week 16
- ss-IGA score of 0 or 1 at Week 16 among participants with a baseline ss-IGA score ≥3
- PSSI 90 response at Week 16 among participants with a baseline ss-IGA score ≥3
- sPGA-G score of 0 or 1 at Week 16 among participants with a baseline sPGA-G score ≥3
- hf-PGA score of 0 or 1 at Week 16 among participants with a baseline hf-PGA score ≥3

4.3.2. Other Secondary Endpoints Analyses

4.3.2.1. Definition of Endpoints

4.3.2.1.1. Psoriasis Area and Severity Index (PASI)

The PASI is a system used for assessing and grading the severity of psoriatic lesions and their response to therapy. In the PASI system, the body is divided into 4 regions: the head, trunk, upper extremities, and lower extremities which account for 10%, 30%, 20%, and 40% of the total BSA, respectively. Each of these areas is assessed separately for erythema, induration, and scaling, which are each rated on a scale of 0 to 4; and the area of involvement for psoriatic lesion is rated on a scale of 0 (no involvement) to 6 (90% to 100% involvement). The PASI produces a numeric score that can range from 0 (no psoriasis) to 72. A higher score indicates more severe disease. PASI 90 responder is defined as at least a 90% reduction from baseline in PASI total score.

Meeting PASI 75 criteria: defined as having ≥75% improvement from baseline in PASI total score.

Meeting PASI 90 criteria: defined as having ≥90% improvement from baseline in PASI total score from baseline.

Meeting PASI 100 criteria: defined as having a 100% improvement from baseline in PASI total score from baseline.

4.3.2.1.2. Body Surface Area (BSA)

Body surface area is a commonly used measure of involvement of skin disease. It is defined as the percentage of surface area of the body involved with the condition being assessed, (ie, plaque psoriasis). The handprint method for assessing BSA will be used in this study, where the surface area of the participant's hand including the palm and all 5 digits is used as a guide to estimate 1% BSA.

4.3.2.1.3. Fingernail Physician's Global Assessment (f-PGA)

The f-PGA is used to evaluate the current status of a participant's fingernail psoriasis on a scale of 0 to 4: clear (0), minimal (1), mild (2), moderate (3), and severe (4).

Meeting f-PGA 0 or 1 criteria: defined as having an f-PGA score of clear (0) or minimal (1).

4.3.2.1.4. Modified Nail Psoriasis Area and Severity Index (mNAPSI)

The mNAPSI is an index used for assessing and grading the severity of nail psoriasis. Each of the participant's ten fingernails are evaluated on 7 features. The first three features are each scored from 0 to 3 in severity and are (1) onycholysis and oil-drop dyschromia, (2) pitting, and (3) nail plate crumbling. The next four features are each scored 0 (absent) or 1 (present), and are (1) leukonychia, (2) splinter hemorrhages, (3) nail bed hyperkeratosis, and (4) red spots in the lunula. The score ranges from 0-13 per nail, and 0-130 for all fingernails.

mNAPSI data is collected only for participants with active nail psoriasis at Week 0, i.e. baseline f-PGA score >0.

4.3.2.1.5. Psoriasis Symptom and Sign Diary (PSSD)

Refer to section 4.3.1.1.6 for details.

Meeting PSSD sign score of 0 criteria: having a PSSD sign score of 0 indicates absence of psoriasis signs.

4.3.2.1.6. Dermatology Life Quality Index/Children's Dermatology Life Quality Index Score

The Dermatology Life Quality Index (DLQI) is a dermatology-specific quality of life instrument designed to assess the impact of the disease on a participant's quality of life. It is a 10-item questionnaire that in addition to evaluating overall quality of life, can be used to assess 6 different aspects that may affect quality of life: symptoms and feelings, daily activities, leisure, work or school performance, personal relationships, and treatment.

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired. A higher score indicates more severe disease. A score of ≤1 indicates no effect at all of disease on participant's health related quality of life, and a reduction of 5 points or more in total DLQI score is considered clinically meaningful improvement.

For a partially answered questionnaire (eg, not all ten questions in a questionnaire were available):

- If one question's answer is not available (missing), this question will be scored missing. The total score will then be calculated.
- If two or more questions' answers are not available (missing), then the questionnaire is not scored. Hence, the total score will be set to missing.
- If one question from one of the 6 component scores is missing, the affected component score will be set to be missing.

The Children's Dermatology Life Quality Index (CDLQI) is a dermatology-specific quality of life instrument designed to assess the impact of the disease on a child's quality of life. It is an adapted version of DLQI. The CDLQI, a 10-item questionnaire has 4 items response options and a recall period of 1 week. In addition to evaluating overall quality of life, the CDLQI can be used to assess 6 different aspects that may affect quality of life: symptoms and feelings, leisure, school or holidays, personal relationships, sleep, and treatment.

The CDLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired. For a partially answered questionnaire (eg, not all ten questions in a questionnaire were available):

- If one question's answer is not available (missing), this question will be scored missing. The total score will then be calculated.
- If two or more questions' answers are not available (missing), then the questionnaire is not scored. Hence, the total score will be set to missing.
- If one question from one of the 6 component scores is missing, the affected component score will be set to be missing.
- If both questions in question 7 are completed, the higher of the two scores should be counted for question 7.

Meeting DLQI/CDLQI 0 or 1 criteria: defined as having a DLQI/CDLQI score of 0 or 1 with baseline DLQI/CDLQI score >1.

4.3.2.1.7. Patient-reported Outcomes Measurement Information System-29 v2.1 (PROMIS-29)

The PROMIS-29 will be utilized in the adult population and is a 29-item generic HRQoL survey, assessing each of the 7 PROMIS domains (depression, anxiety, physical function, pain interference, fatigue, sleep disturbance, and ability to participate in social roles and activities) with 4 questions for each domain. The questions are ranked on a 5-point Likert Scale. There is also one 11-point rating scale for pain intensity.

The total raw score will be converted into a T-score for each participant based on the table in Appendix 9. The T-score rescales the raw score into a standardized score with a mean of 50 and an SD of 10. For PROMIS domains of Depression, Anxiety, Physical Function, Pain Interference, Fatigue, a score of 50 is the average for the United States general population with a standard deviation of 10, because testing was performed on a large sample of the general population.

However, the other two domains (Ability to Participate in Social Roles and Activities and Sleep Disturbance) were not centered in a national sample. For these two domains, a score of 50 represents the average of the calibration sample which was generally more enriched for chronic illness, and a score of 50 likely represents somewhat sicker people than the general population. A higher PROMIS T-score represents more of the concept being measured. For negatively-worded concepts like Anxiety, a T-score of 60 is one SD worse than average. By comparison, an Anxiety T-score of 40 is one SD better than average. However, for positively-worded concepts like Physical Function, a T-score of 60 is better than average while a T-score of 40 is better. The physical component score (PCS) and mental component score (MCS) will be derived from the domain scores.

Change from baseline in PROMIS-29 domain score: defined as the domain score minus the participant's baseline domain score, where a negative change indicates an improvement for the following domains:

- Anxiety
- Depression
- Fatigue
- Sleep disturbance
- Pain interference

and a positive change indicates an improvement for the following domains:

- Physical function
- Ability to participate in social roles and activities
- Physical health component score
- Mental health component score

4.3.2.1.8. PROMIS Pediatric-25 Profile v2.0 (PROMIS-25)

The PROMIS-25 will be utilized in the adolescent population and is a 25-item generic HRQoL survey. Six PROMIS domains (physical function mobility, anxiety, depressive symptoms, fatigue, peer relationships, pain interference) are each assessed with 4 questions. There is also one 11-point rating scale for pain intensity. The instrument is designed for use in ages 8-17 years of age and can be self-administered.

The total raw score will be converted into a T-score for each participant based on the table in Appendix 10. The T-score rescales the raw score into a standardized score with a mean of 50 and an SD of 10.

Change from baseline in PROMIS-25 domain score: defined as the domain score minus the participant's baseline domain score, where a negative change indicates an improvement for the following domains:

- Anxiety

- Depressive symptoms
- Fatigue
- Pain interference

and a positive change indicates an improvement for the following domains:

- Physical function mobility
- Peer relationships

4.3.2.1.9. Palmoplantar Quality of Life Instrument (ppQLI)

The ppQLI assesses impact on patient quality of life due to palmoplantar psoriasis over the past month in adult and adolescent populations. Sixteen items evaluate hand functionality, pain, and social impact due to psoriasis. Fourteen items evaluate foot functionality, pain, and physical limitations due to psoriasis. All items use verbal rating scales ranging from 1 to 5. The ppQLI yields a score for hands, ranging from 16 to 80, and a score for feet, ranging from 14 to 70.

Separately for hands and feet the sum of the scores is categorized according to the following table:

Hands		**Feet**	
No difficulty	=16	No difficulty	=14
Mild	17 - 32	Mild	15 - 28
Moderate	33 - 48	Moderate	29 - 42
Severe	49 - 64	Severe	43 - 56
Totally unstable	65 - 80	Totally unstable	57 - 70

ppQLI data is collected only for participants with active palmoplantar psoriasis at Week 0, ie baseline hf-PGA score >0.

Change from baseline in the ppQLI score is defined as the sum score (the hand and foot sum score, respectively) minus the participant's score at baseline. This measures the change in the impact of the disease on quality of life, where a decrease from baseline in ppQLI score indicates an improvement and an increase indicates a worsening.

4.3.2.1.10. Genital Psoriasis Symptoms Scale (GPSS)

Refer to section 4.3.1.1.9 for details.

Change from baseline in GPSS total score: The change from baseline in GPSS measures the change in disease severity on a continuous scale where a negative change indicates an improvement, and a positive change indicates worsening.

4.3.2.2. Estimands

The estimands for other secondary endpoints have the same attributes as the primary estimand in treatment and strategy used for ICEs. The attributes for variable, population and population level summary for the other secondary endpoints are listed in Table 4.

Table 4: List of Variables, Populations, and Population Level Summary for Other Secondary Endpoints.

Variable	Population	Population Level Summary
To Further Evaluate the Effect of JNJ-77242113		
PASI 90 at Week 16	Same population as the primary estimand	Difference in proportions
PASI 75 at Week 16		
f-PGA score of 0 or 1 at Week 16	Patients ≥12 years of age with plaque psoriasis involving at least one of affecting special areas and with a baseline f-PGA score ≥2	
Change from baseline in PASI at Week 16	Same population as the primary estimand	Difference in treatment means
Percent change from baseline in PASI at Week 16		
Change from baseline in BSA at Week 16		
Percent change from baseline in mNAPSI score at Week 16	Patients ≥12 years of age with plaque psoriasis involving at least one of affecting special areas and with a baseline mNAPSI score >0	
To Further Evaluate the Effect of JNJ-77242113 on PROs		
PSSD symptom score of 0 at Week 8	Patients ≥12 years of age with plaque psoriasis involving at least one of affecting special areas and with a baseline PSSD symptom score >0	Difference in proportions

PSSD sign score of 0 at Week 16	Patients ≥12 years of age with plaque psoriasis involving at least one of affecting special areas and with a baseline PSSD sign score >0	
≥4-point improvement from baseline in PSSD Itch score at Week 4	Patients ≥12 years of age with plaque psoriasis involving at least one of affecting special areas and with a baseline PSSD Itch score ≥4	
DLQI score of 0 or 1 at Week 16	Adult patients with plaque psoriasis involving at least one of affecting special areas and with a baseline DLQI Score >1	
CDLQI score of 0 or 1 at Week 16	Adolescent patients with plaque psoriasis involving at least one of affecting special areas and with a baseline CDLQI Score >1	
Change from baseline in PSSD symptom score at Week 16	Same population as the primary estimand	Difference in treatment means
Change from baseline in PSSD sign score at Week 16		
Change from baseline in each of the 8 individual domain scores, PCS and MCS scores of the PROMIS-29 score at Week 16	Adult patients with plaque psoriasis involving at least one of affecting special areas	
Change from baseline in each of the 7 individual domain scores of the PROMIS-25 pediatric score at Week 16	Adolescent patients with plaque psoriasis involving at least one of affecting special areas	
Change from baseline in ppQLI hands score at Week 16	Patients ≥12 years of age with plaque psoriasis involving at least one of affecting special areas and with a baseline hf-PGA score ≥3	
Change from baseline in ppQLI feet score at Week 16	Patients ≥12 years of age with plaque psoriasis involving at least one of affecting special areas and with a baseline hf-PGA score ≥3	
Change from baseline in GPSS total score at Week 16	Patients ≥12 years of age with plaque psoriasis involving at least one of affecting special areas and with a baseline sPGA-G score ≥3	

4.3.2.3. Analysis Methods

The other secondary endpoints will be analyzed using the estimands described in Section 4.3.2.2 for FAS. All statistical testing will be performed at the 2-sided 0.05 significance level. No adjustments for multiple comparisons will be made for other secondary endpoints. Nominal p-values for other secondary will be reported but should not be used to infer statistical significance.

