Hangzhou PhecdaMed Co., Ltd.

A Randomized, Double-blind, Placebo Parallel-Controlled Phase II Clinical Trial to Evaluate the Efficacy and Safety of TJ0113 Capsule in Patients with Early-stage Parkinson's Disease

TJJS01-201

Statistical Analysis Plan

Version: 1.0

Date: September 22, 2025

Sponsor Approval Page

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Amendment History

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V1.0	September 22, 2025	Qing Li	New created

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List of Abbreviations and Definitions of Terms

Abbreviations/Terms	Full Name
AE	Adverse Event
ALT	Alanine Aminotransferase
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
ASMI	Appendicular Skeletal Muscle Index
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical Classification
ATC2	ATC Level 2 Terminology
BMI	Body Mass Index
Ccr	Creatinine Clearance
CI	Confidence Interval
CTCAE	Common Terminology Criteria for Adverse Events
DXA	Dual-energy X-ray Absorptiometry
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
FAS	Full Analysis Set
GFAP	Glial Fibrillary Acidic Protein
IFN	Interferon
IL	Interleukin
LOCF	Last Observation Carried Forward
Max	Maximum
MDS-UPDRS	Unified Parkinson's Disease Rating Scale
MedDRA	Medical Dictionary for Regulatory Activities
Median	Median
MI	Multiple Imputation
Min	Minimum
MMRM	Mixed-Effects Model for Repeated Measures
NCI	National Cancer Institute

PD	Parkinson's Disease
PN	Preferred Name
PPS	Per-Protocol Set
PT	Preferred Term
Q1	First Quartile
Q3	Third Quartile
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
SS	Safety Set
TBIL	Total Bilirubin
TEAE	Treatment-Emergent Adverse Event
TNF	Tumor Necrosis Factor
TRAE	Treatment Related Adverse Event
ULN	Upper Limit of Normal
WHODrug	World Health Organization Drug Dictionary

1. Introduction

This Statistical Analysis Plan is prepared for study entitled as "A Randomized, Double-blind, Placebo Parallel-controlled Phase II Clinical Trial to Evaluate the Efficacy and Safety of TJ0113 Capsules in Patients with Early Parkinson's Disease" (Protocol No.: TJJS01-201). It provides a detailed description of the statistical analysis content and methodology.

This statistical analysis plan is developed based on the study protocol version 4.0 dated February 11, 2025, and the case report form (CRF) version 4.0 dated April 28, 2025.

2. Study Design

2.1. Overall Design

This study is a randomized, double-blind, placebo parallel-controlled Phase II clinical trial designed to evaluate the efficacy and safety of TJ0113 capsules in patients with early-stage PD. It is planned to include approximately 150 subjects with early-stage PD who will be randomized in a 1:1 ratio into two cohorts (Cohort 1: 200 mg dose group; Cohort 2: 400 mg dose group). Within each cohort, subjects who have been successfully screened will be randomly assigned to TJ0113 capsules group and the placebo group in a ratio of 2:1 within each stratum based on a stratification factor whether they have been receiving levodopa, the background medication for PD (yes vs. no) at a stable dose. Among them, approximately 50 subjects will receive TJ0113 capsules and approximately 25 subjects will receive the placebo. In this study, there will be approximately 50 subjects in each of the TJ0113 capsules 200 mg group, TJ0113 capsules 400 mg group and the placebo group.

After randomization, subjects will receive the oral administration of TJ0113 capsules or the placebo for 12 consecutive weeks and continue to receive follow-up visits for 1 week (telephone follow-up) after the end of treatment. For subjects who have been receiving the anti-PD drug at a stable dose for at least 4 weeks prior to study entry, the original regimen of the background medication for PD should be maintained during the study.

The trial period includes a screening phase (up to 4 weeks), a treatment phase (12 weeks), and a follow-up phase (1 week, via telephone follow-up).

2.2. Randomization and Blinding

This study is a randomized, double-blind, placebo parallel-controlled Phase II clinical trial. The subject randomization numbers and drug randomization numbers will be pre-generated by the randomization statistician (independent of the project) in the statistical department, to create the randomization table. The detailed randomization procedure will be described in the randomization plan.

Throughout the study, all personnel involved in blinding should remain blinded until the database is locked. Refer to Section 5.3.2 of the protocol for the detailed blinding procedure.

