1.0 Title Page

Statistical Analysis Plan

Study M15-741

A 52-Week, open-label, single-arm study to evaluate the safety and tolerability of 24-hour daily exposure of continuous subcutaneous infusion of ABBV-951 in subjects with Parkinson's disease

Date: 10 Mar 2021

Version 4.0

2.0 Table of Contents

List of Figures

List of Appendices

3.0 Introduction

This statistical analysis plan (SAP) describes the statistical analyses for ABBV-951 Study M15-741.

This SAP provides high level summaries of the planned statistical analyses for key efficacy and safety endpoints, interim analysis and multiplicity control strategies where applicable.

Unless noted otherwise, all analyses will be performed using SAS version 9.2 or later (SAS Institute Inc., Carry, NC 27513) under the UNIX operating system.

Pharmacokinetics/pharmacodynamics, pharmacogenetics, and selected biomarkers will be analyzed separately if applicable, and are not included in this SAP.

The SAP will not be updated in case of future administrative or minor amendments to the protocol unless the changes have any impact on the analysis of study data.

4.0 Study Background

4.1 Objective

The primary objective is to assess the local and systemic safety and tolerability of ABBV-951 delivered as a continuous subcutaneous infusion (CSCI) for 24 hours daily for up to 52 weeks.

The secondary objective is to assess the efficacy of ABBV-951 as measured by patient-reported and rater-measured efficacy endpoints.

4.2 Study Design

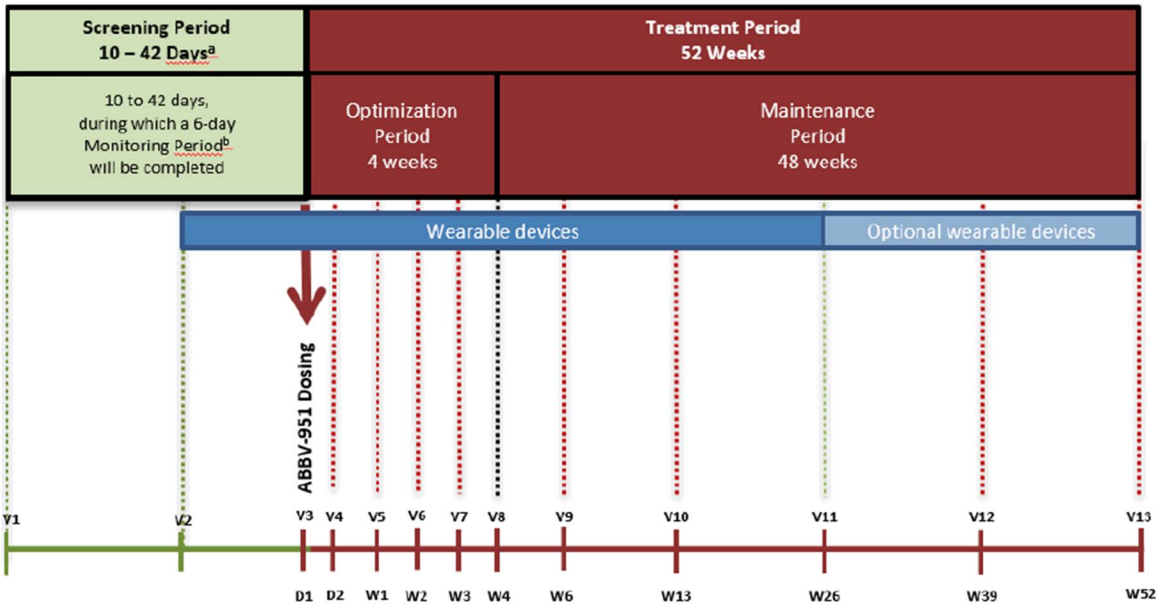
4.2.1 Study Design and Design Diagram

This is a 52-week, Phase 3, open-label, single-arm, multicenter study to assess the local and systemic safety and tolerability, as well as efficacy, of ABBV-951 administered as a

CSCI for 24 hours daily for up to 52 weeks. At study completion, subjects may transition to a 24-hour CSCI of ABBV-951 open-label extension study. Approximately 240 adult subjects with Parkinson's disease (PD) whose motor symptoms are inadequately controlled despite their current optimized PD therapy will be enrolled.

A schematic of the study is shown in Figure 1. Details regarding study procedures are located in Section 3 of the Operations Manual.

Figure 1. Study Design Schematic



D = Day; V = Visit; W = Week

a. The Screening Period may be extended up to a total of 90 days for extenuating circumstances, e.g., supply constraints.

b. The Monitoring Period can occur any time before V3, as long as it lasts for 6 days. PD Diaries will also be collected for at least 2 consecutive days during the Monitoring Period. In countries where the PKG watch is not approved, the Monitoring Period may be reduced to at least 2 days to account for the collection of PD Diaries and pump training.

Screening Period

The 10- to 42-day Screening Period will consist of 2 screening visits (V1 and V2) and a 6-day Monitoring Period during which subjects will become familiar with the wearable device and the PD Diary.

Treatment Period

The Treatment Period starts with the initiation of ABBV-951 and consists of 2 parts: a 4-week Optimization Period and a 48-week Maintenance Period.

Post-treatment Period Activities

There are no post-treatment activities except for subjects who prematurely discontinue study participation. See study protocol for additional information.

4.2.2 Variables Used for Stratification at Randomization

Since this is a single-arm study, there is no randomization.

4.3 Endpoint

4.3.1 Primary Endpoints (Safety)

The primary endpoints include the following safety variables:

1. Percentage of subjects with adverse events (AEs) and serious adverse events (SAEs) during the study
2. Percentage of subjects with AEs of special interest (AESI) during the study
3. Percentage of subjects with numeric grade equal to or higher than 5 and percentage of subjects with letter grade equal to or higher than D on the Infusion Site Evaluation Scale at any time during the study
4. Change in clinical laboratory test data from Baseline to end of study
5. Change in vital sign measurements from Baseline to end of study

6. Change in electrocardiograms (ECGs) from Baseline to end of study

4.3.2 Secondary Endpoints

The efficacy endpoints are change from baseline to end of study for the following:

1. Average normalized daily "Off" time and "On" times as assessed by the PD Diary
2. PD symptoms as assessed by the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-IV scores and Hoehn and Yahr Stage
3. Sleep symptoms as assessed by the PD Sleep Scale-2 (PDSS-2): total score and domain scores
4. Quality of life as assessed by the PD Questionnaire-39 items (PDQ-39): summary index and domain scores
5. Health-related quality of life as assessed by the EuroQol 5-dimensions questionnaire (EQ-5D-5L): summary index and visual analogue scale (VAS)
6. Early morning motor symptom derived from PD Diary

Canè pump-specific endpoints are as follows:

- Safety
    1. Percentage of subjects with AEs and SAEs associated with pump-specific product quality complaints.
    2. The percentage of pumps that were replaced due to pump malfunction
- Effectiveness
    1. The number of times a subject was required to take rescue medication due to pump malfunction.