Binary Endpoints

The same strategies for addressing ICEs for primary analysis (binary endpoint) will be used for other secondary binary endpoints. The proportions of participants achieving a clinical response for the efficacy endpoints will be provided by intervention group. The p-values, difference in proportions and 95% CIs will be provided based on the same model for the primary analysis specified in Section 4.2.3.1.

Continuous Endpoints

The analysis strategies for ICEs:

- Participants experiencing ICEs 1 and 2 will be handled with composite strategy and data will be imputed with a zero change (or zero improvement) from baseline assigned from that point onward.
- Participants experiencing ICE 3 will be handled by the treatment policy strategy and observed data will be used regardless of intercurrent events. For participants experiencing multiple ICEs, ICE 2 will override an ICE 3.
- Missing data will not be imputed after applying the rules for intercurrent events.

For repeated measure continuous endpoints, treatment comparisons will be performed using a MMRM model. The MMRM will include treatment, baseline value, special area involvement, geographic region, and BSA category, as explanatory factors. The MMRM model will also include visit, treatment group by visit interaction, and baseline value by visit interaction as additional explanatory factors. An unrestricted (UN) variance-covariance matrix for repeated measures within a participant will be used. If the model with unstructured covariance structure does not converge, alternative covariance structures will be tried in the following order, with the first structure that converges being used in the analysis: heterogeneous Toeplitz, standard Toeplitz, and autoregressive of order 1. The LS mean estimates and their corresponding 95% CI will be provided at each timepoint. In addition, the estimates of LS mean difference and 95% CIs between treatment groups will be provided. For endpoints related to special areas, the MMRM will not include special area involvement as an explanatory factor. For change from baseline in BSA at Week 16, BSA category will not be included in the MMRM model.

Analysis of covariance (ANCOVA) will be used to analyze some continuous endpoints when appropriate. The ANCOVA will include treatment group, baseline value, special area involvement, geographic region, and BSA category. The LS mean estimates and their corresponding 95% CI will be provided. In addition, LS mean difference and 95% CIs between treatment groups will be

provided. For change from baseline in BSA at Week 16, BSA category will not be included in the ANVOCA model.

4.4. Exploratory Endpoints Analyses

4.4.1. Definition of Endpoints

Endpoints to Further Evaluate the Efficacy of of JNJ-77242113

4.4.1.1. Investigator's Global Assessment (IGA)

Refer to section 4.2.1 for details.

Meeting an IGA of mild or better (≤2) criteria: defined as achieving an IGA score of cleared (0), minimal (1) or mild (2).

4.4.1.2. Psoriasis Area and Severity Index (PASI)

Refer to section 4.3.2.1.1 for details.

4.4.1.3. Body Surface Area (BSA)

Refer to section 4.3.2.1.2 for details.

4.4.1.4. Scalp-specific Investigator Global Assessment (ss-IGA)

Refer to section 4.3.1.1.1 for details.

4.4.1.5. Psoriasis Scalp Severity Index (PSSI)

Refer to section 4.3.1.1.2 for details.

Meeting PSSI 75 criteria: defined as having ≥75% improvement in PSSI from baseline.

Meeting PSSI 100 criteria: defined as having 100% improvement in PSSI from baseline.

4.4.1.6. Static Physician's Global Assessment of Genitalia (sPGA-G)

Refer to section 4.3.1.1.3 for details.

4.4.1.7. Physician's Global Assessment of Hands and/or Feet (hf-PGA)

Refer to section 4.3.1.1.4 for details.

Meeting hf-PGA 0 criteria: defined as having an hf-PGA score of clear (0).

4.4.1.8. Fingernail Physician's Global Assessment (f-PGA)

Refer to section 4.3.2.1.33 for details.

Meeting f-PGA 0 criteria: defined as having an f-PGA score of clear (0).

4.4.1.9. Modified Nail Psoriasis Areas and Severity Index (mNAPSI)

Refer to section 4.3.2.1.44 for details.

Endpoints To Further Evaluate the Effect of JNJ-77242113 on PROs

4.4.1.10. Psoriasis Symptom and Sign Diary (PSSD)

Refer to section 4.3.1.1.6 for details.

4.4.1.11. Dermatology Life Quality Index (DLQI)

Refer to section 4.3.2.1.6 for details.

4.4.1.12. Scalp Itch Numeric Rating Scale (Scalp Itch NRS)

Refer to section 4.3.1.1.8 for details.

4.4.1.13. Genital Psoriasis Symptoms Scale (GPSS)

Refer to section 4.3.2.1.10 for details.

4.4.1.14. Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ)

Refer to section 4.3.1.1.7 for details.

4.4.1.15. Palmoplantar Quality of Life Instrument (ppQLI)

Refer to section 4.3.2.1.9 for details.

4.4.1.16. Patient-reported Outcomes Measurement Information System-29 (PROMIS-29)

Refer to section 4.3.2.1.7 for details.

4.4.1.17. Participant Assessment of Psoriatic Arthritis Pain

This self-administered item is designed to assess the participant's reported pain associated with PsA over the past week on a VAS ranging from 0 (no pain) to 100 (worst possible pain). This assessment will be administered only to adult and adolescent participants who report having PsA at or before Week 0.

4.4.1.18. Participant Assessment of Psoriatic Arthritis Disease Activity

This self-administered item is designed to assess the participant's overall well-being over the past week on a VAS ranging from 0 (very poor) to 100 (very well). This assessment will be administered only to adult and adolescent participants who report having PsA at or before Week 0.

4.4.2. Analysis Methods

In general, the efficacy analyses for exploratory endpoints will be based on FAS (Section 3). Simple descriptive statistics, such as n, mean, SD, median, IQ range, minimum and maximum for continuous variables and counts and percentages for discrete variables will be summarized by study intervention group.

Unless otherwise specified, the treatment comparisons for binary endpoints will be performed using the same analysis methods described in Section 4.3.1.3.1 for the main estimands of the key secondary endpoints. The analysis strategy for ICEs and missing data will be handled in the same manner as the key secondary endpoints. For continuous variables, the analysis strategy for ICEs and missing data will be handled in the same manner as other secondary analyses (section 4.3.2.3). For endpoints related to special areas, the MMRM will not include special area involvement as an explanatory factor. No adjustments for multiple comparisons will be made for exploratory endpoints.

For the efficacy analyses from Week 64 through Week 156, all participants randomized to JNJ-77242113 at Week 0 or placebo cross-over to JNJ-77242113 at or after Week 16 will be included in the analyses. For select binary endpoints (IGA responses, ss-IGA responses, PSSI responses, sPGA-G responses, hf-PGA responses), both modified Non-Responder Imputation (mNRI) and as-observed cases (OC) will be performed to handle the missing data; other binary endpoints will only apply mNRI. mNRI will be the primary method to handle the missing data.

- mNRI for binary endpoints: Participants who meet ICE 1 (discontinuation of treatment due to lack of efficacy, or due to an AE of worsening of psoriasis) will be considered as non-responders for binary endpoints from that point forward. After accounting for the ICE 1, missing data will then be imputed using the same multiple imputations (MI) method specified in Section 4.2.3.2.1 for Sensitivity Analysis 1.
- Observed Cases (OC) for binary endpoints: in the as-observed analyses, no ICE rules will be applied and missing data will not be imputed. Thus, a subject who does not have an evaluation on a scheduled visit will be excluded from the as-observed analysis for that visit.

For continuous endpoints, participants with ICE 1 will be considered as zero change or zero percent change from baseline from that point forward. After accounting for ICE 1, MMRM will be used to account for missing data under the assumption of MAR.

Additionally, graphical data displays may also be used to summarize the over time data if applicable.

4.4.2.1. Analyses Through Week 16

Efficacy analyses at Week 16 and over time through Week 16 will be summarized by the randomized treatment group at Week 0:

- **Placebo**: subjects randomized to placebo group at Week 0
- **JNJ-77242113**: subjects randomized to JNJ-77242113 treatment group at Week 0

4.4.2.2. Analyses From Week 16 Through Week 52

Efficacy analyses from Week 16 through Week 52 will be summarized over time by the following treatment group:

- **Placebo**-> **JNJ-77242113**: adult or adolescent participants randomized to placebo group at Week 0 and crossed over to receive JNJ-77242113 on or after Week 16

- **JNJ-77242113**: adult or adolescent participants randomized to JNJ-77242113 treatment group at Week 0 and received JNJ-77242113

4.4.2.3. Analyses From Week 64 Through Week 156

The efficacy analyses from Week 64 through Week 156 will be summarized:

- **JNJ-77242113**: participants randomized to JNJ-77242113 treatment group at Week 0, or randomized to placebo group at Week 0 and crossed over to received JNJ-77242113 at or after Week 16

4.4.2.4. Analyses Related to IGA

Through Week 16

- The proportions of IGA (overall) responses (IGA 0, IGA 0 or 1 and at least a 2-grade improvement from baseline) will be summarized over time through Week 16 by treatment group.

From Week 16 Through Week 52

- The proportions of IGA (overall) responses (IGA 0, IGA 0 or 1 and at least a 2-grade improvement from baseline) will be summarized over time by treatment group.

- Summary of IGA (overall) 0 or 1 response at Week 52 among participants who are randomized to JNJ-77242113 at Week 0 and are IGA (overall) 0 or 1 responders at Week 16.

From Week 64 Through Week 156

- The proportions of IGA (overall) responses (IGA 0, IGA 0 or 1 and at least a 2-grade improvement from baseline) will be summarized over time.

4.4.2.5. Analyses Related to PASI

Through Week 16

- The proportion of participants achieving PASI 100 at Week 16 will be compared between the JNJ-77242113 group and the placebo group.
- The change from baseline in PASI total score will be summarized over time through Week 16 by treatment group.
- The percent change from baseline in PASI total score will be summarized over time through Week 16 by treatment group.
- The proportion of PASI responses (PASI 75, 90, and 100) will be summarized over time through Week 16 by treatment group.

From Week 16 Through Week 52

- The change from baseline in PASI total score will be summarized over time by treatment group.

- The percent change from baseline in PASI total score will be summarized over time by treatment group.
- The proportion of PASI responses (PASI 75, 90, and 100) will be summarized over time by treatment group.

4.4.2.6. Analyses Related to BSA

Through Week 16

- The change from baseline in BSA will be summarized over time through Week 16 by treatment group.
- The change from baseline in BSA will be summarized over time through Week 16 by treatment group and baseline BSA category (<10%, ≥10%).

From Week 16 Through Week 52

- The change from baseline in BSA will be summarized over time by treatment group.

4.4.2.7. Analyses Related to ss-IGA

Through Week 16

- The proportion of participants who achieve ss-IGA score of 0 will be compared between treatment groups at Week 16 among participants with a baseline ss-IGA score ≥3.
- The proportion of participants who achieve ss-IGA score of 0 will be compared between treatment groups at Week 16 among participants with a baseline ss-IGA score ≥2.
- The proportion of participants who achieve an ss-IGA score of 0 or 1 and at least 2-grade improvement from baseline will be compared between treatment groups at Week 16 among participants with a baseline ss-IGA score ≥2.
- The proportion of ss-IGA responses (ss-IGA score of 0, ss-IGA score of 0 or 1) will be summarized over time through Week 16 by treatment group among participants with a baseline ss-IGA score ≥3
- The proportion of ss-IGA responses (ss-IGA score of 0, ss-IGA score of 0 or 1 and at least 2-grade improvement from baseline) will be summarized over time through Week 16 by treatment group among participants with a baseline ss-IGA score ≥2.
- The proportion of ss-IGA responses (ss-IGA score of 0, ss-IGA score of 0 or 1) will be summarized over time through Week 16 by treatment group and baseline BSA category (<10%, ≥10%) among participants with a baseline ss-IGA score ≥3.

