Janssen Research & Development

Statistical Analysis Plan

A Phase 2a Multicenter, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy, Safety, and Tolerability of an Oral Tablet Formulation of JNJ-77242113 for the Treatment of Moderate-to-Severe Plaque Psoriasis

Protocol 77242113PSO2003; Phase 2a

JNJ-77242113

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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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VERSION HISTORY

Table [xx] – SAP Version History Summary

SAP Version	Approval Date	Change	Rationale
1		Not Applicable	Initial release

1. INTRODUCTION

77242113PSO2003 is a randomized, double-blind placebo-controlled, parallel, multicenter, interventional study in participants with moderate-to-severe plaque psoriasis. This Phase 2a study is focused on proof of-concept and will assess the efficacy, safety, and tolerability of JNJ-77242113 (an IL-23R peptide antagonist) orally administered as a delayed release tablet formulated with CCI [redacted] This study will be conducted in parallel with the complementary study 77242113PSO2001, a Phase 2b randomized, double-blinded, dose-ranging, placebo-controlled study designed to evaluate the efficacy and safety of JNJ-77242113, formulated as an immediate-release oral tablet CCI [redacted] in adults with moderate-to-severe plaque psoriasis. The target population for this study intervention consists of participants 18 to 75 years of age (or the legal age of consent if it is higher in the jurisdiction in which the study is taking place), with moderate to severe psoriasis of at least 26 weeks duration, primarily defined as a total BSA ≥10%, total PASI ≥12, and total Investigator Global Assessment (IGA) ≥3 at screening and baseline.

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

1.1. Objectives and Endpoints

Objectives	Endpoints
Primary	
To evaluate the efficacy of an oral tablet formulation of JNJ-77242113 compared with placebo in participants with moderate-to-severe plaque psoriasis.	• Proportion of participants achieving PASI 75 (≥75% improvement from baseline in PASI) at Week 16
Secondary	
To assess the safety and tolerability of an oral tablet formulation of JNJ-77242113 compared with placebo in participants with moderate-to-severe plaque psoriasis.	• Frequency and type of adverse events (AEs) and serious adverse events (SAEs).
To evaluate additional measures of efficacy of an oral tablet formulation ofJNJ-77242113 compared with placebo in participants with moderate-to-severe plaque psoriasis.	• Change from baseline in PASI total score at Week 16. • Proportion of participants achieving PASI 90 (≥90% improvement from baseline in PASI) at Week 16. • Proportion of participants achieving PASI100 (100% improvement from baseline in PASI) at Week 16. • Proportion of participants achieving an Investigator Global Assessment (IGA) score of cleared (0) or minimal (1) at Week 16. • Proportion of participants achieving an IGA score of cleared (0) at Week 16. • Change from baseline in body surface area (BSA) at Week 16.
Exploratory	

Objectives	Endpoints
To characterize the pharmacokinetics (PK) of JNJ-77242113 for the oral tablet formulation and explore the PK/pharmacodynamic (PD) relationship of the JNJ-77242113 formulation for biomarkers, efficacy, and safety in participants with moderate-to-severe plaque psoriasis.	• JNJ-77242113 PK parameters (ie, plasma concentration just prior to the beginning or at the end of a dosing interval Ctrough], area under the plasma concentration versus time curve [AUC]). • The relationship between PK parameters and PD (ie, skin, blood cellular and molecular biomarker activity as well as clinical endpoints and safety parameters).
To explore treatment effects of an oral tablet formulation of JNJ-77242113 on biomarkers in participants with moderate-to-severe plaque psoriasis.	• Change from baseline in levels of skin and blood biomarkers.
To evaluate the immunogenicity of JNJ-7242113.	• The incidence of anti-drug antibodies to JNJ-77242113.
To further assess the safety and tolerability of an oral tablet formulation of JNJ-77242113 compared with placebo in participants with moderate-to-severe plaque psoriasis.	• Frequency and type of AEs, SAEs, reasonably related AEs, and AEs leading to discontinuation of study intervention. • Laboratory parameters and change from baseline in laboratory parameters (hematology and chemistry) over time. • Systolic and diastolic blood pressures over time.
To evaluate the treatment effect of an oral tablet formulation of JNJ-77242113 on patient-reported psoriasis severity and dermatology-specific health-related quality of life compared with placebo in participants with moderate-to-severe plaque psoriasis.	• Change from baseline in Psoriasis Symptoms and Signs Diary (PSSD) symptoms score at Week 16. • Change from baseline in PSSD signs score at Week 16. • Proportion of participants achieving a PSSD symptoms score=0 at Week 16 among participants with a baseline symptom score ≥1. • Proportion of participants achieving a PSSD signs score=0 at Week 16 among participants with baseline sign scores ≥1. • Proportion of participants achieving a Dermatological Life Quality Index (DLQI) score of 0 or 1 at Week 16 among participants with baseline DLQI score >1.

1.2. Study Design

This is a randomized, double-blind placebo-controlled, parallel, multicenter, interventional study in participants with moderate-to-severe plaque psoriasis. This Phase 2a study is focused on proof of-concept and will assess the efficacy, safety, and tolerability of JNJ-77242113 (an IL-23R peptide antagonist) orally administered as a delayed release tablet formulated with an CCI [redacted] This study will be conducted in parallel with the complementary study 77242113PSO2001, a Phase 2b randomized, double-blinded, dose-ranging, placebo-controlled study designed to evaluate the efficacy and safety of JNJ-77242113, formulated as an immediate-release oral tablet CCI [redacted] in adults with moderate-to-severe plaque psoriasis. The target population for this study intervention consists of participants 18 to 75 years of age (or the legal age of consent if it is higher in the jurisdiction in which the study is taking place), with moderate to severe psoriasis of at least 26 weeks duration, primarily defined as a total BSA ≥10%, total PASI ≥12, and total Investigator Global Assessment (IGA) ≥3 at screening and baseline.

A target of 80 participants will be enrolled in this study. Participants will be randomized to receive 1 of the 2 JNJ-77242113 doses of an oral delayed release tablet CCI [redacted] or placebo in a 3:3:2 ratio (30:30:20) using dynamic central randomization, stratified by baseline weight (≤90 kg, >90 kg).

The treatment arms for this study will be as follows:

Group 1: 10 mg JNJ-77242113 oral delayed release tablet CCI [redacted] administered once daily from Week 0 through Week 16.

Group 2: 50 mg JNJ-77242113 oral delayed release tablet CCI [redacted] administered once daily from Week 0 through Week 16.

Group 3: Placebo oral delayed release tablet, administered once daily from Week 0 through Week 16.