Neria™ Guard infusion set-specific endpoints are as follows:

- Safety
    1. Percentage of subjects with AEs and SAEs associated with Neria Guard infusion set-specific product quality complaints.
- Effectiveness
    1. The number of product complaints associated with the Neria Guard infusion set that resulted in the subject replacing the infusion set.

4.3.3 Exploratory Endpoint

PD symptoms (including tremor, bradykinesia, dyskinesia and somnolence) as assessed by the Parkinson's KinetiGraph™/Personal KinetiGraph™ (PKG) wearable device (as allowed by local regulations).

- Change from Baseline to Week 26 in median bradykinesia score (BK50)
- Change from Baseline to Week 26 in interquartile range of bradykinesia score (BK75-BK25)
- Change from Baseline to Week 26 in median dyskinesia score (DK50)
- Change from Baseline to Week 26 in interquartile range of dyskinesia score (DK75-DK25)
- Percent change from Baseline to Week 26 in time of tremor and somnolence

4.4 Sample Size Justification

Approximately 240 subjects will be enrolled to obtain exposure data from at least 100 subjects treated with 24-hour daily CSCI of ABBV-951 for at least 12 months and to meet country requirements. With 240 subjects receiving ABBV-951, the probability to observe an AE with an annual incidence rate of 0.005, 0.01, and 0.02 is 70%, 91%, and 99%, respectively.

4.5 Interim Analysis

Two interim analyses will be performed during the course of this study. The first interim analysis will be performed after at least 100 subjects have completed 26 weeks of therapy; the second interim analysis will be performed after at least 100 subjects have completed 52 weeks of therapy. Interim locks will occur to preserve the clinical database to be used for these interim analyses. All the analyses described in this SAP will be performed, except for analysis of change from baseline to the final visit.

4.6 Multiplicity Testing Procedures for Type-I Error Control

No multiplicity adjustment is needed since efficacy is not the primary objective.

4.7 Missing Data Imputation

PD Diary

If more than 2 valid diary days are available prior to Day 1 or post-baseline visits, the 2 days closest to the clinical visit (or closet to Day 1 for Baseline) will be used. If only 1 valid diary day is available, that valid diary day will be used. If no valid diary day is available for a visit, the average daily normalized "Off" or "On" times will be missing for that visit.

MDS-UPDRS

The MDS-UPDRS total score and score of each part will be calculated as long as no more than 15% of the answers are missing for that assessment. The missing item will be imputed as the average of the non-missing items from the same MDS-UPDRS assessment. Imputation for Part I, Part II, Part III or Part IV scores should use the non-missing items within the particular part, but the imputation for the total score of Parts I-III should use the non-missing items from all 59 items across the 3 parts.

PDSS-2

There is no imputation of missing responses. If any item score is missing, the total score and the corresponding domain scores will not be calculated.

PDQ-39

The PDQ-39 summary index will be calculated as long as no more than 15% (i.e., 5) of the answers are missing for that assessment. It will be imputed as the average of the non-missing items from the same PDQ-39 assessment. The domain score will only be calculated if all the questions for that domain are answered.

EQ-5D-5L

The EQ-5D-5L summary index will only be calculated if answers are provided for all 5 individual questions. The EQ-5D-5L VAS is a single value collected and there is no imputation if the VAS value is missing.

5.0 Analysis Populations and Important Subgroups

5.1 Analysis Population

The Full Analysis Set (FAS) consists of all subjects who receive any ABBV-951 infusion and have a baseline and treatment observation for at least 1 efficacy outcome measure.

The Treatment Naive Analysis Set (TNAS) consists of all subjects in the FAS who have the initial exposure to ABBV-951 in Study M15-741, i.e., subjects who had received ABBV-951 in another study prior to participating in Study M15-741 are excluded from the TNAS.

The Safety Analysis Set consists of all subjects who receive any ABBV-951 infusion.

5.2 Subgroup

Unless otherwise noted, all analyses will be conducted by subgroup defined by dose category (low dose or high dose) according to total daily levodopa dose from levodopa phosphate (LDP) by molecular weight calculated from dosing diary. Each subject will be categorized to a dose subgroup based on the modal total daily dose over the treatment period.

Other subgroups are:

- Gender
- Race (White, Asian, Other). Analysis of Other race will be conducted if at least 3 subjects had races other than White or Asian.
- Age category (< 65, ≥ 65)
- Geographic region (North America, Europe and Australia, or Japan)
- PD duration (time since diagnosis) category (< 10 years, ≥ 10 years)

Additional subgroup analyses may be conducted as appropriate.

6.0 Demographics, Baseline Characteristics, Medical History, Prior/Concomitant Medications and Dosing

6.1 Subject Disposition and Accountability

All enrolled subjects will be used for the subject disposition summaries. Number and percentage of subjects for each of the following categories will be provided:

- Analysis Population
  - Full Analysis Set
  - Treatment Naïve Analysis Set
  - Safety Analysis Set
- Prematurely discontinued ABBV-951
- Prematurely discontinued from study

- ABBV-951 ongoing
- Study ongoing
- Completed study

The number of subjects screened, enrolled, screen failure, prematurely discontinued ABBV-951 and prematurely discontinued from study will be provided by country and investigational site.

In addition, the number of sites and countries that screened and enrolled at least 1 subject will be summarized. The number and percentage of subjects who screen failed, prematurely discontinued ABBV-951, and prematurely discontinued study will be summarized by reason (primary and all reasons). Subject disposition will also be summarized by Sample 1 (Subjects enrolled prior to 08-Jul-2020) and Sample 2 (Subjects enrolled on or after 08-Jul-2020).

6.2 Demographics and Baseline Characteristics

Demographics and baseline characteristics will be summarized for the Safety Analysis Set. Categorical variables will be summarized with the number and percentage of subjects. Continuous variables will be summarized with descriptive statistics (number of observations, mean and standard deviation [SD], median, minimum [min] and maximum [max]). Missing observations are excluded from all summary statistics.

Variables to be included in this analysis are listed below.