From Week 16 Through Week 52

- The proportion of ss-IGA responses (ss-IGA score of 0, ss-IGA score of 0 or 1) will be summarized over time by treatment group among participants with a baseline ss-IGA score ≥3.
- The proportion of ss-IGA responses (ss-IGA score of 0, ss-IGA score of 0 or 1 and at least 2-grade improvement from baseline) will be summarized over time by treatment group among participants with a baseline ss-IGA score ≥2.

- Summary of ss-IGA score of 0 or 1 response at Week 52 among participants with a baseline ss-IGA score ≥3 who are randomized to JNJ-77242113 at Week 0 and are ss-IGA score of 0 or 1 responders at Week 16.

From Week 64 Through Week 156

- The proportion of ss-IGA responses (ss-IGA score of 0, ss-IGA score of 0 or 1) will be summarized over time among participants with a baseline ss-IGA ≥3.

4.4.2.8. Analysis Related to PSSI

Through Week 16

- The proportion of PSSI 75 and PSSI 100 responses, respectively, will be compared between treatment groups at Week 16 among participants with a baseline ss-IGA score ≥3 score respectively.
- The change from baseline in PSSI total score will be summarized over time through Week 16 by treatment group among participants with a baseline ss-IGA score ≥3.
- The percent change from baseline in PSSI total score will be summarized over time through Week 16 by treatment group among participants with a baseline ss-IGA score ≥3.
- The proportion of PSSI responses (PSSI 75, 90, and 100) will be summarized over time through Week 16 by treatment group among participants with a baseline ss-IGA score ≥3.

From Week 16 Through Week 52

- The change from baseline in PSSI total score will be summarized over time by treatment group among participants with a baseline ss-IGA score ≥3.
- The percent change from baseline in PSSI total score will be summarized over time by treatment group among participants with a baseline ss-IGA score ≥3.
- The proportion of PSSI responses (PSSI 75, 90, and 100) will be summarized over time by treatment group among participants with a baseline ss-IGA score ≥3.

From Week 64 Through Week 156

- The proportion of PSSI responses (PSSI 75, 90, and 100) will be summarized over time among participants with a baseline ss-IGA score ≥3.

4.4.2.9. Analyses Related to sPGA-G

Through Week 16

- The proportion of participants who achieve sPGA-G score of 0 will be compared between treatment groups at Week 16 among participants with a baseline sPGA-G score ≥3.
- The proportion of participants who achieve sPGA-G score of 0 will be compared between treatment groups at Week 16 among participants with a baseline sPGA-G score ≥2.
- The proportion of participants who achieve an sPGA-G score of 0 or 1 and at least 2-grade improvement from baseline will be compared between treatment groups at Week 16 among participants with a baseline sPGA-G score ≥2.

- The proportion of sPGA-G responses (sPGA-G score of 0, sPGA-G score of 0 or 1) will be summarized over time through Week 16 by treatment group among participants with a baseline sPGA-G score ≥3.
- The proportion of sPGA-G responses (sPGA-G score of 0, sPGA-G score of 0 or 1 and at least 2-grade improvement from baseline) will be summarized over time through Week 16 by treatment group among participants with a baseline sPGA-G score ≥2.
- The proportion of sPGA-G responses (sPGA-G score of 0, sPGA-G score of 0 or 1) will be summarized over time through Week 16 by treatment group and baseline BSA category (<10%, ≥10%) among participants with a baseline sPGA-G score ≥3.

From Week 16 Through Week 52

- The proportion of sPGA-G responses (sPGA-G score of 0, sPGA-G score of 0 or 1) will be summarized over time by treatment group among participants with a baseline sPGA-G score ≥3.
- The proportion of sPGA-G responses (sPGA-G score of 0, sPGA-G score of 0 or 1 and at least 2-grade improvement from baseline) will be summarized over time by treatment group among participants with a baseline sPGA-G score ≥2.
- Summary of sPGA-G score of 0 or 1 response at Week 52 among participants with a baseline sPGA-G score ≥3 who are randomized to JNJ-77242113 at Week 0 and are sPGA-G score of 0 or 1 responders at Week 16.

From Week 64 Through Week 156

- The proportion of sPGA-G responses (sPGA-G score of 0, sPGA-G score of 0 or 1) will be summarized over time among participants with a baseline sPGA-G score ≥3.

4.4.2.10. Analyses Related to hf-PGA

Through Week 16

- The proportion of participants who achieve hf-PGA score of 0 will be compared between treatment groups at Week 16 among participants with a baseline hf-PGA score ≥3.
- The proportion of participants who achieve hf-PGA score of 0 will be compared between treatment groups at Week 16 among participants with a baseline hf-PGA score ≥2.
- The proportion of participants who achieve an hf-PGA score of 0 or 1 and at least 2-grade improvement from baseline will be compared between treatment groups at Week 16 among participants with a baseline hf-PGA score ≥2.
- The proportion of hf-PGA responses (hf-PGA score of 0, hf-PGA score of 0 or 1) will be summarized over time through Week 16 by treatment group among participants with a baseline hf-PGA score ≥3.
- The proportion of hf-PGA responses (hf-PGA score of 0, hf-PGA score of 0 or 1 and at least 2-grade improvement from baseline) will be summarized over time through Week 16 by treatment group among participants with a baseline hf-PGA score ≥2.

- The proportion of hf-PGA responses (hf-PGA score of 0, hf-PGA score of 0 or 1) will be summarized over time through Week 16 by treatment group and baseline BSA category (<10%, ≥10%) among participants with a baseline hf-PGA score ≥3.

From Week 16 Through Week 52

- The proportion of hf-PGA responses (hf-PGA score of 0, hf-PGA score of 0 or 1) will be summarized over time by treatment group among participants with a baseline hf-PGA score ≥3.
- The proportion of hf-PGA responses (hf-PGA score of 0, hf-PGA score of 0 or 1 and at least 2-grade improvement from baseline) will be summarized over time by treatment group among participants with a baseline hf-PGA score ≥2.
- Summary of hf-PGA score of 0 or 1 response at Week 52 among participants with a baseline hf-PGA score ≥3 who are randomized to JNJ-77242113 at Week 0 and are hf-PGA score of 0 or 1 responders at Week 16.

From Week 64 Through Week 156

- The proportion of hf-PGA responses (hf-PGA score of 0, hf-PGA score of 0 or 1) will be summarized over time among participants with a baseline hf-PGA score ≥3.

4.4.2.11. Analyses Related to f-PGA

Through Week 16

- The proportion of f-PGA responses (f-PGA score of 0, f-PGA score of 0 or 1) over time through Week 16 by treatment group among participants with a baseline f-PGA score ≥2.

4.4.2.12. Analyses Related to mNAPSI

Through Week 16

- The percent change from baseline in mNAPSI will be summarized over time through Week 16 by treatment group among participants with a baseline mNAPSI score >0.

4.4.2.13. Analyses Related to PSSD

Through Week 16

- The change from baseline in each PSSD individual scale score will be compared between treatment groups at Week 16.
- The change from baseline in PSSD symptom score and sign score will be summarized over time through Week 16 by treatment group.
- The proportions of participants who achieve a PSSD symptom score of 0 will be summarized over time through Week 16 by treatment group among participants with a baseline PSSD symptom score >0.
- The proportions of participants who achieve a PSSD sign score of 0 will be summarized over time through Week 16 by treatment group among participants with a baseline PSSD sign score >0.

- The proportion of participants who achieve a ≥4-point improvement from baseline in PSSD Itch score will be summarized over time through Week 16 by treatment group among participants with a baseline PSSD Itch score ≥4.

From Week 16 Through Week 52

- The change from baseline in PSSD symptom score and sign score will be summarized over time by treatment group.
- The proportions of participants who achieve a PSSD symptom score of 0, sign score of 0 and ≥4-point improvement from baseline in itch score will be summarized over time by treatment group among participants with a baseline PSSD symptom score >0, baseline sign score >0, and itch score ≥4 at baseline, respectively.

From Week 64 Through Week 156

- The change from baseline in PSSD symptom score and sign score will be summarized over time.
- The proportions of participants who achieve a PSSD symptom score of 0, sign score of 0 and ≥4-point improvement from baseline in itch score will be summarized over time among participants with a baseline PSSD symptom score >0, baseline sign score >0, and itch score ≥4 at baseline, respectively.

4.4.2.14. Analyses Related to DLQI (Adults)

Through Week 16

- The change from baseline in DLQI score will be summarized over time through Week 16 by treatment group among adult participants.
- The proportions of participants with DLQI score of 0 or 1 will be summarized over time through Week 16 by treatment group among adult participants with a baseline DLQI score >1.

From Week 16 Through Week 52

- The change from baseline in DLQI score will be summarized over time by treatment group among adult participants.
- The proportions of participants with DLQI score of 0 and 1 will be summarized over time by treatment group among adult participants with a baseline DLQI score >1.

From Week 64 Through Week 156

- The change from baseline in DLQI score will be summarized over time by treatment group among adult participants.
- The proportions of participants with DLQI score of 0 and 1 will be summarized over time among adult participants with baseline DLQI score >1.

4.4.2.15. Analyses Related to Scalp Itch NRS

Through Week 16

- The proportions of participants who achieve a ≥4-point improvement in Scalp Itch NRS score will be summarized through Week 16 by treatment group among participants with a baseline Scalp Itch NRS score ≥4 and with a baseline ss-IGA score ≥3.
- The change from baseline in Scalp Itch NRS score will be summarized over time through Week 16 by treatment group among participants with a baseline ss-IGA score ≥3.

From Week 16 Through Week 52

- The proportions of participants who achieve a ≥4-point improvement in Scalp Itch NRS score will be summarized over time by treatment group among participants with a baseline Scalp Itch NRS score ≥4 and with a baseline ss-IGA score ≥3.
- The change from baseline in Scalp Itch NRS score will be summarized over time by treatment group among participants with a baseline ss-IGA score ≥3.

From Week 64 Through Week 156

- The proportions of participants who achieve a ≥4-point improvement in Scalp Itch NRS score will be summarized over time among participants with a baseline Scalp Itch NRS score ≥4 and with a baseline ss-IGA score ≥3.
- The change from baseline in Scalp Itch NRS score will be summarized over time among participants with a baseline ss-IGA score ≥3.

4.4.2.16. Analyses Related to GPSS

Through Week 16

- The change from baseline in GPSS total score through Week 16 will be summarized over time through Week 16 by treatment group among participants with a baseline sPGA-G score ≥3.
- The change from baseline in each GPSS domain score through Week 16 will be summarized over time through Week 16 by treatment group among participants with a baseline sPGA-G score ≥3.
- The proportion of participants who achieve a ≥4-point improvement in GPSS Genital Itch NRS score (Item 1 from the GPSS) through Week 16 by treatment group among participants with a baseline GPSS Genital Itch NRS score (Item 1 from the GPSS) ≥4 and with a baseline sPGA-G score ≥3.

From Week 16 Through Week 52

- The change from baseline in GPSS total score will be summarized over time by treatment group among participants with a baseline sPGA-G score ≥3.
- The proportion of participants who achieve a ≥4-point improvement in GPSS Genital Itch NRS score (Item 1 from the GPSS) over time by treatment group among participants with a baseline GPSS Genital Itch NRS score (Item 1 from the GPSS) ≥4 and with a baseline sPGA-G score ≥3.

From Week 64 Through Week 156

- The change from baseline in GPSS total score will be summarized over time among participants with a baseline sPGA-G score ≥3.
- The proportion of participants who achieve a ≥4-point improvement in GPSS Genital Itch NRS score (Item 1 from the GPSS) over time among participants with a baseline GPSS Genital Itch NRS score (Item 1 from the GPSS) ≥4 and with a baseline sPGA-G score ≥3.