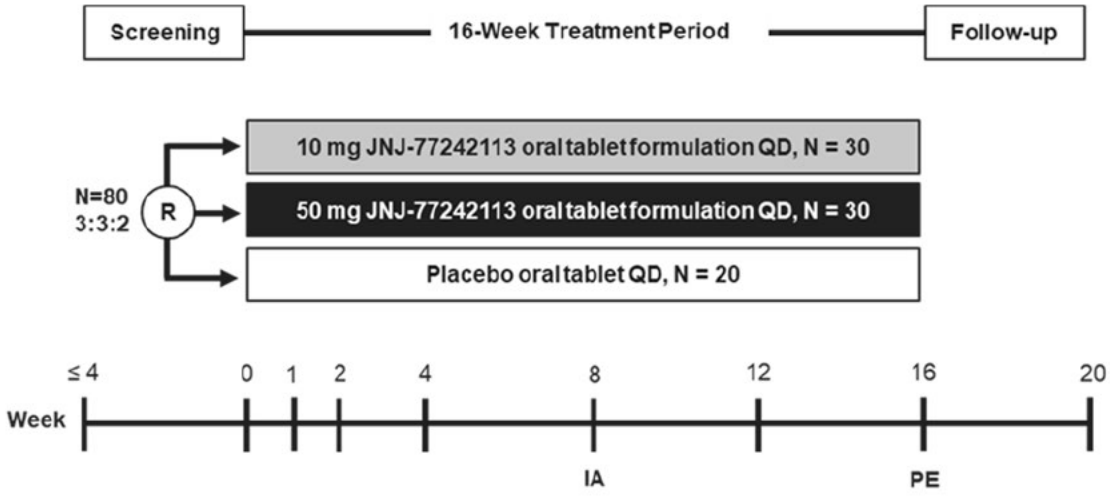
Participants will be instructed to take the study intervention once daily on an empty stomach, at least 2 hours after final food and caloric drink consumption in the evening (water is permitted). The study intervention should be administered with approximately 240 mL (8 ounces) of noncarbonated water. The tablet must be swallowed whole (ie, intact), and participants must not chew, divide, dissolve, or crush the study intervention. Participants should not consume food or drinks, except for water, after study intervention administration until the following morning. Following a 16-week placebo-controlled treatment period, participants will return for a follow-up visit approximately 4 weeks after the last administration of study intervention.

There is 1 database lock (DBL) planned at the end of this intervention cohort. An interim analysis (IA) is planned at Week 8 to inform Phase 3 development. Additional ad hoc IA(s) may be conducted if deemed necessary. No DBLs are planned for any of the IA(s). An external

Independent Data Monitoring Committee (iDMC) will be commissioned to assess the safety at an ongoing basis for this study.

A study design schematic is provided in Figure 1 below.

Figure 1: Schematic Overview of the Study



Abbreviations: IA = interim analysis; PE = primary endpoint; QD = quaque die (once a day)

2. STATISTICAL HYPOTHESES

The hypothesis of this study is that an oral delayed release tablet formulation of JNJ-77242113 CCI will result in superior efficacy compared with placebo as determined by the proportion of participants achieving PASI 75 response at Week 16.

3. SAMPLE SIZE DETERMINATION

This study is designed to assess the clinical response, safety/tolerability, and pharmacology of JNJ-77242113 CCI in participants with moderate-to-severe plaque psoriasis. The sample size is evaluated based on the primary endpoint of a PASI 75 response at Week 16. The sample size of 80 participants was chosen in order to have sufficient power to detect a difference between the JNJ-77242113 CCI (30 participants for each of low and high dose groups) and the placebo group (20 participants).

The assumptions for the sample size and power calculations were mainly based on the clinical data from guselkumab Phase 3 clinical studies that evaluated the safety and efficacy in the treatment of adult participants with moderate-to-severe plaque psoriasis.

The null hypothesis is to be tested at an overall Type 1 error rate of 0.10 (2-sided). Assuming PASI75 response rates at Week 16 are 5% to 10% for placebo and 40% to 80% for JNJ-77242113 CCI a sample size of 20 participants in the placebo group and 30 participants in the JNJ-77242113 CCI will provide at least 90% power to detect a 35% difference between the JNJ-77242113 CCI and placebo groups in the proportion of participants achieving a PASI 75 response at Week 16 based on a 2-sample Z-test.
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4. POPULATIONS (ANALYSIS SETS) FOR ANALYSIS

Unless specified otherwise, data included in the analyses for the study are briefly summarized below:

Table 1: Populations for Analyses

Population	Description
Enrolled	All participants who signed the ICF
Randomized	All participants who were randomized in the study
FAS	All randomized participants who took at least 1 dose of study intervention
Per Protocol (PP)	The per protocol analysis set (PP) includes a subset of participants in the full analysis set (FAS) who were in compliance with the protocol. Compliance is defined as participants in FAS and meet the following criteria: • Has a total BSA ≥10% at the screening and baseline visit. • Has a total PASI score ≥12 at the screening and baseline visit • Has a total IGA score ≥3 at the screening and baseline visit • Overall compliance of study treatment at least 80% prior to Week 16, Or participants who did not complete all scheduled study intervention administration due to intercurrent events (i.e., discontinued the study intervention due to lack of efficacy, an AE of worsening of psoriasis, or started a protocol-prohibited medication or therapy during the study that could improve psoriasis) • Criteria added as needed after the team's review.
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 CCI and had at least 1 valid blood sample drawn for PK analysis after their first dose of JNJ-77242113 CCI
Immunogenicity Analysis Set	All randomized participants who received at least 1 dose of JNJ-77242113 CCI and who had at least 1 sample obtained after the first dose of JNJ-77242113 for the detection of antibodies to JNJ-77242113
PD Analysis Set	All randomized participants who received at least 1 dose of JNJ-77242113

5. STATISTICAL ANALYSES

5.1. General Considerations

Unless specified otherwise, efficacy data summaries will be provided by intervention group for 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 response efficacy endpoints, comparisons between each of the JNJ-77242113 CCI groups versus placebo will be performed using a Cochran-Mantel-Haenszel (CMH) test stratified by the baseline weight (≤90 kg, >90 kg). For continuous efficacy endpoints, treatment comparisons will be performed using a Mixed-Effect Model Repeated Measure (MMRM) model. The MMRM model will have factors for treatment group, baseline weight (≤90 kg, >90 kg), baseline value for the corresponding efficacy endpoint, visit, and treatment group by visit interaction. 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 considered 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 Least Square mean (LSmean) estimates and their corresponding 90% confidence interval (CI) will be provided at each time point. In addition, the estimates of LSmean difference and 90% CIs between the JNJ-77242113 groups and placebo will be provided.

In general, all statistical tests will be performed at a 2-sided significance level of α=0.10. Nominal p-values will be reported. No multiplicity adjustment is planned for this phase 2a proof-of-concept study.

The baseline measurement is defined as the closest measurement taken prior to or at the time of the first study agent administration date unless otherwise specified.

5.1.1. Visit Windows

The schedules for visits of the study will follow per protocol 'Schedule of Activities' table. Visits at Week 1 and Week 2 should occur within ± 2 days of the scheduled visit; and the visits after Week 2 though Week 16 should occur within ± 4 days of the scheduled visit. The final follow-up visit (ie, Week 20) should occur approximately 4 weeks after the last administration of study intervention.

Nominal visits of Week 0 through Week 16 will be used for all by visit analyses. Visit windows will be created around the study day of each scheduled visit and be applied to map early termination visit and final follow-up visit. The visit windows and the targeted study day are indicated in Table 1. Scheduled visit assessments are preferred if more than one assessment falls within the same visit window.

Table 1. Visit Windows

Scheduled Study Day	Visit Window
Week 0 Day 1*	1, 4
Week 1 (Day 8)	5, 11
Week 2 (Day 15)	12, 21
Week 4 (Day 29)	22, 42
Week 8 (Day 57)	43, 70
Week 12 (Day 85)	71, 98
Week 16 (Day 113)	99, 126
Week 20/Final Follow-up	127, 999
* Study Day 1 begins on the day of randomization. Each Week consists of 7 days.	

5.1.2. 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.

5.1.3. Treatment Groups

In the efficacy analyses, FAS will be used, and the participants will be analyzed according to the randomized treatment groups they were assigned to, regardless of the treatments they actually received. Unless otherwise specified, efficacy analyses for placebo comparisons at Week 16 or through Week 16 will be summarized and displayed as follows:

- **Placebo**: Participants randomized to placebo group at Week 0.
- **10 mg JNJ-77242113 oral delayed release tablet** CCI Participants randomized to 10 mg group CCI at Week 0.
- **50 mg JNJ-77242113 oral delayed release tablet** CCI Participants randomized to 50 mg group CCI at Week 0.