- Continuous variables: Age (years), Weight (kg), Height (cm), Body mass index (BMI) (kg/m^2), Mini-Mental State Examination (MMSE) total score
- Categorical variables: Country, Geographic Region (North America, Europe and Australia or Japan), Age (< 65 years, ≥ 65 years), Age (< 75 years, ≥ 75 years), BMI category (< 18.5, 18.5 - < 25.0, 25.0 - < 30.0, ≥ 30.0), Sex (Female, Male), Ethnicity (Hispanic or Latino, Not Hispanic or Latino), Race (White, Black or African American, Asian, American Indian or Alaska Native, Native Hawaiian or Other pacific islander), Tobacco (Current, Former, Never,

Unknown), Alcohol (Current, Former, Never, Unknown), and all Brief Neurological Examination variables.

Additional variables may be included given sufficient data.

6.2.1 Medical History and Parkinson's Disease History

Medical history data will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). The actual version of the MedDRA coding dictionary will be noted in the statistical tables and clinical study report. The number and percentage of subjects in each medical history category (by MedDRA system organ class [SOC] and preferred term [PT]) will be summarized. The SOC will be presented in alphabetical order, and the PT will be presented in alphabetical order within each SOC. Subjects reporting more than one condition/diagnosis will be counted only once in each row (SOC or PT).

Parkinson's Disease history will be summarized with the following variables:

- Continuous variables: Age at PD onset (years), Duration of PD since onset (years), Age at PD diagnosis (years), Duration of PD since diagnosis (years), Age at onset of motor fluctuation (years), Duration since onset of motor fluctuation (years), MDS-UPDRS – Part III score during "Off" state.
- Categorical variables: Duration of PD since diagnosis (< 10 years, ≥ 10 years), History of levodopa induced dyskinesia (Yes, No), Levodopa response for more than 5 years (Yes, No), and Hoehn and Yahr Stage.

The Advanced Parkinson's Disease (APD) tool will be summarized for each question as a categorical variable and for each domain score as a continuous variable.

6.2.2 Prior and Concomitant Medications

Prior and concomitant PD medications and non-PD medications will be summarized separately. A prior medication is defined as any medication taken prior to the date of first ABBV-951 infusion and collected in the electronic case report form (eCRF). A concomitant medication is defined as:

- Any medication that started prior to the date of first ABBV-951 infusion and continued to be taken after ABBV-951 infusion started.

OR

- Any medication that started on or after the date of first ABBV-951 infusion, but not after the date of the last ABBV-951 infusion.

The number and percentage of subjects who take at least one medication will be summarized by generic drug name based on the World Health Organization (WHO) Drug Dictionary for both concomitant PD medications and non-PD medications. For summaries of concomitant medications, if an incomplete start date or end date was collected for a medication, the medication will be assumed to be a concomitant medication unless there is evidence that confirms that the medication was not a concomitant medication (e.g., the medication end date was prior to the first dose of study drug).

Parkinson's disease medications use at Screening (V1) and at baseline (on Day –2) will be summarized, respectively, by the number of PD medications taken.

6.3 Analysis of Dosing

Based on molecular weight, 100 mg of LDP is equivalent to 71 mg of levodopa.

Unless otherwise noted, all analyses of dosing diary data will be performed on valid dosing diary days. A valid dosing diary day is defined as one in which ABBV-951 has been infused ≥ 80% of the entire 24-hour period (i.e., ≥ 19.2 hours).

6.3.1 Analysis of Daily Prescribed Dose

Summary statistics (mean, SD, median, min and max) will be provided for prescribed dose information, including levodopa oral loading dose, F1 (Base), F2 (High) and F3 (Low) continuous infusion rates, and extra dose.

In addition, daily total prescribed dose based on Base rate infused for entire 24-hour period will be calculated and summarized. High and Low infusion rates as percentage of Base infusion rate will also be summarized for the subjects that these alternative infusion rates were enabled by the investigator.

When available, the summary statistics will be provided at initial prescription, first maintenance prescription following the Optimization Period, final prescription in the 48-week Maintenance Period and final prescription in study. Change from initial to first maintenance, initial to maintenance final, initial to final and maintenance first to final will also be summarized.

6.3.2 Analysis of Titration

Duration of Initial Titration is defined as the number of days from Day 1 to the first day where there is no change to F1 rate for at least 15 days.

Duration of Initial Titration will be summarized by the following interval (days): 1, 2, 3 - 7, 8 - 14, 15 - 21, 22 - 28, and > 28. When applicable, the summary statistics will include mean, SD, median, min and max.

6.3.3 Analysis of Daily Levodopa Dose

Daily levodopa dose will be summarized for ABBV-951 and other levodopa at each protocol defined visit. Extra dose (ABBV-951), oral loading dose and oral rescue dose will also be summarized. The summary statistics include mean, SD, median, min and max.

The modal total daily levodopa dose during the study will be determined for each subject by first assigning the subject's total daily levodopa doses to narrow dose ranges in 100-mg increments (e.g., 1000 to < 1100 mg, 1100 to < 1200 mg) and then take the most frequent narrow dose range for the subject. If two or more dose ranges are of the same highest frequency, the highest dose range will be selected.

The modal pump infusion rate (i.e., Base, High, Low) will be similarly defined for each subject.

The modal total daily dose and modal pump infusion rate will be summarized for the Safety Analysis Set.

6.3.4 Other Dosing Analysis

The frequency of subjects taking extra dose, rescue dose and switching among 3 pump flow rates will be summarized by 0 time, 1 time, 2 times and ≥ 3 times categories for each planned visit. In addition, number of subjects with at least one occurrence and the total number of occurrences will be summarized by mean, SD, median, min and max.

In addition, during the 52-week ABBV-951 CSCI, the percentage of time that the ABBV-951 was infused with each rate (Base, High and Low) will be summarized separately. The summary statistics include mean, SD, median, min and max.

6.4 Other Descriptive Analyses

A summary of protocol deviation will be provided.

7.0 Study Drug Duration and Compliance

For the Safety Analysis Set, study drug duration will be calculated in the following two ways and will be summarized by mean, SD, median, min and max:

1. Duration of ABBV-951 exposure: Date of ABBV-951 discontinued/completed – Date of ABBV-951 started + 1
2. Duration of ABBV-951 exposure without interruption: Date of ABBV-951 discontinued/completed – Date of ABBV-951 started + 1 – total duration of infusion interruption

In addition, the number and percentage of subjects in each study drug duration interval (1 to 7, 8 to 14, 15 to 21, 22 to 28, 29 to 42, 43 to 91, 92 to 182, 183 to 273, and ≥ 274) will be summarized.