4.4.2.17. Analyses Related to GenPs-SFQ (Adult)

Through Week 16

- The proportion of participants who achieve a GenPs-SFQ item 2 score of 0, and a GenPs-SFQ item 2 score of 0 or 1, respectively, will be compared between treatment groups at Week 16 among participants with a baseline GenPs-SFQ item 2 score ≥2 and a baseline sPGA-G score ≥2.
- The proportion of GenPs-SFQ responses (GenPs-SFQ item 2 score of 0, GenPs-SFQ item 2 score of 0 or 1) will be summarized through Week 16 by treatment group among adult participants with a baseline GenPs-SFQ item 2 score ≥2 and a baseline sPGA-G score ≥3 .
- The proportion of GenPs-SFQ responses (GenPs-SFQ item 2 score of 0, GenPs-SFQ item 2 score of 0 or 1) will be summarized through Week 16 by treatment group among adult participants with a baseline GenPs-SFQ item 2 score ≥2 and a baseline sPGA-G score ≥2.

From Week 16 Through Week 52

- The proportion of GenPs-SFQ responses (GenPs-SFQ item 2 score of 0, GenPs-SFQ item 2 score of 0 or 1) will be summarized over time by treatment group among adult participants with a baseline GenPs-SFQ item 2 score ≥2 and a baseline sPGA-G score ≥3.
- The proportion of GenPs-SFQ responses (GenPs-SFQ item 2 score of 0, GenPs-SFQ item 2 score of 0 or 1) will be summarized over time by treatment group among adult participants with a baseline GenPs-SFQ item 2 score ≥2 and a baseline sPGA-G score ≥2.

From Week 64 Through Week 156

- The proportion of GenPs-SFQ responses (GenPs-SFQ item 2 score of 0, GenPs-SFQ item 2 score of 0 or 1) will be summarized over time among adult participants with a baseline GenPs-SFQ item 2 score ≥2 and a baseline sPGA-G score ≥3.

4.4.2.18. Analyses Related to ppQLI

Through Week 16

- The change from baseline in ppQLI hands score and the feet score, respectively, over time through Week 16 by treatment group among participants with a baseline hf-PGA score ≥3.

From Week 16 Through Week 52

- The change from baseline in ppQLI hands score and the feet score, respectively, will be summarized over time by treatment group among participants with a baseline hf-PGA score ≥3.

4.4.2.19. Analyses Related to PROMIS-29 (Adult)

Through Week 16

- The change from baseline in each PROMIS-29 domain score (T-score), Physical Component Score (PCS), and Mental Component Score (MCS) will be summarized through Week 16 by treatment group among adult participants.

From Week 16 Through Week 52

- The change from baseline in each PROMIS-29 domain score (T-score), Physical Component Score (PCS), and Mental Component Score (MCS) will be summarized over time by treatment group among adult participants.

From Week 64 Through Week 156

- The change from baseline in Physical Component Score (PCS) and Mental Component Score (MCS) will be summarized over time among adult participants.

4.4.2.20. Participant Assessment of Psoriatic Arthritis Pain

Through Week 16

- The change from baseline in PsA pain assessment score will be summarized at Week 8 and Week 16 by treatment group among participants with a diagnosis of PsA at or before screening.

From Week 16 Through Week 52

- The change from baseline in PsA pain assessment score will be summarized over time by treatment group among participants with a diagnosis of PsA at or before screening.

4.4.2.21. Participant Assessment of Psoriatic Arthritis Disease Activity

Through Week 16

- The change from baseline in PsA disease activity assessment score will be summarized at Week 8 and Week 16 by treatment group among participants with a diagnosis of PsA at or before screening.

From Week 16 Through Week 52

- The change from baseline in PsA disease activity assessment score will be summarized over time by treatment group among participants with a diagnosis of PsA at or before screening.

4.5. Safety Analyses

All safety analyses will be performed using the safety analysis set based on actual intervention received, unless otherwise specified. No formal statistical comparison is planned.

For all continuous safety variables, descriptive statistics by intervention group will include the N, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized by intervention group using frequency counts and percentages.

The cumulative safety data will be analyzed through different study periods as shown below. Unless otherwise specified, tabular summaries of safety events are also presented as follows:

Summary through Week 16 (placebo controlled):

- Placebo
- JNJ-77242113

For participants who were randomized to placebo at Week 0 and discontinued treatment prior to Week 16, the safety events/measurements occurred after Week 16 will be provided in a listing.

Summary through the reporting period (date of last participant completing Week 52 visit):

Safety data will be summarized by intervention group defined as follows:

- Placebo → JNJ-77242113: all participants who were randomized to placebo at Week 0, and later crossed over to receive treatment with JNJ-77242113 at or after Week 16. Only the safety events/measurements from these participants that occurred at or after Week 16 will be included.
- JNJ-77242113: Participants who were randomized to JNJ-77242113 at Week 0 and were treated with JNJ-77242113. All the safety events/measurements from these participants that occurred at and after Week 0 will be included in this group.
- Combined JNJ-77242113: all participants as described above in the Placebo → JNJ-77242113 and the JNJ-77242113 groups.

Summary through Week 160:

- Safety data through Week 160 will be summarized for participants exposure to JNJ-77242113.

4.5.1. Extent of Exposure

The extent of exposure will be summarized for randomized participants who received at least one study agent administration. Distribution of study agent lot through Week 52 reporting period and through Week 156 will be summarized. Descriptive statistics for the average daily dose of study intervention and duration of exposure to study medication (weeks) will be summarized.

The total duration of exposure to study medication (weeks) will be summarized.

Total duration of exposure = last day of study medication - first day of study medication + 1.

Study intervention compliance will be summarized descriptively. See Appendix 6 for further details.

4.5.2. Adverse Events

The verbatim terms used in the CRF by investigators to identify adverse events will be coded using MedDRA. Any AE occurring at or after the initial administration of study intervention up to 4 weeks after the last dose or treatment discontinuation is considered to be treatment emergent. If

the event occurs on the day of the initial administration of study intervention, and either event time or time of administration are missing, then the event will be assumed to be treatment emergent. If the event date is recorded as partial or completely missing, then the event will be considered to be treatment emergent unless it is known to be prior to the first administration of study intervention based on partial onset date or resolution date. All reported treatment-emergent adverse events will be included in the analysis. For each adverse event, the number and percentage of participants who experience at least 1 occurrence of the given event will be summarized by intervention group.

Summary tables will be provided for treatment-emergent adverse events:

- AEs
- Serious AEs (SAE)
- AEs of Special Interest (AESIs)
- AEs leading to discontinuation of study intervention
- AEs of severe intensity
- AEs related to study intervention
- AE of psoriasis

Safety will also be assessed by participants' baseline BSA category. In addition to the summary table, listings will be provided for participants who:

- Had SAEs
- Had AESIs
- Had AEs leading to discontinuation of study intervention
- Had AEs of severe intensity
- Had AEs for psoriasis
- Had suicidal ideation or suicidal behavior
- Had serious hypersensitivity including anaphylactic reactions

A listing of participants who died will be provided.

Since safety should be assessed relative to follow-up, most AE summary tables will include average weeks of follow-up for each intervention group.

An AESI, which may be serious or non-serious, is an AE of scientific and medical concern specific to the sponsor's product or program, for which ongoing monitoring and expedited communication (within 24 hours) by the investigator to the sponsor is warranted. The AESIs for JNJ-77242113 are active TB, malignancy, and possible Hy's Law cases.

A **possible Hy's law case** is defined by the occurrence of ALT/AST ≥3×ULN, together with Tbili ≥2×ULN or INR >1.5 (if measured).

Adjudicated results for events such as Cardiovascular events, TB and Opportunistic Infections will be summarized.

4.5.3. Additional Safety Assessments

4.5.3.1. Clinical Laboratory Tests

Clinical laboratory tests will be displayed for the participants included in the safety analysis set.

Box plots of laboratory measurements and change from baseline will be provided for select laboratory measurements.

Applicable laboratory results will be graded according to National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI-CTCAE). The proportion of participants with post-baseline values by maximum toxicity grade for clinical laboratory tests will be summarized by study intervention group. Participants with toxicity grades ≥2 will be listed.

In addition, for selected laboratory parameters (i.e., ALT, AST), ULN will also be used to identify abnormal laboratory test results. Lipid and hs-CRP will be summarized. The 4-week window after the last dose or treatment discontinuation will also be applied.

4.5.3.2. Vital Signs

Incidence of treatment-emergent markedly abnormal vital signs during intervention, as defined in Table 5, will be summarized for participants who had a baseline assessment and at least 1 postbaseline assessment for that vital sign. A listing of participants with treatment-emergent markedly abnormal vital signs will be presented. The 4-week window after the last dose or treatment discontinuation will also be applied.

Table 5: Markedly Abnormal Vital Signs

Vital Sign	Criteria
Pulse	>120 bpm and with >30 bpm increase from baseline
	<50 bpm and with >20 bpm decrease from baseline
Systolic blood pressure	>180 mm Hg and with >40 mm Hg increase from baseline
	<90 mm Hg and with >30 mm Hg decrease from baseline
Diastolic blood pressure	>105 mm Hg and with >30 mm Hg increase from baseline
	<50 mm Hg and with >20 mm Hg decrease from baseline
Respiratory rate	>20 breaths per minute
Temperature	>38ºC and with ≥1ºC increase from baseline

4.5.3.3. Columbia-Suicide Severity Rating Scale

The C-SSRS will be used as a screening tool to prospectively evaluate suicidal ideation and behavior among study participants as part of a comprehensive evaluation of safety. The C-SSRS defines 5 subtypes of suicidal ideation and 4 possible suicidal behaviors, as well as non-suicidal self-injurious behavior and completed suicide.

Two versions of the C-SSRS will be used in this study, the *Baseline/Screening* version and the *Since Last Visit* version. The *Baseline/Screening* version will be conducted during the screening visit and the *Since Last Visit* version will be conducted at all other visits.

The investigator or trained study-site personnel will interview the participant in a private place and complete the C-SSRS on the eCOA device. At the conclusion of each assessment, the trained personnel administering the C-SSRS will determine the level of suicidal ideation or behavior, if any. They will then determine the next course of action if any level of suicidal ideation or behavior is reported. The participant should not be released from the site until the C-SSRS has been reviewed by the investigator and the participant's risk has been assessed and follow-up determined, as appropriate.

The following are C-SSRS categories and have binary responses (yes/no). A "yes" response to any C-SSRS category will be assigned a score as below:

Suicidal Ideation (1-5)

1 = Wish to be Dead

2 = Non-specific Active Suicidal Thoughts

3 = Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act

4 = Active Suicidal Ideation with Some Intent to Act, without Specific Plan

5 = Active Suicidal Ideation with Specific Plan and Intent

Suicidal Behavior (6-10)

6 = Preparatory Acts or Behavior

7 = Aborted Attempt

8 = Interrupted Attempt

9 = Actual Attempt (non-fatal)

10 = Completed Suicide

If no events qualify for a score of 1 to 10, a score of 0 will be assigned (0 = "Negative result [no suicidal ideation or behavior]"). Higher scores indicate greater severity.

Suicidal ideation and behavior will be summarized by C-SSRS categories and intervention group based on the most severe/maximum post baseline C-SSRS outcome or AE of suicidal ideation, suicidal behavior excluding completed suicide, or completed suicide through Week 16, through reporting period at Week 52 DBL, and through Week 160. The baseline is defined as the most severe/maximum C-SSRS score at either screening or Week 0.

The maximum score assigned for each participant will also be summarized into one of three broad categories: No suicidal ideation or behavior, suicidal ideation, and suicidal behavior. A shift table for change in C-SSRS categories of no suicidal ideation or behavior, suicidal ideation, and suicidal behavior from baseline through Week 16, through the reporting period at Week 52 DBL, and through Week 160 will be presented, where the baseline category is based on C-SSRS score and the post baseline is based on C-SSRS or AE data.

4.5.3.4. Tanner Staging

A listing for Tanner staging will be provided for adolescent participants.