5.2. Participant Dispositions

The number of screened participants 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

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.

The above categories will include summaries over the placebo-controlled period through Week 16.

5.3. Primary Endpoint Analysis

5.3.1. Definition of Primary Endpoints

The primary efficacy endpoint is the proportion of participants achieving PASI 75 response at Week 16, defined as at least a 75% reduction from baseline in PASI total score.

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.

Efficacy endpoints related to the PASI score are defined below:

PASI 50 Responders

Participants with ≥50% improvement in PASI from baseline will be considered PASI 50 responders.

PASI 75 Responders

Participants with ≥75% improvement in PASI from baseline will be considered PASI 75 responders.

PASI 90 Responders

Participants with ≥90% improvement in PASI from baseline will be considered PASI 90 responders.

PASI 100 Responders

Participants with a PASI score of 0 will be considered PASI 100 responders.

5.3.2. Estimands

Primary Trial Objective: To evaluate whether the oral tablet formulation of JNJ-77242113 will result in
superior efficacy compared with placebo in participants with moderate-to-severe plaque psoriasis.

Estimand Scientific Question of Interest: What is the proportion of participants considered to have benefited from JNJ-77242113 versus placebo assessed by the PASI75 response at Week 16?

5.3.2.1. Primary Estimand

The primary estimand, based on the above primary objective, is defined by the following 5 attributes which assess the treatment effects not only based on the variable measurements, but also based on intercurrent events:

Study intervention:

- JNJ77242113 10 mg CCI oral delayed release tablet administered once a day.
- JNJ77242113 50 mg CCI oral delayed release tablet administered once a day.
- Placebo, oral tablet administered once a day.

Population: adult participants with moderate to severe psoriasis

Variable/endpoint: Binary response variable, where a responder is defined as a participant achieving a PASI75 response at Week 16. A participant with an intercurrent event in categories 1-2 defined below will be considered as a non-responder.

Intercurrent Events (ICEs) and their corresponding strategies.

ICEs	Analysis Strategy for Addressing Intercurrent Events
1. Discontinuation of study intervention due to lack of efficacy, or an AE of worsening of psoriasis prior to Week 16 2. Initiation of a protocol-prohibited medication or therapy during the study that could improve psoriasis prior to Week 16	**Composite Strategy:** Participants with these intercurrent event are considered as non-responders. The occurrence of these intercurrent event being captured in the variable definition.
3. Discontinuation of study intervention for reasons other than ICE 1	**Treatment Policy:** observed data will be used regardless of whether or not this intercurrent event had occurred.

For participants experiencing multiple ICEs, ICE 2 will override ICE 3.

A list of Participants who experienced ICEs 1-3 will be provided.

Population level summary: Difference in the proportions of participants achieving a PASI 75 responses at Week 16 between the treatment groups.

5.3.2.2. Supplementary Estimands

5.3.2.2.1. Supplementary Estimand 1 (Hypothetical Estimand):

In this supplementary estimand, the only component that changes from the definition of the primary estimand is the hypothetical strategy will be used for addressing ICEs 1-3.

Hypothetical strategy: assess the treatment effect as if the intercurrent event would not have occurred. Under the hypothetical strategy, data collected after ICEs 1-3 will not be used in analysis and will be imputed using a MAR multiple imputation method.

5.3.2.2.2. Supplementary Estimand 2 (Treatment Policy Estimand):

This supplementary estimand has the same components as the primary estimand, except for the strategies used for ICEs 1-3.

Treatment policy strategy: assess the treatment effect regardless of whether or not intercurrent events had occurred. Under the treatment policy strategy, observed data collected after ICEs will be used in analysis.

5.3.3. Analysis Methods

5.3.3.1. Analysis Methods for the Primary Estimand

The primary endpoint will be analyzed based on the primary estimand and the data from all participants in FAS will include data from all randomized participants who received at least one administration of study intervention based on their assigned intervention group, regardless of the actual intervention received.

Comparisons of each JNJ-77242113 treatment group versus the placebo group will be performed for the primary endpoint of PASI 75 at Week 16. The Cochran-Mantel-Haenszel chi-square statistic stratified by baseline weight category (≤ 90 kg, > 90 kg) at a 2-sided significance level of 0.1 will be used. Difference in response rates between each of the active groups and the placebo group adjusted for baseline weight category (≤ 90 kg, > 90 kg) using Mantel-Haenszel weight and the corresponding 90% CI will be presented. Pairwise comparisons will not be adjusted for multiplicity.

Participants with ICEs 1-2 before Week 16 will be considered as PASI75 non-responders at Week 16. Participants with ICE 3, observed PASI data after this ICE will be utilized in the analysis. After accounting for the ICEs for the primary estimand, participants with the missing data of the primary endpoint at Week 16 will be considered as non-responders.

5.3.3.2. Additional Analysis for the Primary Estimand

The primary estimand for the completers will be analyzed using the Cochran-Mantel-Haenszel statistic stratified by baseline weight category (≤ 90 kg, > 90 kg).

5.3.3.3. Analysis for Supplementary Estimands

The analyses specified below for supplementary estimands will be applied for the primary endpoint.

5.3.3.3.1. Supplementary Analysis 1 (Hypothetical Estimand)

Under this estimand, PASI 75 response will be considered missing after an intercurrent event and missing data will be imputed using multiple imputations (MI) by fully conditional specification (FCS).

More specifically, the missing PASI75 responses will be imputed with FCS logistic regression including treatment group, baseline PASI score, and PASI75 response status through Week 16 in the model with seed = 789 and 500 imputations. The proportion difference of PASI75 response between each JNJ-77242113 group and placebo group at Week 16 adjusted for baseline weight category (≤ 90 kg, > 90 kg) using Mantel-Haenszel weight and its 90% CI combining multiple datasets will also be provided. A CMH test stratified by baseline weight category (≤ 90 kg, > 90 kg) will be used to obtain the CMH statistic for each imputed dataset.

The values of the general association test statistics from the CMH test for each imputed dataset will be transformed using the Wilson-Hilferty transformation 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 sing SAS PROC MIANALYZE and obtain the overall p-value for the CMH test. Difference in PASI75 response rates at Week 16 between each of the active intervention groups and the placebo group at Week 16 adjusted for baseline weight category using Mantel-Haenszel weight and its 90% CI combining multiple datasets will also be provided.

5.3.3.3.2. Supplementary Analysis 2 (Treatment Policy Estimand)

The primary endpoint will also be analyzed utilizing the treatment policy estimand. For participants who experience an intercurrent event through Week 16, the analysis will be performed using observed data regardless of intercurrent events. Missing data will be imputed use multiple imputation method specified in Section 5.3.2.2.1.

5.3.3.4. Per Protocol Analysis

The primary efficacy endpoint will be evaluated in the PP population based on the primary estimand except that ICE 3 will not be applied. Participants with ICE 3 who do not complete all scheduled study administration prior to Week 16 will be excluded from the per protocol analysis. The same data handling rule and analysis method specified in Section 5.3.3.1will be applied.

5.4. Secondary Endpoints Analysis

No multiplicity adjustment will be made for the secondary endpoints. All statistical testing will be performed at the 2-sided 0.1 significance level. Nominal p-values will be presented.

5.4.1. Secondary Endpoint(s)

The secondary objective is to characterize additional efficacy of JNJ-77242113 versus placebo in participants with moderate-to-severe plaque psoriasis.