For each subject, study drug compliance will be summarized and is defined as the number of hours the pump is infusing per day relative to the 24-hour/day goal and averaged across all dosing diary days.

Compliance categories are defined as:

- Low compliance: study drug compliance < 60%
- Medium compliance: study drug compliance ≥ 60% to < 80%
- High compliance: study drug compliance ≥ 80% to 100%

Study drug compliance will be summarized for each visit that dosing diary is collected for the Safety Analysis Set by compliance category. In addition, number of subjects with non-missing observations, mean, SD, median, min and max of study drug compliance will be summarized for the entire study period.

In addition, patient-years of exposure will also be summarized.

8.0 Efficacy Analyses

8.1 General Considerations

This is a single-arm, open-label study. Unless stated otherwise, all analyses on efficacy variables will be performed with the FAS using data collected no more than 1 day after the end of the infusion of ABBV-951. Paired-sample t-test will be performed for testing the change from baseline.

Variables Derived from PD Diary

A PD Diary recording day is defined as a full 24-hour period across two calendar days, specifically, from current calendar day 6:00 am to next calendar day 5:30 am.

On PD diary recording days, the subject will be instructed to make an entry upon waking and every 30 minutes during their normal waking time and upon awakening from time asleep for a full 24-hour PD diary day from 6:00 am to 5:30 am of the next day (48 entries with each entry representing 0.5 hour). Each entry could be in one of 5 categories: Asleep, "Off," "On" without dyskinesia, "On" with non-troublesome dyskinesia, and "On" with troublesome dyskinesia. For each PD diary recording day, the absolute time spent in each category will be summed. The daily awake time will be the sum of the absolute time spent in the 4 non-asleep categories. The daily "Off" and "On" times will be normalized to a typical waking day (16 hours) to account for different sleep patterns across subjects, e.g.,

$$\text{Normalized "Off" time} = (\text{Absolute "Off" time}/\text{Awake time}) \times 16$$

Daily normalized "Off" and "On" times are averaged over valid diary days for each visit to obtain the average daily normalized "Off" and "On" times.

A valid PD diary day is defined as a PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) OR at least 12 awake hours (i.e., at least 24 "Off" or "On" time entries)for the entire 24-hour diary.

Only valid PD diary days are used in the analysis for "Off" and "On" times.

The early morning motor symptom will also be summarized and is defined to be the first non-sleep entry between 0:00 am and 12:00 pm within a calendar day, after at least 4 consecutive entries of "Asleep" (i.e., at least 2 hours of continuous sleep).

The analysis of early morning motor symptoms will be performed if there are ≤ 2 missing entries during the period between 0:00 am and 12:00 pm.

8.2 Efficacy Analysis

For all efficacy endpoints, the change from baseline to each planned visit and to the final visit will be summarized in a descriptive manner for each dose category subgroup and

overall subjects. The statistics include the number of observations, mean, SD, median, min and max.

8.3 Exploratory Efficacy Analysis

The change from baseline to each planned visit and to the final visit in normalized daily "Off" time and "On" times will be summarized on the TNAS. The analysis of PKG related exploratory endpoints defined in Section 4.3.3 will also be performed on the FAS.

In addition, a sensitivity analysis will be performed for average normalized daily "Off" time and "On" times by modifying the definition of the valid PD diary day as "a PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) for the entire 24-hour diary."

The change from baseline to each planned visit and to the final visit in normalized daily "Off" time and "On" times will also be summarized by Sample 1 (Subjects enrolled prior to 08-Jul-2020) and Sample 2 (Subjects enrolled on or after 08-Jul-2020).

8.4 Efficacy Subgroup Analyses

The change from baseline to each planned visit and to the final visit on the average normalized "Off" time and "On" times will be summarized for each of the subgroups defined in Section 5.2.

9.0 Safety Analyses

9.1 General Considerations

Safety analyses will be performed using the Safety Analysis Set. All analyses on safety variables, with the exception of Adverse Events and Infusion Site Evaluation Scale, will be performed using data collected no more than 1 day after the end of the infusion of ABBV-951. For continuous safety outcomes, the change from baseline will be analyzed in a descriptive manner by visit for each dose category subgroup and overall subjects. For categorical safety outcomes, the number and percentage of each category will be

summarized by visit for each dose category subgroup and overall subjects. Hypothesis testing will not be performed.

9.2 Analysis of Adverse Events

All adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). The MedDRA version will be noted on the statistical tables and in the CSR. Treatment Emergent Adverse Events (TEAE) will be defined as all events that begin or worsen on or after CSCI initiation through 30 days after the last infusion. Adverse events will be summarized by primary MedDRA system organ class (SOC) and preferred term (PT). Subjects reporting more than one adverse event for a given PT will be counted only once for that term. Subjects reporting more than one adverse event within an SOC will be counted only once for the SOC total. Subjects reporting more than one adverse event will be counted only once in the overall adverse event total. For summaries by SOC and PT, the SOCs will be presented in alphabetical order and the PTs will be presented in alphabetical order within each SOC.

Adverse events will be summarized by time interval for the Optimization Period, the Maintenance Period, and the entire Treatment Period. For subjects who received less than 29 days of ABBV-951 infusion, all TEAEs will be assigned to the Optimization Period. For subjects who received at least 29 days of ABBV-951 infusion, adverse events with onset from Study Day 1 through Study Day 28 will be assigned to the Optimization Period and all other TEAEs will be assigned to the Maintenance Period.

9.2.1 Adverse Event Overview

The number and percentage of subjects experiencing one or more TEAEs in the following adverse event categories will be summarized for the Optimization Period, the Maintenance Period and the entire study:

- Any TEAE
- Any severe TEAE
- Any TEAE that are considered associated with study drug

- Any TEAE that are considered associated with product complaint: ABBV-951
- Any TEAE that are considered associated with product complaint: Infusion Pump
- Any TEAE that are considered associated with product complaint: Vial Adapter
- Any TEAE that are considered associated with product complaint: Syringes
- Any TEAE that are considered associated with product complaint: Cleo 90 Infusion Set 6 mm
- Any TEAE that are considered associated with product complaint: Cleo 90 Infusion Set 9 mm
- Any TEAE that are considered associated with product complaint: Neria Guard Infusion Set 6 mm
- Any TEAE that are considered associated with product complaint: Neria Guard Infusion Set 9 mm
- Any TEAE that are considered associated with product complaint: PKG Wearable Watch
- Any TEAE that are considered associated with loading dose
- Any TEAE that are considered associated with rescue dose
- Any TEAE that are considered associated with COVID-19 infection
- Any TEAE leading to prematurely discontinuation of study drug
- Any TEAE leading to death (fatal TEAE)
- Any serious TEAE
- Any TESAE that are considered associated with infusion pump
- Any TESAE that are considered associated with Neria Guard infusion set
- Any TESAE that are considered associated with Cleo90 infusion set
- All Deaths
- Death related to COVID-19
- AESI: infusion site related infections
- AESI: infusion site related non infection reactions
- AESI: polyneuropathy

- AESI: weight loss
- AESI: hallucinations/psychosis
- AESI: somnolence
- AESI: falls and associated injuries

In addition, the number and percentage of subjects experiencing one or more TEAEs in the above adverse event categories will also be summarized by Sample 1 (Subjects enrolled prior to 08-Jul-2020) and Sample 2 (Subjects enrolled on or after 08-Jul-2020).