4.5.3.5. PHQ-9

The PHQ-9 is self-administered, 9-item questionnaire measuring symptoms and severity of depression. The recall period for all items is the past 2 weeks. The items include: diminished interest or pleasure, depressed mood, insomnia/hypersomnia, fatigue or loss of energy, weight loss or weight gain/appetite loss or appetite gain, feelings of worthlessness, diminished concentration/indecisiveness, psychomotor agitation/retardation, and thoughts of death/suicide. Each item is rated on a 4-point Likert scale ranging from 0 “not at all” to 3 “nearly every day”. Higher scores indicate more severe depressive symptoms. Higher scores indicate more severe depressive symptoms. The PHQ-9 scores for depression range from 0 to 27 with higher scores indicating worse state (more severe depressive symptoms). A score of 5 to 9 is considered to be minimal symptoms of depression. A score of 10 to 14 is considered minor depression, dysthymia, or mild major depression. A score of 15 to 19 is considered to indicate moderately severe major depression, and a score ≥20 is considered to be severe major depression.

- The shift table will be provided to summarize the shift in values from baseline to postbaseline.
- A listing will be produced for all PHQ-9 score including unscheduled visits for participants with PHQ-9 score ≥15.

4.5.3.6. Electrocardiogram

Electrocardiogram data will be summarized by ECG parameter. Descriptive statistics will be calculated at baseline and for observed values and change from baseline at each scheduled time point.

In addition, summary of post-baseline ECG abnormalities different from Week 0 and a listing of subjects with any post-baseline ECG abnormalities different from Week 0 measurement will be provided. The 4-week window after the last dose or treatment discontinuation will also be applied.

4.6. Other Analyses

4.6.1. Pharmacokinetics

4.6.1.1. JNJ-77242113 Concentrations

PK analyses will be performed on the PK analysis set, defined as participants who have received at least 1 dose of JNJ-77242113 and have at least 1 valid blood sample drawn for PK analysis after their first dose of JNJ-7724113.

Descriptive statistics (N, mean, SD, median, range, coefficient of variation [%CV] and IQ range) will be used to summarize JNJ-77242113 concentrations at post-dose sampling time intervals classified as peak, intermediate and trough. PK data may be displayed graphically, such as mean +/- SD PK concentrations over time by intervention group.

The following analyses will be performed as appropriate.

- Summary of plasma JNJ-77242113 concentration over time
- Proportion of participants with plasma JNJ-77242113 concentration below the lowest quantifiable concentration in a sample at each visit
- Plots of median plasma JNJ-77242113 concentrations over time

JNJ-77242113 concentrations below the lowest quantifiable concentration will be imputed as zero in the summary statistics. All plasma concentrations below the lowest quantifiable concentration or missing data will be labeled as such in the concentration database.

All participants and samples excluded from the analysis will be clearly documented.

PK data may be displayed graphically, such as mean +/- SD PK concentrations over time by weight group.

If sufficient data are available, then population PK analysis using plasma concentration-time data of JNJ-77242113 will be performed using nonlinear mixed-effects modeling. Data may be combined with those of other selected studies to support a relevant structural model. Available baseline participant characteristics (eg, demographics, laboratory variables, race) will be evaluated as potential covariates affecting PK parameters. Details will be given in a population PK analysis plan and the results of the analysis will be presented in a separate report.

4.6.1.2. Data Handling Rules

Unless otherwise specified, the following data handling rules will apply to PK sample analyses:

- Plasma concentration summaries will be based on the actual treatment received.
- All plasma concentration summaries for a particular timepoint will include data obtained from treated participants at the timepoint of interest without imputing any missing data.

- A concentration not quantifiable (below the lower limit of quantification) will be treated as 0 in the summary statistics and shown as the lower limit of quantification (< LLOQ) in the data listings.
- The data from a participant who discontinued study agent will be excluded from the by-visit data analyses from that point onwards. In addition, the data from a participant who received an incomplete/ incorrect or skipped dose based on the dose prior to the PK sample collection will be excluded for that visit.

4.6.2. Immunogenicity

4.6.2.1. Antibodies to JNJ-77242113

The incidence and titers of anti-JNJ-77242113 antibodies will be summarized for all participants who receive at least 1 dose of JNJ-77242113 and have appropriate samples for detection of antibodies to JNJ-77242113 (ie, participants with at least 1 sample obtained after their first dose of JNJ-77242113).

Sample ADA status and sample titer, as well as the cumulative subject ADA status and peak titer through the visit will be coded and provided by the bioanalytical group.

Participants with treatment-emergent antibodies to JNJ-77242113 include participants with treatment-induced antibodies to JNJ-77242113 and treatment-boosted antibodies to JNJ-77242113.

Participants with treatment-induced antibodies to JNJ-77242113 will have a sample that is negative for antibodies to JNJ-77242113 prior to JNJ-77242113 administration and at least one sample that is positive for antibodies to JNJ-77242113 after JNJ-77242113 administration.

Participants with treatment-boosted antibodies to JNJ-77242113 will have a sample that is positive for antibodies to JNJ-77242113 prior to JNJ-77242113 administration and at least one sample that is positive for antibodies to JNJ-77242113 after JNJ-77242113 with a 4-fold increase in titer over baseline.

If the titer remains the same or increases less than 4-fold after intervention or if ADA titer reduces or ADA disappears, the participant is classified as “treatment-emergent ADA negative”. Participants with baseline negative and all post intervention samples negative are also classified as “treatment-emergent ADA negative”. Participants that are unavailable for treatment-emergent ADA following intervention will be classified as “participants with baseline samples only”, ie, no appropriate sample is available after intervention.

The antibodies to JNJ-77242113 summary and analysis will be based on the observed data; therefore, no imputation of missing data will be performed. Note: participant status is through each visit, thus, participant status and peak titers may change as the study progresses over time. Therefore, the ‘subject ADA status’ at a visit represents the cumulative ADA status through that visit. For example, if a study has a lock at Week 16, datasets through Week 16 will have participant level status (eg, negative) but at Week 52, they may have developed ADA and the participant status

becomes "treatment-emergent ADA positive" from the interim to the final DBL. Peak titers can also change (increase) if a higher titer occurs after an initial DBL.

Incidence of antibody (evaluable, treatment-emergent ADA positive, treatment-emergent ADA negative) status will be summarized.

In addition, listings of participants with baseline positive ADA samples, participants who are classified as positive for treatment-emergent antibodies to JNJ-77242113 and participants who discontinue the study agent by antibodies to JNJ-77242113 status may be presented. The sample antibody status, and the titer will be listed by visit. This listing will also provide information regarding JNJ-77242113 plasma concentration and select efficacy endpoints.

4.6.2.2. Other Immunogenicity Analyses

The following analyses will be conducted if there is a sufficient number (eg, ≥20) of participants that are ADA positive.

Treatment-induced Onset (data summarized will be exclusive to baseline negative participants)

Descriptive statistics for days from first administration of study intervention to the date of first instance of treatment-induced ADA (positive for treatment-induced antibody) will be summarized.

Number of days until first instance of treatment-induced ADA = (First date for positive antibody-Date of first administration of study intervention+1).

Duration of Treatment-induced ADA (data summarized is exclusive to baseline negative participants).

The duration of treatment-induced ADA refers to the longevity of treatment-induced ADA.

Descriptive statistics for duration of treatment-induced ADA among those who developed antibody will be summarized.

4.6.2.3. Neutralizing Antibodies to JNJ-77242113

The incidence of neutralizing antibodies (NAbs) to JNJ-77242113 will be summarized for participants who are positive for antibodies to JNJ-77242113 and have samples evaluable for NAbs JNJ-77242113.

4.6.2.4. Antibody vs Efficacy/PK/Safety

To explore the relationship between antibodies to JNJ-77242113 status and plasma JNJ-77242113 concentrations and efficacy, the following analysis may be performed as appropriate:

- Summary of select clinical response (e.g., IGA 0/1 (overall) with 2-grade improvement, and ss-IGA 0/1 among participants with baseline ss-IGA ≥3) by antibody to JNJ-77242113 status.
- Summary of plasma JNJ-77242113 concentration over time by antibody to JNJ-77242113 status.

- Summary of plasma JNJ-77242113 concentration over time by first positive ADA timepoint
- Summary of safety by antibody to JNJ-77242113 status.
- Plots of median (IQ) plasma JNJ-77242113 concentrations over time by antibody to JNJ-77242113 status.
- Plots of median (IQ) plasma JNJ-77242113 concentrations over time by first positive ADA timepoint.

4.6.3. Pharmacokinetic/Pharmacodynamic Relationships

To explore the relationship between JNJ-77242113 plasma concentrations and efficacy endpoints, the following analyses may be explored:

- The relationship between JNJ-77242113 plasma trough concentrations and IGA (overall) 0/1 responses and ss-IGA 0/1 response among participants with baseline ss-IGA ≥3 at Week 16 and/or other timepoints may be explored. The relationship between JNJ-77242113 plasma concentration and other endpoints may also be explored.

If data permit, the relationships between JNJ-77242113 concentrations and efficacy may be analyzed graphically. If any visual trend is observed, a suitable exposure-response (E-R) model may be developed to describe the E-R relationship. Details will be given in an E-R analysis plan and results will be presented in a separate technical report.

4.6.4. Biomarkers

Planned biomarker analyses may be deferred if emerging study data show no likelihood of providing useful scientific information.

Changes in biomarkers over time will be summarized by intervention group. Associations between baseline levels and changes from baseline in select markers and clinical response to treatment will be explored. Biomarker analyses will be summarized in separate technical reports.

4.6.5. Pharmacogenomic Analyses

Genetic (DNA) analyses will be conducted only in participants who sign the consent form to participate in the optional pharmacogenetics substudy.
These results are considered exploratory and will be presented in a separate report.

4.6.6. Subgroup Analyses

4.6.6.1. Definition

To evaluate the consistency of the primary efficacy endpoint IGA (overall) 0 or 1 responders and select key secondary endpoints at Week 16, subgroup analyses of the primary endpoint and select key secondary endpoints for IGA 0 and special areas (ss-IGA score of 0 or 1, PSSI 90 response, sPGA-G score of 0 or 1, and hf-PGA score of 0 or 1) may be performed when the number of participants in the subset permits.

For each of the subgroups defined below, the difference between the JNJ-77242113 treatment group and placebo group in the proportion of the IGA (overall) 0) or 1 responders, and select key

secondary endpoints for IGA 0 and special areas (ss-IGA score of 0 or 1, PSSI 90 response, sPGA-G score of 0 or 1, and hf-PGA score of 0 or 1) at Week 16, and their 95% confidence intervals will be calculated. No p-values will be provided.

Subgroup	**Definition**
Baseline demographics:	
Region	Define based on UN guidance as per the M49 standard • AMER • EU • APAC
Sex	• male • female • other
Race	• American Indian or Alaska Native • Asian • Black or African American • Native Hawaiian or other Pacific Islander • White • Multiple • Not Reported • Unknown
Ethnicity	• Hispanic or Latino • Not Hispanic or Latino • Not Reported • Unknown
Age Group (years)	• <18 • ≥18 to <45 years • ≥45 to <65 years • ≥65 years
BMI	• normal <25 kg/m^2 • overweight 25-<30 kg/m^2 • obese ≥30 kg/m^2
Body Weight Group (kg)	• ≤90 kg • >90 kg
Baseline disease characteristics:	
Age at diagnosis (years)	• <median • ≥median
Psoriasis disease duration (years)	• <median • ≥median
Baseline PASI	• <12 • ≥12 to <20 • ≥20
Baseline IGA	• =4 • =3 • =2
Baseline BSA	• <10% • ≥10% to <20% • ≥20%
Baseline DLQI	• <10 • ≥10
Psoriatic arthritis	• Yes

	• No
Psoriasis medication history:	
Phototherapy (ultraviolet B light [UVB] or psoralen and ultraviolet A light therapy [PUVA])	• Never used • Ever used
Systemics (Conventional non-biologic systemics, novel non-biologic systemics, 1,25-vitamin D3 and analog, phototherapy, biologics)	• Never used • Ever used
Conventional non-biologic systemics (PUVA, MTX, cyclosporine, acitiretin, azathioprine, or fumarate)	• Never used • Ever used
Novel non-biologic systemics (apremilast, deucravacitinib, or tofacitinib)	• Never used • Ever used
Biologics (etanercept, infliximab, adalimumab, ustekinumab, briakinumab, secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab, alefacept, efalizumab, natalizumab, certolizumab pegol)	• Never used • Ever used
Anti-TNFα agent (etanercept, infliximab, certolizumab pegol, or adalimumab)	• Never used • Ever used
IL-12/23 inhibitors (ustekinumab, briakinumab)	• Never used • Ever used
IL-23 inhibitors (guselkumab, tildrakizumab, Risankizumab)	• Never used • Ever used
IL-17 inhibitors (secukinumab, ixekizumab, or brodalumab)	• Never used • Ever used

In addition, for each of the subgroups defined below, the difference between the JNJ-77242113 treatment group and placebo group in the proportion of IGA (overall) responses (IGA 0, IGA 0 or 1 and at least a 2-grade improvement from baseline) at Week 16, and their 95% confidence intervals will be calculated by baseline special area severity.