The secondary endpoints to address these objectives are the following:

1. Proportion of participants achieving PASI 90 (≥ 90% improvement from baseline in PASI) at Week 16
2. Proportion of participants achieving PASI 100 (100% improvement from baseline in PASI) at Week 16
3. Proportion of participants achieving an IGA score of cleared (0) or minimal (1) at Week 16
4. Proportion of participants achieving an IGA score of cleared (0) at Week 16
5. Change from baseline in PASI total score at Week 16
6. Change from baseline in BSA at Week 16

5.4.1.1. Definition of Endpoint(s)

5.4.1.1.1. Psoriasis Area and Severity Index (PASI)

Refer to section 5.3.1 for details.

5.4.1.1.2. Investigator's Global Assessment (IGA)

The IGA documents the investigator's assessment of the participant's psoriasis at a given time point. Overall lesions are graded for induration, erythema, and scaling. The participant's psoriasis is assessed as cleared (0), minimal (1), mild (2), moderate (3), or severe (4).

5.4.1.1.3. Body Surface Area (BSA)

Body Surface Area is a commonly used measure of severity 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 patient's hand including the palm and all five digits is used as a guide to estimate 1% BSA (Long 1992; Rossiter 1996; Thomas 2007).

5.4.1.2. Main Estimands for Secondary Endpoints

The secondary endpoints will be analyzed using the primary estimand described in section 5.3.2.1. as the main estimand. This main estimand will be considered for both binary and continuous

secondary endpoints. The analysis strategy for ICEs and missing data will be handled in the same manner as the primary estimand for the primary endpoint.

- ICEs 1-2: Composite strategy
- ICE 3: Treatment policy strategy

The study intervention and population are the same as the primary estimand.

BINARY ENDPOINTS

Variables: Binary response variable (eg, PASI 90 responses at Week 16). A participant with an intercurrent event in categories 1-2 defined below will be considered as a non-responder.

Population-level summary: Difference in the proportions of participants achieving a clinical response between the treatment groups.

The variables and population -level summaries for the other secondary binary endpoints are similarly described.

CONTINUOUS ENDPOINTS

Variable (Endpoint): change from baseline to Week 16 (change = Week 16 - baseline).

- Participants who have intercurrent events in categories 1, 2 through Week 16 will be assigned a zero change from baseline from the point of the ICE, regardless of the observed data.

Population-level summary: LSMean difference in change from baseline in eg, PASI score at Week 16 between JNJ-77242113 treatment groups and the placebo group.

The variables and population -level summaries for the other secondary continuous endpoints are similarly described.

5.4.1.3. Supplementary Estimands

The supplementary estimands defined in Section 5.3.3.3.1 (Hypothetical Strategy) and Section 5.3.3.3.2 (Treatment Policy Strategy) for the primary endpoint will also be used for binary secondary endpoints:

- Proportion of participants achieving PASI 90 (≥ 90% improvement from baseline in PASI) at Week 16
- Proportion of participants achieving PASI 100 (100% improvement from baseline in PASI) at Week 16
- Proportion of participants achieving an IGA score of cleared (0) or minimal (1) at Week 16

- Proportion of participants achieving an IGA score of cleared (0) at Week 16

The following table provides the list of variables, summary measure (population-level summary) and intercurrent event strategy for secondary endpoints.

Endpoint	**Variable**	**Summary Measure (Population-level summary)**	**Intercurrent Event Strategy**
1	Binary response variable, where a responder is defined as a participant achieving a PASI 90 response at Week 16	Difference in the proportions of participants achieving a PASI 90 response at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand as specified in section 5.3.2.1 and two supplementary estimands specified in section 5.3.2.2
2	Binary response variable, where a responder is defined as a participant achieving a PASI 100 response at Week 16	Difference in the proportions of participants achieving a PASI 100 response at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand as specified in section 5.3.2.1 and two supplementary estimands specified in section 5.3.2.2
3	Binary response variable, where a responder is defined as a participant achieving an IGA scores of cleared (0) or minimal (1) at Week 16	Difference in the proportions of participants achieving an IGA score of cleared (0) or minimal (1) at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand as specified in section 5.3.2.1 and two supplementary estimands specified in section 5.3.2.2
4	Binary response variable, where a responder is defined as a participant achieving an IGA scores of cleared (0) at Week 16	Difference in the proportions of participants achieving an IGA score of cleared (0) at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand as specified in section 5.3.2.1 and two supplementary estimands specified in section 5.3.2.2
5	Continuous variable, change from baseline in PASI score at Week 16 (change = Week 16 - baseline)	LSMean difference in change from baseline in PASI at Week 16 between JNJ-77242113 treatment groups and the placebo group.	Same analysis strategies as the primary estimand specified in section5.4.1.2. Participants who have intercurrent events in categories 1, 2 through Week 16 will be assigned a zero change from baseline from the

			point of the ICE, regardless of the observed data.
6	Continuous variable, change from baseline in BSA at Week 16 (change = Week 16 - baseline)	LSMean difference in change from baseline at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand specified in section 5.4.1.2. Participants who have intercurrent events in categories 1, 2 through Week 16 will be assigned a zero change from baseline from the point of the ICE, regardless of the observed data.

5.4.2. Analysis Methods

The secondary efficacy analysis of data will be based on the FAS. The endpoints will be summarized by intervention group. 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 used to summarize most data. All statistical testing will be performed at the 2-sided 0.1 significance level. Nominal p-values will be presented. No adjustments for multiple comparisons will be made for the secondary endpoints.

5.4.2.1. Binary Endpoints

The binary secondary endpoints at Week 16 will be analyzed using the estimand described in section 5.4.1.2. The analysis strategy for ICEs and missing data will be handled in the same manner as the primary estimand for the primary analysis. The proportions of participants achieving the above secondary efficacy endpoints will be summarized for each intervention group.

The Cochran-Mantel-Haenszel chi-square statistic stratified by baseline weight category (≤ 90 kg, > 90 kg) at a 2-sided significance level of 0.1 will be used. Difference in response rates between each of the active and placebo groups at Week 16 adjusted for baseline weight category (≤ 90 kg, > 90 kg) using Mantel-Haenszel weight and the corresponding 90% CI will be presented.

The Fisher's Exact test will be used for treatment comparisons in binary response endpoints. The proportion differences between JNJ-77242113 groups and placebo and the exact confidence intervals will be provided.

5.4.2.1.1. Analysis for Supplementary Estimands

The analyses specified in Section 5.3.2.2.1 (Hypothetical Estimand) and Section 5.3.2.2.2 (Treatment Policy Estimand) for supplementary estimands will be applied to the following secondary endpoints:

- Proportion of participants achieving PASI 90 (≥ 90% improvement from baseline in PASI) at Week 16
- Proportion of participants achieving PASI 100 (100% improvement from baseline in PASI) at Week 16
- Proportion of participants achieving an IGA score of cleared (0) or minimal (1) at Week 16
- Proportion of participants achieving an IGA score of cleared (0) at Week 16

5.4.2.2. Continuous Endpoints

Unless otherwise specified, the analyses for continuous secondary endpoints at Week 16 will be based on the following strategies to handle ICEs and missing data.

- ICEs in categories 1 - 2 in the primary estimand (definitions in Section 5.4.1.2) will be handled with the Composite Strategy. Participants experiencing ICEs 1-2 will have a zero change (or zero improvement) from baseline assigned from that point onward.
- ICEs in category 3 in the primary estimand (definitions in Section 5.4.1.2) will be handled by the Treatment Policy strategy. The analysis will be performed using observed data regardless of intercurrent events.
- For participants experiencing multiple ICEs, an ICE in category 2 of the primary estimand will override an ICE in category 3.
- Missing data will not be imputed after applying the rules for intercurrent events.