9.2.2 Adverse Event Summary

The number and percentage of subjects experiencing one or more TEAEs, one or more TESAEs, one or more TEAEs leading to premature discontinuation of study drug will be summarized by primary SOC and PT by time interval for the Optimization period, the Maintenance Period and the entire Treatment Period.

A listing contains all subjects numbers associated with each PT will be presented for all TEAEs.

9.2.3 Adverse Event by Maximum Severity

The number and percentage of subjects experiencing one or more TEAEs will also be summarized by maximum severity category (mild, moderate, severe, or unknown) and primary SOC and PT for the entire study. Subjects reporting more than one TEAE for a given PT will be counted only once for that term in the most severe category reported. If a subject has an adverse event with unknown severity, then the subject will be counted in the severity category of "unknown," even if the subject has another occurrence of the same event with a severity present. The only exception is if the subject has another occurrence of the same adverse event with the most extreme severity – "Severe." In this case, the subject will be counted under the "Severe" category.

9.2.4 Adverse Event by Relationship to Study Drug

The number and percentage of subjects experiencing one or more TEAEs will also be summarized by maximum relationship category (reasonable possibility, no reasonable possibility, or unknown), as assessed by the investigator, and primary SOC and PT for the entire study. Subjects reporting more than one TEAE for a given PT will be counted only once for that term in the most related category reported. If a subject has an adverse event with unknown relationship, then the subject will be counted in the relationship category of "unknown," even if the subject has another occurrence of the same event with a relationship present. The only exception is if the subject has another occurrence of the same adverse event with a relationship assessment of "reasonable possibility." In this case, the subject will be counted under the "reasonable possibility" category.

9.2.5 Adverse Event by Relationship to Product Quality Complaints

The number and percentage of subjects experiencing one or more TEAEs that are associated with Product Quality Complaints will also be summarized by the products listed below:

- ABBV-951
- Infusion Pump
- Vial Adapter
- Syringes
- Cleo 90 Infusion Set 6 mm
- Cleo 90 Infusion Set 9 mm
- Neria Guard Infusion Set 6 mm
- Neria Guard Infusion Set 9 mm
- PKG Wearable Watch

9.2.6 Adverse Event Leading to Study Drug Discontinuation, Interruption, and Dose Reduction

The number and percentage of subjects experiencing one or more TEAEs leading to study drug discontinuation, interruption, and dose reduction will also be summarized by primary system organ class and preferred term, respectively.

9.2.7 Adverse Event Associated with Loading Dose Drug and Rescue Dose Drug

The number and percentage of subjects experiencing one or more TEAEs associated with oral loading dose drug, and rescue dose drug will also be summarized by primary system organ class and preferred term, respectively.

9.2.8 Serious Adverse Events

In addition to Section 9.2.2, the number and percentage of subjects experiencing one or more serious adverse events related to infusion pump and Neria Guard infusion set will be summarized by primary SOC and PT, respectively.

9.2.9 Adverse Events of Special Interest

Adverse events of special interest (AESIs) include:

- Infusion Site Related Infections
- Infusion Site Related Non Infection Reactions
- Polyneuropathy
- Weight loss
- Hallucinations/psychosis
- Somnolence
- Falls and associated injuries

The search strategy for each AESI is defined in Appendix E.

The analysis of AESI includes an overview summary of each AESI and for each AESI, the number and percentage of subjects experiencing one or more adverse events will be summarized in descending frequency by PT.

9.2.10 Adverse Events by Subgroup

The number and percentage of subjects in each of the subgroups (defined in Section 5.2) experiencing one or more TEAEs during the study will be summarized by primary SOC and PT.

9.2.11 Listings of Adverse Events

The following additional summaries of adverse events will be prepared.

- Listing of all deaths for all subjects screened
- Listing of all serious TEAEs
- Listing of all TEAEs that led to discontinuation of study treatment
- Listing of all AESIs (As defined in Section 9.2.9)

9.2.12 Treatment-Emergent Adverse Events per Patient-Years of Exposure

Exposure-adjusted AEs per 100 patient-years will be provided, where AEs per 100 patient-years of exposure are defined as the number of AEs divided by the total exposure in 100 patient-years.

9.3 Analysis of Laboratory Data

Data collected from central and local laboratories, including additional laboratory testing due to an SAE, will be used in all analyses, except for baseline where SAE-related laboratory assessments on or before the date of first ABBV-951 infusion will be excluded. The clinical laboratory tests defined in the protocol operations manual (e.g., hematology and clinical chemistry) will be summarized.

9.3.1 Analysis of Mean Changes for Laboratory Tests

Change from baseline to each planned visit and to the minimum, maximum and final value will be summarized in a descriptive manner for each continuous hematology, chemistry, urinalysis, and special laboratory variable.

For each change from baseline analysis, the following summary statistics will be presented: sample size, baseline mean, visit mean, and the summary statistics (i.e., mean, SD, and median) of the change from baseline. The summary statistics of the change from baseline will only be calculated for subjects who have both baseline and visit values.

9.3.2 Analysis of Laboratory Tests by NCI CTC Criteria

Changes in laboratory parameters will be tabulated using shift tables either by Common Terminology Criteria for Adverse Events (CTCAE) criteria or categorized as low, normal, or high based on the normal ranges of the laboratory used for each sample. A shift table from baseline either to the worse value (based on CTCAE criteria) or to minimum and maximum value (based on normal range) during study, will be created.

A similar shift table will be provided to summarize shifts from baseline to the final post-baseline value during study.

9.3.3 Potentially Clinically Significant (PCS) Laboratory Values

Criteria for potentially clinically significant (PCS) values have been predefined for selected laboratory variables as outlined in Appendix B. For each variable, a summary of the number and percentage of subjects who have at least one post-baseline observation that meets the PCS criteria and is more extreme than their baseline value will be provided.