Subgroup	**Definition**
Baseline ss-IGA	• = 0 • = 1 or 2 • = 3 • = 4
Baseline sPGA-G	• = 0 • = 1 or 2 • = 3 • = 4 or 5
Baseline hf-PGA	• = 0 • = 1 or 2 • = 3 • = 4

4.7. Interim Analysis

No formal interim analysis is planned. However, a Data Monitoring Committee (DMC) will monitor the safety for this study.

4.7.1. Data Monitoring Committee or Other Review Board

An independent external DMC will monitor data on an ongoing basis to ensure the continuing safety of the participants enrolled in the psoriasis studies and to provide recommendations to the Sponsor Committee. The DMC will make recommendations concerning the conduct of the study including changes to the informed consent.

The DMC will consist of 5 members with 4 clinicians (including 2 dermatologists, one cardiologist and 1 infectious disease specialist), and one statistician with all DMC members having voting rights.

The major function of the DMC is to monitor the safety of the study agent and provide recommendations for placing the study on hold or stopping the study in the event of serious safety concerns. The content of the safety summaries, the DMC roles and responsibilities and the general procedures (including communication plan) and their possible recommendations on study conduct will be defined and documented in the DMC Charter prior to the first DMC review.

In addition, during the study, the sponsor's study responsible physician (or designee) will regularly review blinded safety data from the sites and notify the DMC and appropriate sponsor personnel of any issues.

5. SAMPLE SIZE DETERMINATION

This study is designed to evaluate the efficacy of JNJ-77242113 vs. placebo. The sample size was also chosen to ensure a reasonable safety database to assess the overall safety of JNJ-77242113. These study objectives were taken into consideration in determining the sample size.

The assumptions of the sample size and power calculations for the primary endpoint were based on placebo response rates from the historical psoriasis clinical studies and response rates observed from the JNJ-77242113 Phase 2b study (77242113PSO2001) for JNJ-77242113.

- The proportion of placebo participants achieving an IGA (overall) score of 0 or 1 and at least 2-grade improvement from baseline at Week 16 is 8%.
- The proportion of JNJ-77242113 participants achieving an IGA (overall) score of 0 or 1 and at least 2-grade improvement from baseline at Week 16 is 64%.

Based on the above assumptions, a total of approximately 300 participants to be randomized in a 2:1 ratio to JNJ-77242113 (n=200) or placebo (n=100) at Week 0 will provide >99% power to detect significant difference for the primary endpoint at a 2-sided significance level of 0.05.

Table 6 provides the power for detecting a treatment difference under varying assumptions for the primary endpoint.

Table 6:	**Power to Detect a Treatment Effect Based on Different Proportions of Participants Achieving the Primary Endpoints**	
Placebo (n=100)	**JNJ-77242113 (n=200)**	**Power**
8%	60%	>99%
	65%	**>99%**
	70%	>99%

Note: The power calculation is based on a 2-sample Z-test (pooled variance) under the normal distribution approximation.

The assumptions of the sample size and power calculations for select key secondary endpoints were based on the data from:

- the guselkumab Phase 3 psoriasis studies (CNTO1959PSO3001 [VOYAGE 1] and CNTO1959PSO3002 [VOYAGE 2]),
- the JNJ-77242113 Phase 2b psoriasis study (77242113PSO2001 [FRONTIER 1]) and the secukinumab SCALP psoriasis study for scalp psoriasis,
- the ixekizumab IXORA-Q and 77242113PSO2001 studies for genital psoriasis,
- the CNTO1959PSO3001, CNTO1959PSO3002, and 77242113PSO2001 studies for hand/foot psoriasis.

To achieve at least a 90% power at a two-sided significance level of 0.05, approximately 75 participants are needed for each subpopulation (ie, baseline hf-PGA score ≥3, baseline sPGA-G score ≥3, or baseline ss-IGA score ≥3). Of note, these 3 subpopulations are not mutually exclusive.

Table 7 provides the sample size for detecting a treatment difference under varying assumptions for the selected key secondary endpoints for special areas.

Table 7:	**Sample Size Needed to Achieve 90% Power to Detect a Treatment Difference in the Key Secondary Endpoints for Specific Special Areas Under Varying Assumptions**		
Placebo	**JNJ-77242113**	**Delta**	**Sample Size**
15%	50%	35%	93 (31:62)
	55%	**40%**	**75 (25:50)**
	60%	45%	60 (20:40)

Note: The sample size calculations are based on a 2-sample Fisher's exact test.

6. SUPPORTING DOCUMENTATION

6.1. Appendix 1 Participant Dispositions

Screened participants and reason for screen failures will be summarized overall.

The number of participants in the following disposition categories will be summarized throughout the study by intervention group and overall:

- Participants randomized
- Participants who received study intervention
- Participants who completed the study
- Participants who discontinued study intervention
- Reasons for discontinuation of study intervention
- Participants who terminated study prematurely
- Reasons for termination of study

The above categories will include summaries through Week 16, through the reporting period (date of last participant completing Week 52 visit), and through Week 160.

Listings of participants will be provided for the following categories:

- Participants who discontinued study intervention
- Participants who terminated study prematurely
- Participants who were unblinded during the study period
- Participants who were randomized yet did not receive study intervention.
- Participants who were randomized with incorrect stratum will be provided

6.2. Appendix 2 Baseline Characteristics and Demographics

The number of participants in each analysis set will be summarized and listed by intervention group and overall. In addition, the distribution of participants by region, country, and site ID will be presented unless otherwise noted.

Table 8 presents a list of the demographic variables that will be summarized by intervention group and overall for the full analysis set. Demographics will also be summarized by special areas using FAS.

Table 8: Demographic Variables

Continuous Variables:	**Summary Type**
Age (years)	Descriptive statistics (N, mean, standard deviation [SD], median and range [minimum and maximum], and IQ range).
Weight (kg)	
Height (cm)	
BMI (kg/m^2)	
Categorical Variables	
Age (<18 years, ≥18 to <45 years, ≥45 to <65 years, ≥65 years)	Frequency distribution with the number and percentage of participants in each category.
Sex (male, female, undifferentiated, unknown)	
Weight (≤90 kg, >90 kg)	
Race[a] (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Multiple, Not Reported, Unknown)	
Ethnicity (Hispanic or Latino, not Hispanic or Latino, Not Reported, Unknown)	
BMI (normal <25 kg/m^2, overweight ≥25 to <30 kg/m^2, obese ≥30 kg/m^2)	

[a] If multiple race categories are indicated, the Race is recorded as 'Multiple'

Participants' Psoriasis Baseline Clinical Disease Characteristics [eg, psoriasis disease duration (years), age at diagnosis (years), BSA (%), IGA score, PASI score, ss-IGA score, f-PGA score, mNAPSI, hf-PGA score, sPGA-G score, and PSSI total score] will be summarized. Patient Reported Outcomes at baseline [e.g. PSSD (sign, symptom score), DLQI, CDLQI, Scalp Itch NRS score, PROMIS-29 (PCS, and MCS), GenPs-SFQ, GPSS symptom score, ppQLI (hand score, foot score), PsA pain, PsA disease activity] will be summarized. In addition, summaries of participants' medical history, alcohol intake, and smoking status will be provided by treatment group.

6.3. Appendix 3 Protocol Deviations

In general, the following list of major protocol deviations may have the potential to impact participants' rights, safety or well-being, or the integrity and/or result of the clinical study. Participants with major protocol deviations will be identified prior to database lock and the participants with major protocol deviations will be summarized by category.

- Developed withdrawal criteria but not withdrawn
- Entered but did not satisfy criteria
- Received a disallowed concomitant treatment
- Received wrong treatment or incorrect dose
- Other

A listing of participants with major protocol deviations will also be provided by randomized treatment group.

QTL parameters and thresholds are defined and will be monitored in this study. QTL parameters will be summarized. More details are described in the Integrated Analytical Risk-Based Monitoring Plan.

6.4. Appendix 4 Prior and Concomitant Medications

Prior medications are defined as any therapy used before the day of first dose (partial or complete) of study intervention. Previous psoriasis medications/therapy will be summarized by intervention group.

Concomitant medications will be coded using the World Health Organization Drug Dictionary (WHO-DD). Concomitant medications are defined as any therapy used on or after the same day as the first dose of study intervention, including those that started before and continued after the first dose of study intervention.

Summaries of concomitant medications will be presented by anatomic and therapeutic class (ATC) term, and intervention group. The proportion of participants who receive each concomitant medication will be summarized as well as the proportion of participants who receive at least 1 concomitant medication.

Participants' psoriasis medication history with topical agents, phototherapy, non-biologic systemic therapies, and biologic medications will be summarized by treatment group for all randomized participants. If data are available, total cumulative duration of treatment with these medications will be summarized. In addition, reasons for which participants discontinued previous systemic therapies (contraindication, inadequate response, intolerance [ie, AEs], or other) will be summarized by randomized treatment group.

Participants who received concomitant corticosteroids for indications other than psoriasis and/or psoriatic arthritis will be listed. Participants with concomitant prophylactic treatments for latent TB infection will also be listed.

6.5. Appendix 5 Medical History

Summaries of participants' medical history, general medical history, alcohol intake, and smoking status will be provided by treatment group. In addition, the distribution of participants by prior biologic use (yes/no) and type of biologic therapy will also be provided.

6.6. Appendix 6 Intervention Compliance

Treatment compliance will be assessed through Week 16 and through Week 52 based on the full analysis set (FAS). Compliance will be summarized descriptively (sample size, mean, standard deviation, median, and range). Overall compliance will be categorized as >120%, 80 to ≤120%, and <80%.

Compliance will be calculated as follows:

Compliance (%) = (actual number of tablets taken/total number of tablets supposed to be taken) x100.

In addition, treatment compliance will be summarized by protocol deviation reporting for incorrect study agent administration or for treatment compliance that is less than 80% or greater than 120% of the number of expected tablets during participation in this study, unless study intervention is withheld for safety reasons.

6.7. Appendix 7 Medications of Special Interest

Other medication or therapy that could improve psoriasis (Intercurrent Event 2)
(1) any topical therapies used for psoriasis (with the exception of topical moisturizers and shampoos containing tar or salicylic acid only)

(2) any phototherapy or systemic corticosteroid used for psoriasis with the exception of intra-articular corticosteroids

(3) any other anti-psoriatic systemic therapy or biologic therapy

(4) Phototherapy of UVB or PUVA or any other phototherapy used for psoriasis.

Psoriasis Concomitant Medications

Topical Therapy

Week 0 to Week 52

Medicated shampoos containing salicylic acid and bland emollients are allowed on all body regions but should not be used within 24 hours before any study visit. Nonmedicated shampoos may be used on the day of the study visit.