To account for the missing data for continuous endpoints of change (or percent change) from baseline measured at more than one post-baseline visit, a MMRM will be used. In MMRM, missing data will not be imputed, but rather missing data will be accounted for through correlation of repeated measures in the model.

Treatment comparisons for the secondary continuous endpoints at Week 16 will be performed using a Mixed-Effect Model Repeated Measure (MMRM) model. The model has factors for treatment group, visit, baseline weight category (≤ 90 kg, > 90 kg), baseline value for the efficacy endpoint and treatment by visit interaction. Additionally, the MMRM model will be also performed with factors for treatment group, visit, baseline weight category (≤ 90 kg, > 90 kg), baseline value for the efficacy endpoint, treatment by visit interaction and additional interaction terms of baseline weight category by visit and baseline value by visit. 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 considered in the following order, with the first structure that converges being used in the analysis: heterogeneous Toeplitz, standard Toeplitz, and autoregressive of order 1.

5.5. Exploratory Endpoint(s) Analysis

Objectives are: (a) To evaluate the effect of JNJ-77242113 treatment on patient-reported psoriasis severity versus placebo and (b) To evaluate the effect of JNJ-77242113 treatment on dermatology-specific and general health-related quality of life versus placebo in participants with moderate-to-severe plaque psoriasis.

The exploratory endpoints to address these objectives are the following:

To evaluate the effect of JNJ-77242113 treatment on patient-reported psoriasis severity versus placebo

1. Change from baseline in Psoriasis Symptoms and Signs Diary (PSSD) symptoms score at Week 16

2. Change from baseline in PSSD signs score at Week 16

3. Proportion of participants achieving PSSD symptoms score=0 at Week 16 among participants with a baseline symptoms score ≥1.

4. Proportion of participants achieving PSSD signs score=0 at Week 16 among participants with a baseline signs score ≥1.

To evaluate the effect of JNJ-77242113 treatment on dermatology-specific and general health-related quality of life versus placebo

5. Proportion of participants achieving a DLQI of 0 or 1 at Week 16 among participants with baseline DLQI score >1

In addition to the primary and secondary efficacy endpoints, the analyses for exploratory efficacy endpoints (including the over time summaries through Week 16) will be performed. These efficacy endpoints include the endpoints related to

- PASI
- IGA
- BSA
- Patient-reported Outcomes

  PSSD

  DLQI

5.5.1. Endpoint Definitions

5.5.1.1. Psoriasis Area and Severity Index (PASI)

Refer to section 5.3.1 for details.

5.5.1.2. Investigator's Global Assessment (IGA)

Refer to section 5.4.1.1.2 for details.

5.5.1.3. Body Surface Area (BSA)

Refer to section 5.4.1.1.3 for details.

5.5.1.4. Psoriasis Symptom and Sign Diary (PSSD)

The PSSD includes PRO questionnaires designed to measure the severity of psoriasis symptoms and signs for the assessment of treatment benefit (Feldman 2016). This study uses a 7-day recall version of the PSSD that asks the participant to answer the questions thinking about the last 7 days. The PSSD is a self-administered PRO instrument and includes 11 items covering symptoms (itch, pain, stinging, burning, and skin tightness) and patient-observable signs (skin dryness, cracking, scaling, shedding or flaking, redness, and bleeding) using 0 to 10 numerical rating scales for severity. Two subscores are derived each ranging from 0 to 100: the psoriasis symptom score and the psoriasis sign score. A higher score indicates more severe disease.

5.5.1.5. Dermatological Life Quality Index (DLQI)

The DLQI is a dermatology-specific health-related quality of life (HRQoL) instrument designed to assess the impact of the disease on a participant's HRQoL (Finlay 1994). It is a 10-item questionnaire that assesses HRQoL over the past week and in addition to evaluating overall HRQoL, 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 total score ranges from 0 to 30 with a higher score indicating greater impact on QoL.

5.5.2. Analysis Methods

The efficacy data from all participants in FAS will be included and analyzed by study intervention group through Week 16.

Similar to the secondary efficacy analyses, the endpoints will be summarized by intervention group. 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 used to summarize most data. All statistical testing will be performed at a 2-sided 0.1 significance level. Nominal p-values will be presented. No adjustments for multiple comparisons will be made for the secondary endpoints.

5.5.2.1. At Week 16

The exploratory endpoints at Week 16 will be analyzed using the same main estimands and the same analysis methods described in section 5.4.1.2 and section 5.4.2 for secondary endpoints. The analysis strategy for ICEs and missing data will be handled in the same manner as the main estimand for the secondary analyses (section 5.4.1.2).

- Change from baseline in Psoriasis Symptoms and Signs Diary (PSSD) symptoms score at Week 16
- Change from baseline in PSSD signs score at Week 16
- Proportion of participants achieving PSSD symptoms score=0 at Week 16 among participants with a baseline symptoms score ≥1.
- Proportion of participants achieving PSSD signs score=0 at Week 16 among participants with a baseline signs score ≥1.
- Proportion of participants achieving a DLQI of 0 or 1 at Week 16 among participants with baseline DLQI score >1

5.5.2.2. Over Time Summaries Through Week 16

In general, all endpoints with over time analyses will be descriptively summarized by treatment groups using descriptive statistics, such as mean, median, standard deviation, interquartile range, minimum and maximum for continuous variables, and counts and percentages for categorical variables.

Similar to the Week 16 analyses for the secondary continuous endpoints, MMRM model approach specified in Section 5.4.2.2 will be used for the overtime summaries through Week 16. Least Square means (LSmeans), LS means differences and their corresponding 90% confidence interval will be provided over time through Week 16 by visit and treatment group in addition to the descriptive summary statistics.

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

5.5.2.2.1. Analyses Related to PASI

- The change from baseline in PASI total score will be summarized by treatment group over time through Week 16.
- The proportions of PASI 75 responders, PASI 90 responders, and PASI 100 responders; the proportions of PASI 75 responders, PASI 90 responders, and PASI 100 responders by weight (≤90 kg, >90 kg) will be summarized by treatment group over time through Week 16.
- The proportions of participants achieving ≥75% improvement, ≥90%, or achieving 100% improvement from baseline in PASI disease component (Induration, Erythema, and Scaling) and region component (head, trunk, upper extremities, and lower extremities) will also be summarized at Week 16.

5.5.2.2.2. Analysis Related to IGA

- The proportions of participants achieving an IGA score of cleared (0); IGA score of cleared (0) or minimal (1) and the proportion of participants achieving a IGA score of mild or better

(≤2) overall and by weight (≤90 kg, >90 kg) will be summarized by treatment group over time through Week 16.

5.5.2.2.3. Analyses Related to BSA

- The change from baseline in BSA will be summarized by treatment group over time through Week 16.

5.5.2.2.4. Psoriasis Symptom and Sign Diary

The analyses for PSSD data are specified below and in general can be summarized in 3 categories as follows:

(a) Proportion of subjects who achieved clinically meaningful improvement in PSSD symptom score, sign score, and each individual scale score.

- The threshold for a clinically meaningful change from baseline in PSSD scores is defined as a change of ≥40 points in PSSD symptom and sign scores, change of ≥3 points in bleeding and stinging scores, change of ≥4 points in itch, dryness, cracking, skin tightness, burning and pain scores, and change of ≥5 points in scaling, shedding or flaking and redness scores.