A listing will also be prepared that will include, for each variable, all observations for each subject that met the PCS criteria for that variable at any time during the study.

In addition, a summary of the number and percentage of subjects who have at least one observation that meets the HY's Law criteria will be provided.

A listing will also be prepared that will include, for each variable, all observations for each subject that met the HY's Law criteria for that variable at any time during the study.

9.4 Analysis of Vital Signs and Weight Variables

Vital sign variables include: body temperature, pulse (supine, standing and orthostatic), diastolic blood pressure (supine, standing and orthostatic), and systolic blood pressure (supine, standing and orthostatic).

Weight variables include: weight and BMI.

Orthostatic variables will be calculated as the change from supine to standing (standing measurement minus supine measurement).

9.4.1 Vital Sign and Weight Variable Mean Changes

Change from baseline to each planned visit and to the minimum, maximum and final value will be summarized in a descriptive manner for each vital sign and weight variable.

For each change from baseline analysis, the following summary statistics will be presented: sample size, baseline mean, visit mean, and the summary statistics (i.e., mean, SD, and median) of the change from baseline. The summary statistics of the change from baseline will only be calculated for subjects who have both baseline and visit values.

9.4.2 Potentially Clinically Significant (PCS) Vital Sign and Weight Variable Values

Criteria for PCS values have been predefined for selected vital sign and weight variables as outlined in Appendix C. For each variable, a summary of the number and percentage of subjects who have at least one post-baseline observation that meets the PCS criteria and is more extreme than their baseline value will be provided. A listing will also be prepared that will include, for each variable, all observations for each subject that met the PCS criteria for that variable at any time during the study.

9.5 Analysis of ECG Parameters

Electrocardiogram (ECG) variables include: heart rate (HR), PR interval, QRS interval, uncorrected QT interval, and QT interval corrected for heart rate using Fridericia's formula (QTcF).

9.5.1 ECG Mean Changes

Change from baseline to each planned visit and to the minimum, maximum and final value will be summarized in a descriptive manner for each ECG variable.

For each change from baseline analysis, the following summary statistics will be presented: sample size, baseline mean, visit mean, and the summary statistics (i.e., mean, SD, and median) of the change from baseline. The summary statistics of the change from baseline will only be calculated for subjects who have both baseline and visit values.

9.5.2 Potentially Clinically Significant (PCS) ECG Values

Criteria for PCS values have been predefined for selected ECG variables as outlined in Appendix D. For each variable, a summary of the number and percentage of subjects who have at least one post-baseline observation that meets the PCS criteria and is more extreme than their baseline value will be provided. A listing will also be prepared that will include, for each variable, all observations for each subject that met the PCS criteria for that variable at any time during the study.

9.6 Infusion Site Evaluation Scale

All observations from the Infusion Site Evaluation Scale will be included in the analysis, regardless the date of assessment relative to the last date of study drug infusion. The number and percentage of subjects with each category for numeric and letter grade will be presented at each planned visit. The number and percentage of subjects with numeric grade equal or higher than 5 or letter grade equal or higher than D at any time during the study will be presented.

A listing will also be prepared that includes all subjects with numeric grade equal or higher than 5 and letter grade equal or higher than D at any time during the study.

9.7 Analysis of Questionnaire for Impulsive-Compulsive Disorders in PD-Rating Scale (QUIP-RS)

The QUIP-RS is a brief, self-completed or rater-administered rating scale to assess the severity of symptoms of impulse control disorders (ICDs) and related behaviors reported to occur in PD.

Change from Baseline to each planned visit and to the final value will be summarized in a descriptive manner for QUIP-RS total score and domain scores.

For each change from baseline analysis, the following summary statistics will be presented: sample size, baseline mean, visit mean, and the summary statistics (i.e., mean, SD, and median) of the change from baseline. The summary statistics of the change from baseline will only be calculated for subjects who have both baseline and visit values.

9.8 Analysis of Columbia-Suicide Severity Rating Scale (C-SSRS)

The Columbia-Suicide Severity Rating Scale (C-SSRS) is a systematically administered instrument developed to track suicidal adverse events across a treatment study. At Screening (V1) the C-SSRS will be administered to collect lifetime history as well as experience during the past year. At all other visits, the C-SSRS will collect experience since the last visit. Affirmative responses on the C-SSRS will be summarized for the initial screening and each subsequent visit.

Each summary will include the number and percentage of subjects with one or more affirmative responses to each of the 5 suicidal ideation questions, each of the 6 suicidal behavior questions, any of the 5 suicidal ideation questions, any of the 6 suicidal behavior questions, any suicidal ideation or behavior question, and the non-suicidal self-injurious behavior question.

A listing will also be prepared that includes all subjects with 1 or more affirmative responses.

10.0 References

1. U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute, Common Terminology Criteria for Adverse Events (CTCAE), Version 4.0 Published: May 28, 2009 (v4.03: June 14, 2010) [accessed 03 December 2018]. Available from: https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf.10.0 References.

11.0 Summary of Changes

11.1 Summary of Changes Between the Previous Version and the Current Version

The following changes are made in SAP Version 4.0 since SAP Version 3.0, consistent with updates in protocol Version 4.0, 4.1, 4.1.1, 5.0, 6.0, 6.1, 6.2 and 7.0:

- Sample size increased.
- Added analysis by Sample 1 and Sample 2.
- Added a second planned interim analysis.
- Updated Figure 1.
- Updated language in 'Post-treatment Period Activities'
- Updated language in Section 4.3.2.
- Added Canè pump-specific endpoints.
- Added Neria Guard-specific endpoints.
- Updated language in Section 4.3.3.
- Updated language in Section 4.5.
- Updated language in Section 4.7
- Renamed the analysis population:

  - ITT data set is renamed as Full Analysis Set (FAS)
  - TN ITT data set is renamed as Treatment Naïve Analysis Set (TNAS)
  - Safety data set is renamed as Safety Analysis Set.
- Renamed subgroup and updated language in Section 5.2.
- Added 'Descriptive Analyses' section as Section 6.0.
- Added 'Study Drug Duration and Compliance' section as Section 7.0
- Added missing data imputation method for efficacy endpoints.
- Added the derivation algorithm for variables derived from PD diary.
- Added the analysis of early morning symptom from PD diary.
- Added a new AESI: Falls and related injuries.
- Adjusted analysis for AESI and SAE.
- Added a new summary analysis for subjects who met HY's Law.
- Updated language in Section 8.4.
- Updated language in Section 9.1, Section 9.2 and Section 9.3.
- Added reference for CTCAE criteria.
- Added sensitivity analysis by using a different definition for valid PD diary day.
- Added COVID-19 related analysis.
- Change 'average dose' to 'modal dose' for low/high dose subgroup definition.
- Added analysis for modal dose.