Other topical therapies that could affect psoriasis evaluations including but not limited to topical corticosteroids, topical calcineurin inhibitors, vitamin D analogs, vitamin A analogs, retinoids, tar, anthralin, calcipotriene, tazarotene, methoxsalen, trimethylpsoralens, fumarate, PDE4 inhibitors, topical JAK inhibitors, aryl hydrocarbon receptor-modulating agents; shampoos that contain corticosteroids, coal tar, or vitamin D3 analogs; and herbal treatments and traditional Taiwanese, Korean, or Chinese medicines are not permitted.

Week 52 to Week 160

After the Week 52 visit, most topical therapies are permitted for treatment of psoriasis; ultrahigh potency corticosteroids and topical JAK inhibitors are still prohibited during this period.

Phototherapy or Systemic Therapy

The use of phototherapy or systemic medications that could affect psoriasis evaluations is not permitted at any time during the study.

These medications include:

- those targeted for reducing TNFα (including but not limited to adalimumab, infliximab, or etanercept).
- drugs targeted for reducing IL-12/23, IL17, or IL-23 (including but not limited to ustekinumab, briakinumab, guselkumab, tildrakizumab, secukinumab, risankizumab, ixekizumab, or brodalumab).

- alpha-4 integrin antagonists (including but not limited to natalizumab).
- JAK inhibitors (including but not limited to TYK2 inhibitors).
- PDE4 inhibitors (including but not limited to apremilast).
- oral and injectable (IV, intramuscular, or intralesional) corticosteroids.
- any other conventional systemic therapies that could affect psoriasis evaluations (including but not limited to methotrexate, cyclosporine A, acitretin, or other retinoids).
- antimalarial agents.
- herbal treatments.
- traditional Taiwanese, Korean, or Chinese medicines.

Concomitant Medications for Indications Other Than Psoriasis

The use of systemic corticosteroids for indications other than psoriasis should be limited to situations for which, in the opinion of the treating physician, there are no adequate alternatives. Systemic corticosteroids should be used on a short-term basis, preferably for ≤2 weeks. Longer term use of corticosteroids should be discussed with the medical monitor or designee and may require discontinuation of study intervention. Inhaled, otic, ocular, nasal, or other routes of mucosal delivery of corticosteroids are allowed throughout the study. After Week 16, intra-articular corticosteroids are allowed for indication other than psoriasis. Vitamin D3 and analogs for dietary supplementation are permitted.

6.8. Appendix 8 Laboratory Toxicity Grading

The grading scale use for lab assessments is based on 'NCI-CTCAE v5.0'.

If a laboratory value falls within the grading as specified below but also within the laboratory normal limits, the value is considered to be normal and will be reset to grade 0.

Pre-baseline measurements will use the same grading ranges as applied to baseline measurements. In case a test has two sets of ranges – one for baseline normal and one for baseline abnormal, the one for baseline normal will be applied for all measurements taken pre-baseline and on baseline.

Text in gray italic in the table is present in the grading scale, but is not applied by Janssen when grading lab data.

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	J&J Implementation Notes
Blood and lymphatic system disorders					
Anemia	Hemoglobin (Hgb) <LLN - 10.0 g/dL; <LLN - 6.2 mmol/L; <LLN - 100 g/L	Hemoglobin (Hgb) <10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 - 80g/L	Hemoglobin (Hgb) <8.0 g/dL; <4.9 mmol/L; <80 g/L; *transfusion indicated*	*Life-threatening consequences; urgent intervention indicated*	Clinical signs and symptoms are not taken into consideration for grading.
Leukocytosis	-	-	>100,000/mm3; >100 x 10e9 /L	*Clinical manifestations of leucostasis; urgent intervention indicated*	Clinical signs and symptoms are not taken into consideration for grading; Added ranges in SI unit (x 10e9 /L)
Investigations					
Activated partial thromboplastin time prolonged	>ULN - 1.5 x ULN	>1.5 - 2.5 x ULN	>2.5 x ULN; *bleeding*	-	Clinical signs and symptoms are not taken into consideration for grading.
Alanine aminotransferase increased	>ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	Ranges defined for "abnormal baseline" are applied only if baseline > ULN. If baseline < LLN, then ranges for "normal baseline" are applied.
Alkaline phosphatase increased	>ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal	>2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	Ranges defined for "abnormal baseline" are applied only if baseline > ULN. If baseline < LLN, then ranges for "normal baseline" are applied.
Aspartate aminotransferase increased	>ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	Ranges defined for "abnormal baseline" are applied only if baseline > ULN. If baseline < LLN, then ranges for "normal baseline" are applied.
Blood bilirubin increased	>ULN - 1.5 x ULN if baseline was normal;	>1.5 - 3.0 x ULN if baseline was normal;	>3.0 - 10.0 x ULN if baseline was normal;	>10.0 x ULN if baseline was normal;	Ranges defined for "abnormal baseline" are

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	J&J Implementation Notes
	> 1.0 - 1.5 x baseline if baseline was abnormal	>1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 10.0 x baseline if baseline was abnormal	>10.0 x baseline if baseline was abnormal	applied only if baseline > ULN. If baseline < LLN, then ranges for "normal baseline" are applied.
CD4 lymphocytes decreased	<LLN - 500/mm3; <LLN - 0.5 x 10e9 /L	<500 - 200/mm3; <0.5 - 0.2 x 10e9 /L	<200 - 50/mm3; <0.2 x 0.05 - 10e9 /L	<50/mm3; <0.05 x 10e9 /L	
Cholesterol high	>ULN - 300 mg/dL; >ULN - 7.75 mmol/L	>300 - 400 mg/dL; >7.75 - 10.34 mmol/L	>400 - 500 mg/dL; >10.34 - 12.92 mmol/L	>500 mg/dL; >12.92 mmol/L	
CPK increased	>ULN - 2.5 x ULN	>2.5 x ULN - 5 x ULN	>5 x ULN - 10 x ULN	>10 x ULN	CPK (Creatine Phosphokinase) and CK (Creatine Kinase) are synonyms
Creatinine increased	>ULN - 1.5 x ULN	>1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	>3.0 x baseline; >3.0 - 6.0 x ULN	>6.0 x ULN	
Fibrinogen decreased	<1.0 - 0.75 x LLN; if abnormal, <25% decrease from baseline	<0.75 - 0.5 x LLN; if abnormal, 25 - <50% decrease from baseline	<0.5 - 0.25 x LLN; if abnormal, 50 - <75% decrease from baseline	<0.25 x LLN; if abnormal, 75% decrease from baseline; absolute value <50 mg/dL	Ranges defined for "abnormal" are applied only on values < LLN. Grade 0 will be assigned to values > ULN.
GGT increased	>ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal	>2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	Ranges defined for "abnormal baseline" are applied only if baseline > ULN. If baseline < LLN, then ranges for "normal baseline" are applied.
Haptoglobin decreased	<LLN	-	-	-	
Hemoglobin increased	Increase in >0 - 2 g/dL; Increase in >0 - 20 g/L	Increase in >2 - 4 g/dL; Increase in >20 - 40 g/L	Increase in >4 g/dL; Increase in >40 g/L	-	The increase indicates the level of increase above normal (above ULN). Applied as, e.g. grade 1 (g/dL): >ULN – ULN+2 g/dL; Added ranges in SI unit (g/L).
INR increased	>1.2 - 1.5; *>1 - 1.5 x baseline if on anticoagulation;*	>1.5 - 2.5; *>1.5 - 2.5 x baseline if on anticoagulation;*	>2.5; *>2.5 x baseline if on anticoagulation;* *bleeding*	-	Concomitant therapy or clinical signs and symptoms are not taken

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	J&J Implementation Notes
	monitoring only indicated	*dose adjustment indicated*			into consideration for grading.
Lipase increased	>ULN - 1.5 x ULN	>1.5 - 2.0 x ULN; *>2.0 - 5.0 x ULN and asymptomatic*	>2.0 - 5.0 x ULN with signs or symptoms; *>5.0 x ULN and asymptomatic*	>5.0 x ULN and with signs or symptoms	"Asymptomatic" ranges are not taken into consideration for grading, i.e. worst case grading is applied.
Lymphocyte count decreased	<LLN - 800/mm3; <LLN - 0.8 x 10e9/L	<800 - 500/mm3; <0.8 - 0.5 x 10e9 /L	<500 - 200/mm3; <0.5 - 0.2 x 10e9 /L	<200/mm3; <0.2 x 10e9 /L	
Lymphocyte count increased	-	>4000/mm3 - 20,000/mm3; >4 - 20 x 10e9 /L	>20,000/mm3; >20 x 10e9 /L	-	Added ranges in SI unit (x 10e9 /L).
Neutrophil count decreased	<LLN - 1500/mm3; <LLN - 1.5 x 10e9 /L	<1500 - 1000/mm3; <1.5 - 1.0 x 10e9 /L	<1000 - 500/mm3; <1.0 - 0.5 x 10e9 /L	<500/mm3; <0.5 x 10e9 /L	Both Neutrophils and segmented neutrophils are graded using these criteria.
Platelet count decreased	<LLN - 75,000/mm3; <LLN - 75.0 x 10e9 /L	<75,000 - 50,000/mm3; <75.0 - 50.0 x 10e9 /L	<50,000 - 25,000/mm3; <50.0 - 25.0 x 10e9 /L	<25,000/mm3; <25.0 x 10e9 /L	
Serum amylase increased	>ULN - 1.5 x ULN	>1.5 - 2.0 x ULN; *>2.0 - 5.0 x ULN and asymptomatic*	>2.0 - 5.0 x ULN *with signs or symptoms; >5.0 x ULN and asymptomatic*	>5.0 x ULN *and with signs or symptoms*	"Asymptomatic" ranges are not taken into consideration for grading, i.e. worst case grading is applied.
White blood cell decreased	<LLN - 3000/mm3; <LLN - 3.0 x 10e9 /L	<3000 - 2000/mm3; <3.0 - 2.0 x 10e9 /L	<2000 - 1000/mm3; <2.0 - 1.0 x 10e9 /L	<1000/mm3; <1.0 x 10e9 /L	
Metabolism and nutrition disorders					
Acidosis	pH <normal, but ≥7.3	-	pH <7.3	*Life-threatening consequences*	pH <normal is implemented as pH <LLN. Clinical signs and symptoms are not taken into consideration for grading.
Alkalosis	pH >normal, but ≤7.5	-	pH >7.5	*Life-threatening consequences*	pH >normal is implemented as pH >ULN. Clinical signs and symptoms are not taken

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	J&J Implementation Notes
					into consideration for grading.
Hypercalcemia	Corrected serum calcium of >ULN - 11.5 mg/dL; >ULN - 2.9 mmol/L; Ionized calcium >ULN - 1.5 mmol/L	Corrected serum calcium of >11.5 - 12.5 mg/dL; >2.9 - 3.1 mmol/L; Ionized calcium >1.5 - 1.6 mmol/L; *symptomatic*	Corrected serum calcium of >12.5 - 13.5 mg/dL; >3.1 - 3.4 mmol/L; Ionized calcium >1.6 - 1.8 mmol/L; *hospitalization indicated*	Corrected serum calcium of >13.5 mg/dL; >3.4 mmol/L; Ionized calcium >1.8 mmol/L; *life-threatening consequences*	Clinical signs and symptoms are not taken into consideration for grading. Note: For Hypercalcemia or Hypocalcemia in the CTCAE Lab Toxicity grading scale, the reference ranges from serum calcium (ULN /LLN) from the local or central lab are being utilized.
Hyperkalemia	Potassium >ULN - 5.5 mmol/L	Potassium >5.5 - 6.0 mmol/L; *intervention initiated*	Potassium >6.0 - 7.0 mmol/L; *hospitalization indicated*	Potassium >7.0 mmol/L; *life-threatening consequences*	Clinical signs and symptoms are not taken into consideration for grading.
Hypermagnesemia	Magnesium >ULN - 3.0 mg/dL; >ULN - 1.23 mmol/L	-	Magnesium >3.0 - 8.0 mg/dL; >1.23 - 3.30 mmol/L	Magnesium >8.0 mg/dL; >3.30 mmol/L; *life-threatening consequences*	Clinical signs and symptoms are not taken into consideration for grading.
Hypernatremia	Sodium >ULN - 150 mmol/L	Sodium >150 - 155 mmol/L; *intervention initiated*	Sodium >155 - 160 mmol/L; *hospitalization indicated*	Sodium >160 mmol/L; *life-threatening consequences*	Clinical signs and symptoms are not taken into consideration for grading.
Hypertriglyceridemia	Triglycerides 150 mg/dL - 300 mg/dL; 1.71 mmol/L - 3.42 mmol/L	Triglycerides >300 mg/dL - 500 mg/dL; >3.42 mmol/L - 5.7 mmol/L	Triglycerides >500 mg/dL - 1000 mg/dL; >5.7 mmol/L - 11.4 mmol/L	Triglycerides >1000 mg/dL; >11.4 mmol/L; *life-threatening consequences*	Clinical signs and symptoms are not taken into consideration for grading.
Hypoalbuminemia	Albumin <LLN - 3 g/dL; <LLN - 30 g/L	Albumin <3 - 2 g/dL; <30 - 20 g/L	Albumin <2 g/dL; <20 g/L	*Life-threatening consequences; urgent intervention indicated*	Clinical signs and symptoms are not taken into consideration for grading.