- These analyses include only subjects who had at least minimal severity by each corresponding measure at baseline, i.e., a score of ≥40 in PSSD symptom and sign scores, ≥3 in bleeding and stinging scores; ≥4 in itch, dryness, cracking, skin tightness, burning, and pain scores, and ≥5 in scaling, shedding or flaking and redness scores, respectively.

(b) The proportions of subjects who achieve a score of 0 in PSSD symptom score, sign score, and each individual scale score among those who have a baseline PSSD symptom score, baseline sign score, and each individual baseline scale score that is >=1

(c) Change from baseline in PSSD symptom score, sign score, and each individual scale score

5.5.2.2.5. Analyses Related to Psoriasis Symptom and Sign Diary

- The proportion of subjects with clinically meaningful improvement from baseline in PSSD symptom score, sign score, and each individual scale score at Week 16 will be compared between each of the JNJ-77242113 group and the placebo group among participants with at least minimal severity in PSSD individual scale scores at baseline.
- The proportion of subjects with clinically meaningful improvement from baseline in PSSD symptom score, sign score, and each individual scale score will be summarized among participants with at least minimal severity in PSSD individual scale scores at baseline by treatment group.
- The change from baseline in each PSSD individual scale score at Week 16 will be compared between each of the JNJ-77242113 groups and the placebo group.

- The proportions of participants who achieve a score of 0 in each individual PSSD scale score at Week 16 will be compared between each of the JNJ-77242113 groups and the placebo group among participants with a baseline PSSD individual scale score >0.
- The change from baseline in PSSD symptoms score, signs score, and each PSSD individual scale score will also be summarized at Week 8 by treatment group.
- The proportions of participants who achieve a PSSD symptoms score of 0, signs score of 0 and each individual scale score of 0 will be summarized at Week 8 among participants with a baseline PSSD symptoms score, baseline signs score >0, and baseline each individual scale score >0 by treatment group.

5.5.2.2.6. Analyses Related to DLQI

- The change from baseline in DLQI score will be summarized at Week 8 and Week 16; and the change from baseline in DLQI score at Week 16 will be compared between each of the JNJ-77242113 groups and the placebo group.
- The proportions of participants with DLQI score of 0 and 1 for the participants with baseline DLQI score >1 will be summarized at Week 8.
- The proportion of participants with a reduction of 5 or more points in DLQI score for the participants with baseline DLQI score ≥ 5 at Week 16 will be compared between each JNJ-77242113 treatment group and the placebo group and will also be summarized by treatment group at Week 8.
- The change from baseline in DLQI component scores at Week 16 will be compared between each JNJ-77242113 treatment group and the placebo group.

5.6. Safety Analyses

All safety analyses will be performed using safety analysis set based on actual intervention received. 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. Unless otherwise specified, tabular summaries of safety events are also presented as following:

Safety data through Week 20 will be summarized by following intervention group:

- Placebo
- JNJ-77242113 10 mg qd CCI
- JNJ-77242113 50 mg qd CCI
- Combined JNJ-77242113 groups

5.6.1. Extent of Exposure

The extent of exposure will be summarized for randomized participants that received at least one study agent administration. Distribution of participants through Week 16 by study agent lot will be analyzed. In addition, the number (%) of participants receiving the study drug during double blind treatment phase will be summarized by treatment group.

The total duration of exposure to study medication (days), including days off medication, will be calculated as:

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

5.6.2. Adverse Events

The verbatim terms used in the CRF by investigators to identify adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). Any AE occurring at or after the initial administration of study intervention 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 (SAEs)
- AEs leading to discontinuation of study intervention
- AEs of severe intensity
- AEs related to study intervention

In addition to the summary tables, listings will be provided for participants who:

- Had SAEs
- Had AEs leading to discontinuation of study intervention
- Had AEs of severe intensity
- Had AE for psoriasis

- Had suicidal ideation or suicidal behavior
- Had anaphylactic or serum sickness 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.

5.6.3. Additional Safety Assessments

5.6.3.1. Clinical Laboratory Tests

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

Descriptive statistics and graphical displays will be presented for selected chemistry and hematology laboratory tests at scheduled time points.

Change from baseline through Week 20 will be summarized for chemistry, and hematology tests and displayed by intervention group. Box plots of laboratory measurements and change from baseline will be provided for the selected laboratory measurement.

- **Hematology** will include but are not limited to the following: Basophils, Eosinophils, Hemoglobin, Lymphocytes, Monocytes, Neutrophils, Platelets, WBC, CRP and ESR.
- **Chemistry** will include but are not limited to the following: ALT, AST, Albumin, Alkaline Phosphatase, Bicarbonate (CO2), Calcium, Chloride, Creatinine, GGT, Glucose, Potassium, SGOT, SGPT, Sodium, Total Bilirubin, Total Protein, Urea Nitrogen.

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, LLN and ULN will also be used to identify abnormal laboratory test results, and the incidence and severity of abnormal laboratory parameters (hematology and chemistry) will be summarized by treatment group. Participants with maximum post-baseline elevated liver function tests through Week 20 relative to ULN will be summarized in categories as shown below will be provided.:

- > 1 to ≤ 3 x ULN
- > 3 to ≤ 5 x ULN
- > 5 to ≤ 10 x ULN
- > 10 to ≤ 20 x ULN

- > 20 x ULN

In addition, Summary of potential Hy's Law case (ALT or AST ≥3 x ULN and total bilirubin ≥2 x ULN or INR >1.5) through Week 20 will also be provided.

5.6.3.2. Vital Signs

Continuous vital sign parameters including pulse, blood pressure (systolic and diastolic) will be summarized at each assessment time point. Change from baseline will be summarized. Descriptive statistics (mean, standard deviation, median, minimum and maximum) will be presented.

Incidence of treatment-emergent abnormal vital signs during intervention, as defined in Table 6, will be summarized for participants who had a baseline assessment and at least 1 postbaseline assessment for that vital sign.

Table 2: Clinically Important/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

5.6.3.3. 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. The C-SSRS measures 5 possible levels of suicidal ideation and 4 possible suicidal behaviors, as well as non-suicidal self-injurious behavior. The assessment is a fully-structured, participant self-report C-SSRS questionnaire, including standardized questions, follow-up prompts, error handling routines, and scoring conventions. Two versions of the C-SSRS will be used in this study, the *Lifetime* version and the *Since Last Contact* version. The *Lifetime* version will be conducted during the screening visit and the *Since Last Contact* version will be conducted at all other visits.

At the screening visit, the C-SSRS should be completed as the first assessment after signing informed consent and before any other tests, procedures, or other consultations. For subsequent visits, the C-SSRS should be completed after all PROs and before any other tests, procedures, or

other consultations. Participants will be interviewed by the investigator or trained study site personnel in a private, quiet place.

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 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 20. In addition, frequency distribution of the most severe/maximum post baseline C-SSRS outcome will be tabulated by C-SSRS categories and intervention group through Week 20. 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, 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 20 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.

5.7. Other Analyses

5.7.1. Pharmacokinetics

5.7.1.1. JNJ-77242113 Concentrations

The PK evaluable population is defined as all the participants who received at least 1 complete dose of JNJ-77242113 and had at least 1 valid blood sample drawn for PK analysis after their first dose of JNJ-77242113.

Plasma JNJ-77242113 concentrations will be summarized by visit and treatment group. Plasma, concentration will be summarized using descriptive statistics (i.e., n, arithmetic mean, standard deviation [SD], coefficient of variation [%CV], median, range [minimum and maximum], and interquartile [IQ] range) at each visit. PK data may be displayed graphically.