11.2 Summary of Changes in Previous Versions

The following changes were made in SAP Version 2.0 since SAP Version 1.0:

- Added one efficacy endpoint EQ-5D-5L
- Added an analysis population TN ITT data set for exploratory efficacy analysis.
- Added subgroup analysis for race.

The following changes were made in SAP Version 3.0 since SAP Version 2.0, consistent with updates in protocol Version 3.0:

- Hallucinations/psychosis and somnolence were added as AESIs.
- The Minnesota Impulsive Disorders Interview (MIDI) was replaced with the QUIP-RS.
- The sample size could be increased up to 160 if needed.

12.0 Appendices

Appendix A. Activity Schedule

The required study activities are shown in the following table. Individual activities are described in detail in the Operations Manual.

Study Activities Table

Activity	Screening (V1)	Screening (V2)	Treatment Period: Optimization Period 4 Weeks: Enrollment Day 1 (V3)	Day 2 (V4)	Week 1 (V5)	Week 2 (V6)	Week 3 (V7)	Week 4 (V8)	Treatment Period: Maintenance Period 48 Weeks: Week 6 (V9)	Week 13 (V10)	Week 26 (V11)	Week 39 (V12)	Week 52 (V13)/ Premature Discontinuation	Post-treatment Follow-up Call[d]	Dispensing Visits[c]
INTERVIEWS & QUESTIONNAIRES															
Subject information and informed consent	✓														
Eligibility criteria	✓	✓	✓ (predose)												
Medical history	✓														
Clinical assessment	✓														
Advanced Parkinson's Disease (aPD) Clinician Assessment	✓														
Infusion site evaluation (dermatologic assessment if applicable)			✓ (postdose)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Drug and alcohol screen	✓														
AE assessment	✓	✓	✓ (postdose)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	

Activity	Screening (V1)	Screening (V2)	Treatment Period: Optimization Period 4 Weeks: Enrollment Day 1 (V3)	Day 2 (V4)	Week 1 (V5)	Week 2 (V6)	Week 3 (V7)	Week 4 (V8)	Treatment Period: Maintenance Period 48 Weeks: Week 6 (V9)	Week 13 (V10)	Week 26 (V11)	Week 39 (V12)	Week 52 (V13)/ Premature Discontinuation	Post-treatment Follow-up Call[d]	Dispensing Visits[c]
Product complaints			✓ (pre- and postdose)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Prior/concomitant therapy	✓	✓	✓ (pre- and postdose)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Patient Reported Outcomes															
Patient Administered Measures (specific time points)															
Subject dosing diary					2 days before visit ✓	2 days before visit ✓	2 days before visit ✓	2 days before visit ✓	2 days before visit ✓	2 days before visit ✓	2 days before visit ✓	2 days before visit ✓	2 days before visit ✓		
Parkinson's Disease Diary	✓ (concor-dance evalu-ation)		2 days before visit ✓		2 days before visit ✓				2 days before visit ✓		2 days before visit ✓	2 days before visit ✓	2 days before visit ✓		
PKG wearable device	✓[a]	✓[a]	✓[a]	✓	✓	✓	✓	✓	✓	✓	✓	optional	optional		
EQ-5D-5L			✓ (predose)						✓	✓	✓	✓	✓		

Activity	Screening (V1)	Screening (V2)	Treatment Period: Optimization Period 4 Weeks: Enrollment Day 1 (V3)	Day 2 (V4)	Week 1 (V5)	Week 2 (V6)	Week 3 (V7)	Week 4 (V8)	Treatment Period: Maintenance Period 48 Weeks: Week 6 (V9)	Week 13 (V10)	Week 26 (V11)	Week 39 (V12)	Week 52 (V13)/ Premature Discontinuation	Post-treatment Follow-up Call[d]	Dispensing Visits[c]
Rater Administered Measures (specific time points)															
C-SSRS	✓	✓	✓ (predose)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
PDQ-39			✓ (predose)						✓	✓	✓	✓	✓		
MDS-UPDRS/UPDRS	✓		✓ (pre- and postdose)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
PDSS-2			✓ (predose)						✓	✓	✓	✓	✓		
MMSE	✓														
QUIP-RS			✓ (predose)						✓	✓	✓	✓	✓		
LABS & EXAMS															
Clinical laboratory tests	✓		✓ (predose)						✓		✓	✓	✓		
Special laboratory tests (vitamins B_6 and B_{12}, folic acid, MMA, homocysteine)	✓		✓ (predose)						✓		✓		✓		

Activity	Screening (V1)	Screening (V2)	Treatment Period: Optimization Period 4 Weeks: Enrollment Day 1 (V3)	Day 2 (V4)	Week 1 (V5)	Week 2 (V6)	Week 3 (V7)	Week 4 (V8)	Treatment Period: Maintenance Period 48 Weeks: Week 6 (V9)	Week 13 (V10)	Week 26 (V11)	Week 39 (V12)	Week 52 (V13)/ Premature Discontinuation	Post-treatment Follow-up Call[d]	Dispensing Visits[c]
Optional biomarker samples (pharmacogenetic DNA)			✓ (predose)								✓				
12-lead ECG	✓		✓ (postdose)						✓				✓		
Height (V1 only) and weight	✓		✓ (predose)						✓		✓		✓		
Orthostatic vital signs			✓ (postdose)		✓				✓		✓		✓		
Vital signs	✓	✓		✓		✓	✓	✓		✓		✓			
Physical exam	✓		✓ (predose)						✓		✓		✓		
Neurological exam	✓		✓ (predose)						✓	✓	✓	✓	✓		
Serum pregnancy test at central lab	✓														
Local urine pregnancy test[b]			✓ (predose)										✓		