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	J&J Implementation Notes
Hypocalcemia	Corrected serum calcium of <LLN - 8.0 mg/dL; <LLN - 2.0 mmol/L; Ionized calcium <LLN - 1.0 mmol/L	Corrected serum calcium of <8.0 - 7.0 mg/dL; <2.0 - 1.75 mmol/L; Ionized calcium <1.0 - 0.9 mmol/L; *symptomatic*	Corrected serum calcium of <7.0 - 6.0 mg/dL; <1.75 - 1.5 mmol/L; Ionized calcium <0.9 - 0.8 mmol/L; *hospitalization indicated*	Corrected serum calcium of <6.0 mg/dL; <1.5 mmol/L; Ionized calcium <0.8 mmol/L; *life-threatening consequences*	Clinical signs and symptoms are not taken into consideration for grading. Note: For Hypercalcemia or Hypocalcemia in the CTCAE Lab Toxicity grading scale, the reference ranges from serum calcium (ULN /LLN) from the local or central lab are being utilized.
Hypoglycemia	Glucose <LLN - 55 mg/dL; <LLN - 3.0 mmol/L	Glucose <55 - 40 mg/dL; <3.0 - 2.2 mmol/L	Glucose <40 - 30 mg/dL; <2.2 - 1.7 mmol/L	Glucose <30 mg/dL; <1.7 mmol/L; *life-threatening consequences; seizures*	Clinical signs and symptoms are not taken into consideration for grading. Urine glucose is not graded.
Hypokalemia	*Potassium <LLN - 3.0 mmol/L*	*Symptomatic with* Potassium <LLN - 3.0 mmol/L; intervention indicated	Potassium <3.0 - 2.5 mmol/L; *hospitalization indicated*	Potassium <2.5 mmol/L; *life-threatening consequences*	"Symptomatic" ranges are applied for grade 2, grade 1 not assigned, i.e. worst case applied. Clinical signs and symptoms are not taken into consideration for grading of grade 3 and 4.
Hypomagnesemia	Magnesium <LLN - 1.2 mg/dL; <LLN - 0.5 mmol/L	Magnesium <1.2 - 0.9 mg/dL; <0.5 - 0.4 mmol/L	Magnesium <0.9 - 0.7 mg/dL; <0.4 - 0.3 mmol/L	Magnesium <0.7 mg/dL; <0.3 mmol/L; *life-threatening consequences*	Clinical signs and symptoms are not taken into consideration for grading.
Hyponatremia	Sodium <LLN - 130 mmol/L	*Sodium 125-129 mmol/L and asymptomatic*	*Sodium 125-129 mmol/L symptomatic; 120-124 mmol/L regardless of symptoms*	Sodium <120 mmol/L; *life-threatening consequences*	Clinical signs and symptoms are not taken into consideration for grading.

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	J&J Implementation Notes
			Sodium <130-120 mmol/L		Worst case ("<130-120 mmol/L" for grade 3 added by J&J) is applied across grade 2/3 ranges: 120-129 mol/L assigned to grade 3, grade 2 not used.
Renal and urinary disorders					
Proteinuria	1+ proteinuria; urinary protein ≥ULN - <1.0 g/24 hrs; urinary protein ≥ULN - <1000 mg/day	**Adult:** 2+ and 3+ proteinuria; urinary protein 1.0 - <3.5 g/24 hrs; urinary protein 1000 - <3500 mg/day **Pediatric:** Urine P/C (Protein/Creatinine) ratio 0.5 - 1.9; Urine P/C (Protein/Creatinine) 56.5 – 214.7 g/mol	**Adult:** 4+ proteinuria; urinary protein ≥3.5 g/24 hrs; urinary protein ≥3500 mg/day; **Pediatric:** Urine P/C (Protein/Creatinine) ratio >1.9; Urine P/C (Protein/Creatinine) >214.7 g/mol	-	In case both 24-h urine collection and dipstick are collected, then worst case is taken, as opposed to having 24-h urine collection take precedence over dipstick. Added ranges in SI unit for urinary protein (mg/day) and for urine P/C (g/mol). Pediatric grading is applied to age range [0-18]. Adult grading is applied for ages [>18].

* Grade 0 is assigned to a lab assessment when the lab test is described in the table, but the lab value is not assigned a grade 1 or higher.

6.9. Appendix 9 PROIMIS-29 T-score

PROMIS 29 – PROFILE v2.1
PROMIS 29 + 2 PROFILE v2.1 (PROPr)

Adult v2.0 - Physical Function 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	22.5	4.0
5	26.6	2.8
6	28.9	2.5
7	30.5	2.4
8	31.9	2.3
9	33.2	2.3
10	34.4	2.3
11	35.6	2.3
12	36.7	2.3
13	37.9	2.3
14	39.2	2.4
15	40.5	2.4
16	41.9	2.5
17	43.5	2.6
18	45.5	2.8
19	48.3	3.3
20	57.0	6.6
*SE = Standard Error on T-score metric		

Adult v1.0 - Anxiety 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	40.3	6.1
5	48.0	3.6
6	51.2	3.1
7	53.7	2.8
8	55.8	2.7
9	57.7	2.6
10	59.5	2.6
11	61.4	2.6
12	63.4	2.6
13	65.3	2.7
14	67.3	2.7
15	69.3	2.7
16	71.2	2.7
17	73.3	2.7
18	75.4	2.7
19	77.9	2.9
20	81.6	3.7
*SE = Standard Error on T-score metric		

Adult v1.0 - Depression 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	41.0	6.2
5	49.0	3.2
6	51.8	2.7
7	53.9	2.4
8	55.7	2.3
9	57.3	2.3
10	58.9	2.3
11	60.5	2.3
12	62.2	2.3
13	63.9	2.3
14	65.7	2.3
15	67.5	2.3
16	69.4	2.3
17	71.2	2.4
18	73.3	2.4
19	75.7	2.6
20	79.4	3.6
*SE = Standard Error on T-score metric		

Adult v1.0 - Fatigue 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	33.7	4.9
5	39.7	3.1
6	43.1	2.7
7	46.0	2.6
8	48.6	2.5
9	51.0	2.5
10	53.1	2.4
11	55.1	2.4
12	57.0	2.3
13	58.8	2.3
14	60.7	2.3
15	62.7	2.4
16	64.6	2.4
17	66.7	2.4
18	69.0	2.5
19	71.6	2.7
20	75.8	3.9
*SE = Standard Error on T-score metric		

Adult v1.0 - Sleep Disturbance 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	32.0	5.2
5	37.5	4.0
6	41.1	3.7
7	43.8	3.5
8	46.2	3.5
9	48.4	3.4
10	50.5	3.4
11	52.4	3.4
12	54.3	3.4
13	56.1	3.4
14	57.9	3.3
15	59.8	3.3
16	61.7	3.3
17	63.8	3.4
18	66.0	3.4
19	68.8	3.7
20	73.3	4.6
*SE = Standard Error on T-score metric		

Adult v1.0 – Ability to Participate in Social Roles and Activities 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	27.5	4.1
5	31.8	2.5
6	34.0	2.3
7	35.7	2.2
8	37.3	2.1
9	38.8	2.2
10	40.5	2.3
11	42.3	2.3
12	44.2	2.3
13	46.2	2.3
14	48.1	2.2
15	50.0	2.2
16	51.9	2.2
17	53.7	2.3
18	55.8	2.3
19	58.3	2.7
20	64.2	5.1
*SE = Standard Error on T-score metric		

Adult v1.0 - Pain Interference 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	41.6	6.1
5	49.6	2.5
6	52.0	2.0
7	53.9	1.9
8	55.6	1.9
9	57.1	1.9
10	58.5	1.8
11	59.9	1.8
12	61.2	1.8
13	62.5	1.8
14	63.8	1.8
15	65.2	1.8
16	66.6	1.8
17	68.0	1.8
18	69.7	1.9
19	71.6	2.1
20	75.6	3.7
*SE = Standard Error on T-score metric		

6.10. Appendix 10 PROIMIS-25 T-score

PROMIS Pediatric – 25 v2.0 scoring tables

Anxiety 4b
Short Form Conversion Table

Raw Score	T-score	SE*
4	35.6	6.4
5	40.9	5.6
6	44.1	5.4
7	47.2	5.2
8	49.9	5.1
9	52.4	5
10	54.8	5
11	57.2	5
12	59.5	5
13	61.8	5
14	64	5.1
15	66.3	5.1
16	68.7	5.1
17	71.1	5.1
18	73.7	5.2
19	76.3	5.1
20	79.5	5.1

*SE = Standard Error

Depressive Symptoms 4b
Short Form Conversion Table

Raw Score	T-score	SE*
4	37.7	6.4
5	43.5	5.2
6	46.8	5
7	49.8	4.6
8	52.3	4.5
9	54.6	4.4
10	56.7	4.4
11	58.8	4.3
12	60.7	4.3
13	62.6	4.3
14	64.6	4.3
15	66.6	4.3
16	68.6	4.3
17	70.7	4.4
18	73	4.5
19	75.4	4.5
20	78.7	4.8

*SE = Standard Error

Fatigue 4a
Short Form Conversion Table

Raw Score	T-score	SE*
4	35.4	6.5
5	40.6	5.6
6	44.1	5.4
7	47.2	5.2
8	49.8	5.1
9	52.2	5
10	54.4	5
11	56.5	4.9
12	58.6	4.9
13	60.6	4.9
14	62.6	4.9
15	64.7	4.9
16	66.9	4.9
17	69.1	4.9
18	71.5	5
19	74.1	5
20	77.6	5.2

*SE = Standard Error

Mobility 4a
Short Form Conversion Table

Raw Score	T-score	SE*
4	20.1	4.4
5	23.1	4
6	25.1	3.9
7	26.9	3.9
8	28.4	3.8
9	30	3.8
10	31.5	3.8
11	32.9	3.8
12	34.4	3.8
13	35.9	3.8
14	37.6	3.9
15	39.3	4.1
16	41.2	4.4
17	42.9	4.2
18	45.5	4.4
19	48.9	4.7
20	57.1	7

*SE = Standard Error

Pain Interference 4a
Short Form Conversion Table

Raw Score	T- Score	SE*
4	36.7	6.1
5	42	4.9
6	44.4	4.8
7	47.2	4.4
8	49.3	4.3
9	51.3	4.1
10	53.2	4.1
11	55	4
12	56.7	4
13	58.4	4
14	60.1	4
15	61.8	4
16	63.6	4.1
17	65.5	4.1
18	67.7	4.2
19	70	4.3
20	74	4.9

*SE = Standard Error on T-score

Peer Relationships 4a
Short Form Conversion Table

Raw Score	T- Score	SE*
4	23	5.1
5	25.7	4.7
6	27.7	4.7
7	29.8	4.5
8	31.7	4.5
9	33.6	4.4
10	35.4	4.4
11	37.2	4.4
12	38.9	4.4
13	40.7	4.4
14	42.6	4.5
15	44.5	4.6
16	46.7	4.8
17	48.9	4.7
18	51.9	5.1
19	55.3	5.4
20	61.1	6.6

*SE = Standard Error on T-score

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