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
- Summary of plasma JNJ-77242113 concentrations over time by baseline body weight (quartiles). Other covariates may also be applied.
- Summary of plasma JNJ-77242113 concentrations at each visit by treatment group and baseline PASI score categories (PASI <20 or PASI ≥20
- Plots of median plasma JNJ-77242113 concentrations over time
- Plots of median plasma JNJ-77242113 concentrations over time by baseline body weight (≤median, >median).

Concentrations below the lowest quantifiable concentration will be treated 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. PK data may also be displayed graphically.

If feasible, population PK analysis of plasma concentration-time data of JNJ-77242113 may 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, genotypes, race) will be tested as potential covariates affecting PK parameters. Details will be given in a population PK analysis plan and the results of the population PK analysis will be presented in a separate report.

PK analysis set will be used and the analyses will be summarized through Week 16.

For the analyses, a participants included in one and only one treatment group on the basis of the treatment regimen followed. The description of treatment groups is as follows:

- JNJ-77242113 10 mg QD CCI [redacted]

- JNJ-77242113 50 mg QD CCI [redacted]

5.7.1.2. 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 meets 1 of the following dosing deviation criteria based on 2 previous doses prior to the PK sample collection will be excluded for that visit:
  - Skipped a visit
  - Received an incomplete/ incorrect dose

5.7.1.3. PK vs Efficacy

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

- The relationship between JNJ-77242113 plasma concentrations (quartiles) and PASI 75 response and IGA 0/1 response at Week 16 may be explored.

5.7.2. Immunogenicity

5.7.2.1. Antibodies to JNJ-77242113

Immune response analyses will be based on the Immunogenicity Analysis Set.

The incidence and titers of antibodies to JNJ-77242113 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).

The antibody to JNJ-77242113 status (positive at any time, negative) and titers will be summarized by treatment group for participants who receive a 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).

Participants evaluable for immunogenicity are defined as having at least 1 dose of JNJ-77242113 and have at least 1 valid blood sample drawn for antibody detection. The antibodies to JNJ-

77242113 summary and analysis will be based on the observed data; therefore, no imputation of missing data will be performed.

The following analysis of antibodies to JNJ-77242113 will be performed by treatment group:

- Summary of incidence of antibody to JNJ-77242113 status
- Summary of neutralizing antibodies (NAb) to JNJ-77242113

A listing of participants who are positive for antibodies to JNJ-77242113 will be provided. The sample antibody status, the titer, and the neutralizing antibody status to JNJ-77242113 will be listed by visit. This listing will also provide information regarding dose administered, JNJ-77242113 plasma concentration, PASI score, PASI75 response status, and IGA 0/1 response status for all applicable visits. In addition, a list of antibodies to JNJ-77242113 status in participants who discontinued study agent early will be provided.

5.7.2.2. Neutralized 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 to JNJ-77242113.

5.7.2.3. Antibody vs Efficacy/PK

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

- Summary of clinical response (e.g., PASI75 and IGA 0/1) by antibody to JNJ-77242113 status
- Summary of plasma JNJ-77242113 concentrations by antibody to JNJ-77242113 status
- Plots of median (IQ) plasma JNJ-77242113 concentrations over time by antibody to JNJ-77242113 status

5.7.3. Pharmacokinetic/Pharmacodynamic Relationships

The relationship between plasma concentration of JNJ-77242113 and PD may be analyzed graphically. If any visual trend is observed, a suitable PK/PD model may be developed to describe the exposure-response relationship. In the latter case, the results of the PK/PD modeling analysis will be presented in a separate technical report.

5.7.4. Biomarkers

Planned biomarker analyses may be deferred if emerging study data show no likelihood of providing useful scientific information. Any biomarker samples received by the contract vendor or sponsor after the cutoff date will not be analyzed, and therefore, excluded from the biomarker analysis.

Change in biomarkers over time will be summarized by treatment group. Associations between baseline levels and changes from baseline in select markers and response to treatment will be explored. The analyses will aim to identify biomarker relevant to treatment. Results of biomarker analyses will be reported in separate technical reports.

5.7.5. Definition of Subgroups

To evaluate the consistency of the primary efficacy endpoint PASI75 response and IGA at Week 16, subgroup analyses may be performed when the number of participants in the subset permits. The subgroups for subgroup analysis may include, but are not limited to the following:

Demographic subgroups

Subgroup	Variant	Definition
Region	1	Define based on UN guidance as per the M49 standard • North America • Europe
Sex	1	• male • female
Race	1	• American Indian or Alaska Native • Asian • Black or African American • White • Other
Age Group	1	• <45 • 45-64 • >=65
BMI	1	• <25 kg/m^2 • 25-<30 kg/m^2 • >=30 kg/m^2
Body Weight Group	1	• ≤90 kg • >90 kg

Baseline disease characteristics and psoriasis medication subgroups

Subgroup	Variant	Definition
Age at diagnosis (years)	1	• < median • ≥ median
Psoriasis disease duration (years)	1	• < median • ≥ median
Baseline PASI	1	• <20 • ≥20
Baseline IGA	1	• < 4 • = 4
Baseline BSA	1	• < 20% • ≥ 20%
Baseline DLQI		• <10 • ≥ 10
Psoriatic arthritis		• Yes • No

Subgroup	Variant	Definition
Phototherapy (ultraviolet B light [UVB] or psoralen and ultraviolet A light therapy [PUVA])	1	• Never used • Ever used
Conventional non-biologic systemics (PUVA, MTX, cyclosporine, acitiretin, or Azathioprine)		• Never used • Ever used
Novel non-biologic systemic (apremilast, deucravacitinib, tofacitinib, baricitinib)		• Never used • Ever used
Biologics (Etanercept, Infliximab, Adalimumab, Ustekinumab, Briakinumab, Secukinumab, Ixekizumab, Brodalumab, Guselkumab, Risankizumab, Tildrakizumab, Alefacept, Efalizumab, Certolizumab pegol)		• Never used • Ever used
Systemic Therapy (conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, biologics, systemic herbal treatments/traditional Taiwanese, Korean, or Chinese medicines)		• Never used • Ever used
TNFα agents (adalimumab, certolizumab pegol, infliximab, etanercept)		• Never used • Ever used
IL-12/23 inhibitors (ustekinumab, briakinumab)		•
IL-23 inhibitors (guselkumab, risankizumab, tildrakizumab)		• Never used • Ever used
IL-17(R) inhibitors (secukinumab, ixekizumab, brodalumab)		• Never used • Ever used

5.8. Interim Analyses

An internal independent interim analysis committee (IAC) will be established to review the interim data available at the time of the IA to formulate recommended decisions and/or actions in accordance with the objectives of the interim analyses. The IAC will consist of at least a clinician and a statistician (neither of whom are involved in study conduct), one of whom will chair the committee, and other members as required. The details will be provided in a separate IAC charter.

The IAC will review the unblinded efficacy data and provide recommendations about the next step of study conduct and the future development of the compound based upon the results of the interim efficacy analyses. The interim analysis will occur after approximately 67% of the participants who received at least one administration of study intervention have completed their Week 8 visit or have terminated their study participation before Week 8. The objective of the interim analysis is to determine whether the efficacy of JNJ-77242113, which is the proportion of participants achieving a PASI 75 response at Week 8, is sufficient to initiate the at-risk planning for the future development of JNJ-77242113 CCI for psoriasis based on the data accrued up to the interim

analysis. No changes to the current study are planned. Other selected supportive efficacy endpoints could also be reviewed. The unblinded results will be limited to specific sponsor personnel not involved in the study conduct. Interim analysis results will not be disseminated to investigators or individuals associated with the conduct of the study.