Activity	Screening (V1)	Screening (V2)	Treatment Period											Post-treatment Follow-up Call[d]	Dispensing Visits[c]
			Optimization Period 4 Weeks						Maintenance Period 48 Weeks						
			Enrollment Day 1 (V3)	Day 2 (V4)	Week 1 (V5)	Week 2 (V6)	Week 3 (V7)	Week 4 (V8)	Week 6 (V9)	Week 13 (V10)	Week 26 (V11)	Week 39 (V12)	Week 52 (V13)/ Premature Discontinuation		
℞ TREATMENT															
Drug delivery system training		✓	✓												
Study drug infusion			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			
Verify supply of drug, investigational devices and ancillaries			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓
Verify reconciliation of drug and investigational devices			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓
Dispense/return drug delivery system			Investigational product will be dispensed on Day 1, at Week 1, and every 2 weeks thereafter through Week 51. Used and unused vials dispensed at the previous visit should be returned by the subject (before dispensing new vials) at Week 1 and every 2 weeks thereafter; all drug delivery components should be returned by the subject at Week 52/premature discontinuation.												
Study drug prescription record			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			

a. As allowed by local regulations, the PKG watch will be given to the subject following V1, after being received by the study site, and prior to the monitoring period. The 6-day Monitoring Period can occur any time before V3 once the PKG watch has been received by the study site, lasting for a minimum of 6 consecutive days. PD Diaries will also be collected for at least 2 consecutive days during the same 6-day Monitoring Period. In countries where the PKG watch is not approved, the Monitoring Period may be reduced to at least 2 days to account for the collection of PD Diaries and pump training.

b. Urine pregnancy tests will be performed monthly for women of childbearing potential. If there is a scheduled visit, the test will be performed on site; if there is not a scheduled visit, the test may be performed at an unscheduled visit or at home.

c. Dispensing visits may occur with or without a clinic visit being completed.

d. If the subject is willing, the post-treatment follow-up call will occur 30 days after premature discontinuation from the study or 30 days after completion of Week 52 for subjects not enrolling in the extension study.

Appendix B. Potentially Clinically Significant Laboratory Values

Clinical Laboratory Tests	Very Low (VL)	Very High (VH)
Hematology		
Activated partial thromboplastin time	NA	> ULN
Hemoglobin	< 100 g/L (6.2 mmol/L)	> 40 g/L above ULN
Prothrombin Intl. Normalized Ratio	NA	> ULN
Leukocytes (white blood cell)	$< 2 \times 10^9$/L	$> 100 \times 10^9$/L
Lymphocyte	$< 0.5 \times 10^9$/L	$> 20 \times 10^9$/L
Neutrophil	$< 1 \times 10^9$/L	NA
Platelets	$< 75 \times 10^9$/L	NA
Chemistry		
Bilirubin	NA	> 1.5 × ULN
Cholesterol	NA	> 12.92 mmol/L (500 mg/dL)
Creatinine	NA	> 1.5 × ULN
Calcium (corrected serum)	< 1.75 mmol/L (7.0 mg/dL)	> 3.1 mmol/L (12.5 mg/dL)
Glucose (fasting)	< 2.2 mmol/L (40 mg/dL)	> 13.9 mmol/L (250 mg/dL)
Potassium	< 3.0 mmol/L	> 6.0 mmol/L
Magnesium	< 0.4 mmol/L (0.9 mg/dL)	> 1.23 mmol/L (3 mg/dL)
Triglycerides	NA	> 5.7 mmol/L (500 mg/dL)
Uric acid	NA	> 590 umol/L (10 mg/dL)
Albumin	< 20 g/L	NA
Sodium	< 130 mmol/L	> 155 mmol/L
Inorganic phosphorus	< 0.6 mmol/L (2 mg/dL)	NA
Enzymes		
Alanine aminotransferase (ALT)	NA	> 3 × ULN
Alkaline phosphatase	NA	> 2.5 × ULN
Aspartate aminotransferase (AST)	NA	> 3 × ULN
Creatine phosphokinase (CPK)	NA	> 5 × ULN

NA = not applicable; ULN = upper limit of normal

Adapted from the Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0 Published: May 28, 2009 (v4.03: June 14, 2010).

Appendix C. Criteria for Potentially Clinically Significant Vital Sign and Weight Values

Vital Signs	Unit	Very Low (VL)	Very High (VH)
Systolic blood pressure (supine and standing)	mmHg	≤ 80 and decreased ≥ 45 from baseline	≥ 160 and increased ≥ 45 from baseline
Orthostatic systolic blood pressure	mmHg	Decrease ≥ 30 from supine to standing	NA
Diastolic blood pressure (supine and standing)	mmHg	≤ 50 and decreased ≥ 40 from baseline	≥ 95 and increased ≥ 40 from baseline
Orthostatic diastolic blood pressure	mmHg	Decrease ≥ 20 from supine to standing	NA
Pulse rate (supine and standing)	bpm	≤ 45 and decreased ≥ 35 from baseline	≥ 120 and increased ≥ 35 from baseline
Orthostatic pulse rate	bpm		Increase ≥ 30 from supine to standing
Temperature	degrees C	NA	≥ 38.3 and increase ≥ 1.1 from baseline
Weight	kg	Decreased ≥ 7% from baseline	Increased ≥ 7% from baseline

Appendix D. Criteria for Potentially Clinically Significant ECG Values

ECG Parameters	Unit	Very Low (VL)	Very High (VH)
Heart rate	bpm	≤ 45 and decreased ≥ 35 from baseline	≥ 120 and increased ≥ 35 from baseline
PQ (PR)	ms	≤ 120	≥ 220
QTcF Interval	ms	NA	≥ 480 OR Increased ≥ 60 from baseline

Appendix E. Definition of Adverse Events of Special Interest

Adverse Events of Special Interest (AESI) will be identified using the following search criteria:

Area of Safety Interest	Search Criteria
Infusion Site Related Infections	Infusion Site Related Infections (AbbVie ABBV-951 product-specific) Company MedDRA Query (CMQ) (code 80000194)
Infusion Site Related Non Infection Reactions	Infusion Site Related Non Infection Reactions (AbbVie ABBV-951 product-specific) CMQ (code 80000193)
Polyneuropathy	Broad search and narrow search of the Standardized MedDRA Queries (SMQ) • SMQ Peripheral Neuropathy (code 20000034)
Weight Loss	Weight Loss CMQ (code 80000109)
Hallucinations/Psychosis	Search of combined terms in: • CMQ Hallucinations (code 80000088) • SMQ Psychosis and Psychotic Disorders (code 20000117). Note: all terms in this SMQ are narrow search.
Somnolence	Preferred terms (PT) "Somnolence." "Hypersomnia," "Microsleep," "Sudden onset of sleep," "Sleep disorder due to general medical condition, hypersomnia type," "sleep attacks"
Falls and associated injuries	Separate and combined searches: • Falls and Associated Injuries (ABBV-951 product-specific) CMQ (code 80000204) • Orthostatic Hypotension PTs "blood pressure ambulatory decreased," "blood pressure orthostatic," "blood pressure orthostatic decreased," "dizziness," "dizziness postural," "orthostatic hypotension," "syncope"