Details of the plan for the interim analyses will be specified in the Interim Analysis SAP.

5.8.1. Data Monitoring Committee (DMC) or Other Review Board

An external independent data monitoring committee (iDMC) whose members are not directly involved in the conduct of the study, will review unblinded safety data to ensure the safety of the participants enrolled in this study. The committee will meet regularly to review unblinded safety data. After the review, the iDMC will make recommendations to the sponsor regarding the conduct of the study. The iDMC will consist of at least one clinical physician and one statistician, not involved in the conduct of the study. The iDMC responsibilities, authorities, and procedures will be documented in the iDMC charter

An independent, external DMC has been established to monitor data on an ongoing basis to ensure the continuing safety of the participants enrolled in this study. The DMC consists of 3 members (including 1 dermatologist, one cardiologist and one statistician) who are independent of the sponsor. None of the members is participating as an investigator in the current study.

The major function of the DMC is to monitor the safety of the study agent by reviewing the serious adverse events (SAEs) each month and by reviewing the study safety data approximately every 4 months. The content of the safety summaries for this study are defined and documented in the DMC SAP developed by the sponsor. No hypothesis testing will be conducted. An independent statistical supporting group, provided by SGS, supports the DMC and is the liaison between sponsor and the DMC.

In addition, the DMC roles and responsibilities, and the general procedures (including communications) are defined and documented in the Data Monitoring Plan developed by the sponsor detailing the safety data monitoring to be conducted by the DMC.

6. SUPPORTING DOCUMENTATION

6.1. Appendix 1 List of Abbreviations

ADA	anti-drug antibody
AE	adverse event
ALT/SGPT	alanine aminotransferase
AST/SGOT	aspartate aminotransferase
ATC	anatomic and therapeutic class
AUC	area under the curve
BMI	body mass index
BSA	body surface area
CI	confidence interval
Cmax	maximum concentration
CRF	case report form
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
CV	coefficient of variation
DMC	Data Monitoring Committee
DPS	Data Presentation Specifications
eCRF	electronic case report form
F (%)	absolute SC bioavailability
FAS	full analysis set
FDA	Food and Drug Administration
ICH	International Conference on Harmonisation
IQ	interquartile
IWRS	interactive web response system
LLOQ	lower limit of quantification
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed-Effect Model Repeated Measure
MRD	minimum required dilution
NAb	neutralizing antibodies
PD	pharmacodynamic(s)
PI	principal investigator
PK	pharmacokinetic(s)
PP	per protocol
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	standard deviation
SMQs	standardised MedDRA queries
TEAE	treatment-emergent adverse event
Tmax	time to maximum concentration
US NCI	United States National Cancer Institute
V	volume distribution
Vz	volume of distribution based on terminal phase
Vz/F	apparent volume of distribution based on terminal phase after extravascular administration
WHO	World Health Organization
WHO-DD	World Health Organization Drug Dictionary

6.2. Appendix 2 Changes to Protocol-Planned Analyses

N/A

6.3. Appendix 3 Demographics and Baseline Characteristics

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

Table 3: Demographic Variables presents a list of the demographic variables that will be summarized by intervention group, combined active intervention group, and overall for the FAS analysis set.

Table 3: 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)	
Body Mass Index (BMI) (kg/m2)	
Body Surface Area (BSA) (m2)	
Categorical Variables	
Age (<45 years, 45-64 years, and >=65 years)	Frequency distribution with the number and percentage of participants in each category.
Sex (male, female)	
Weight (<90 kg, >=90 kg)	
Race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, White, Unknown, Not Reported)	
Ethnicity (Hispanic or Latino, not Hispanic or Latino)	
BMI ([normal <25 kg/m2, overweight 25-<30 kg/m2, obese >=30 kg/m2])	

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

Baseline disease characteristics (e.g., duration of psoriasis disease, baseline Hurley stage status, baseline PASI score, baseline IGA score, baseline BSA, baseline PRO related measurements, and baseline reginal psoriasis related measurements) will be summarized by treatment group. In addition, summaries of participants' medical history and current diagnoses, alcohol intake, and smoking status will be provided by treatment group will also be provided.

6.4. Appendix 4 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 through Week 16 and through the end of study.

- 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 and a listing of patients who missed scheduled study agent administration will also be provided by randomized treatment group. In addition, analyses of COVID-19 related protocol deviations will be provided.

6.5. Appendix 5 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 continue on 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.

The number of participants who received concomitant treatment of moisturizer for psoriasis 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.

6.6. Appendix 6 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.

6.7. Appendix 7 Intervention Compliance

Treatment compliance will be assessed based through Week 16 on the full analysis set (FAS) for the study. Descriptive summaries (sample size, mean, standard deviation, median, and range) will be presented for the percent of compliance defined as the number of doses taken divided by the number of doses that should have been taken. Overall compliance will be categorized as > 100%, 80 to ≤ 100%, 60 to < 80%, and <60%. In addition, treatment compliance will be assessed by summarizing the protocol deviation of the study agent administration related to incorrect study agent or dose received and missed administrations.

6.8. Appendix 8 Extent of Exposure

The extent of exposure will be summarized for randomized participants that received at least one study agent administration. Distribution of participants through Week 16 by study agent lot will be analyzed. In addition, the number (%) of participants receiving the study drug during double blind treatment phase will be summarized by treatment group.

6.9. Appendix 8 Adverse Events of Special Interest

Not Applicable.

6.10. Appendix 9 Medications of Special Interest

Not Applicable.

6.11. Appendix 10 Laboratory Toxicity Grading

The grading scale use for lab assessments is based on 'Common Terminology Criteria for Adverse Events (CTCAE) v5.0'.

If a laboratory value falls within the grading as specified below but also within the local 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	Janssen 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	Janssen 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	
Creatinine increased	Creatine Kinase >ULN - 1.5 x ULN	Creatine Kinase >1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	Creatine Kinase >3.0 x baseline; >3.0 - 6.0 x ULN	Creatine Kinase >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; monitoring only indicated*	>1.5 - 2.5; *>1.5 - 2.5 x baseline if on anticoagulation; dose adjustment indicated*	>2.5; *>2.5 x baseline if on anticoagulation; bleeding*	-	Concomitant therapy or clinical signs and symptoms are not taken into consideration for grading.

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Janssen implementation notes
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 into consideration for grading.

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Janssen implementation notes
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.
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.
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;	Corrected serum calcium of <7.0 - 6.0 mg/dL; <1.75 - 1.5 mmol/L; Ionized calcium <0.9 - 0.8 mmol/L;	Corrected serum calcium of <6.0 mg/dL; <1.5 mmol/L; Ionized calcium <0.8 mmol/L;	Clinical signs and symptoms are not taken into consideration for grading.

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Janssen implementation notes
		symptomatic	*hospitalization indicated*	*life-threatening consequences*	
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 <130-120 mmol/L	Sodium <120 mmol/L; *life-threatening consequences*	Clinical signs and symptoms are not taken into consideration for grading. Worst case ("<130-120 mmol/L" for grade 3 added by Janssen) 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;	**Adult:** 4+ proteinuria; urinary protein >=3.5 g/24 hrs;	-	In case both 24-h urine collection and dipstick are collected, then worst case is taken, as opposed to having 24-h urine

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Janssen implementation notes
		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	urinary protein >=3500 mg/day; **Pediatric:** Urine P/C (Protein/Creatinine) ratio >1.9; Urine P/C (Protein/Creatinine) >214.7 g/mol		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.

7. REFERENCES

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