3. Study Objectives and Endpoints

Trial Objectives	Trial Endpoints
Primary Objective	**Primary Endpoint**
To assess the efficacy of TJ0113 capsules in the treatment of patients with early-stage PD.	Changes from baseline in scores of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III (motor examination) in subjects after 12 weeks of treatment. Evaluation time point: ≥ 12 hours from the most recent dose of anti-PD drug.
Secondary Objectives	**Secondary Endpoints**
To assess the efficacy of TJ0113 capsules in the treatment of patients with early-stage PD.	• Changes from baseline in scores of MDS-UPDRS Part III (motor examination) in subjects after 1, 4, 8 weeks of treatment. Evaluation time point at each visit: ≥ 12 hours from the most recent dose of anti-PD drug; • Changes from baseline in scores of MDS-UPDRS Part III (motor examination) in subjects after 1, 4, 8, 12 weeks of treatment. Evaluation time point at each visit: 2 ± 1 hours from the most recent dose of anti-PD drug; • Changes from baseline in scores of MDS-UPDRS Part I, II and IV in subjects after 1, 4, 8 and 12 weeks of treatment; • Changes from baseline in the total scores of MDS-UPDRS in subjects after 1, 4, 8, 12 weeks of treatment, including: - Total score 1: II+III; wherein, the evaluation time point for MDS-UPDRS Part III (motor examination) is ≥ 12 hours from the most recent dose of anti-PD drug; - Total score 2: II+III; wherein, the evaluation time point for MDS-UPDRS Part III (motor examination) is 2 ± 1 hours from the most recent dose of anti-PD drug; - Total score 3: I+II+III; wherein, the evaluation time point for MDS-UPDRS Part III (motor examination) is ≥ 12 hours from the most recent dose of anti-PD drug; - Total score 4: I+II+III; wherein, the evaluation time point for MDS-UPDRS Part III (motor examination) is 2 ± 1 hours from the most recent dose of anti-PD drug;

	- Total score 5: I+II+III+IV; wherein, the evaluation time point for MDS-UPDRS Part III (motor examination) is ≥ 12 hours from the most recent dose of anti-PD drug; - Total score 6: I+II+III+IV; wherein, the evaluation time point for MDS-UPDRS Part III (motor examination) is 2 ± 1 hours from the most recent dose of anti-PD drug.
To assess the safety of TJ0113 capsules in the treatment of patients with early-stage PD.	• AE; • Laboratory test; • Vital signs; • Physical examination; • 12-lead ECG.
Exploratory Objectives	**Exploratory Endpoints**
To explore the changes in inflammatory indicators in early-stage PD patients treated with TJ0113 capsules.	Changes in inflammatory markers from baseline at 4, 8, and 12 weeks of treatment.
To investigate the impact of TJ0113 capsules on PD biomarkers in early-stage PD patients.	Changes in α-synuclein and glial fibrillary acidic protein (GFAP) from baseline after 12 weeks of treatment.
To explore the effect of TJ0113 capsules on skeletal muscle mass and function in early-stage PD patients.	• Changes from baseline in appendicular skeletal muscle mass index (ASMI) measured by dual-energy X-ray absorptiometry (DXA) after 12 weeks of treatment; • Changes from baseline in muscle strength (grip strength) after 12 weeks of treatment; • Changes from baseline in 6-meter walking speed test after 12 weeks of treatment.
To explore the association between the efficacy of TJ0113 capsules and the genomic characteristics in early-stage PD patients.	The association between the efficacy of TJ0113 capsules and the genomic characteristics in early-stage PD patients.

3.1. Estimand

The primary estimands of this study are as follows:

- Population: Early-stage PD patients who meet the inclusion criteria (refer to Section 4.1 of the protocol) and do not meet the exclusion criteria (refer to Section 4.2 of the protocol).
- Treatment: Patients will be randomized into one of two cohorts (200 mg and 400 mg dose groups) in a 1:1 ratio. Within each cohort, patients will be further randomized in a 2:1 ratio to receive either TJ0113 capsules or placebo.
- Endpoint: Change from baseline in the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III (Motor Examination) score after 12 weeks of treatment. Evaluation time point: ≥ 12 hours from the most recent dose of anti-PD drug.
- Concomitant Events and Management Strategies: Any concomitant medications (excluding the investigational product and stable anti-PD drugs at enrollment) or treatments that may affect the PD progression will be addressed using therapeutic strategies.
- Population-level Summary: Least squares mean difference in the change from baseline in MDS-UPDRS Part III (Motor Examination) scores between the TJ0113 capsule group and the placebo group after 12 weeks of treatment. Evaluation time point: ≥ 12 hours from the most recent dose of anti-PD drug. (Refer to Section 6.10.1.1)

3.2. Efficacy Endpoints

MDS-UPDRS

The MDS-UPDRS consists of four parts: Part I (Nonmotor Experiences of Daily Living), Part II (Motor Experiences of Daily Living), Part III (Motor Examination), and Part IV (Motor Complications). Throughout the study, each subject should have a fixed rater to evaluate his/her score using MDS-UPDRS.

- For subjects who have received the anti-PD drug at a stable dose for at least 4 weeks prior to study entry, the MDS-UPDRS assessment time points and corresponding assessment parts are as follows:

Visit	MDS-UPDRS assessment part	Assessment time points
V1	Part I	No special requirements
	Part III	Before administration of background medication for PD (≥ 12 hours from the most recent dose of the background medication for PD)
V2, Early Withdrawal	Part III	Before administration of background medication for PD (≥ 12 hours from the most recent dose of the background

Visit (if applicable)		medication for PD)
		After administration of background medication for PD (to be performed at 2 ± 1 hours after the administration of background medication for PD at this visit)
	Parts I, II, and IV	No special requirements
V3~V6	Part III	Before administration of the investigational product and the background medication for PD (≥ 12 hours from the most recent administration of background medication for PD and the investigational product)
		After administration of the investigational product and the background medication for PD (to be performed at 2 ± 1 hours after the administration of the background medication for PD and the investigational product at this visit)
	Parts I, II, and IV	No special requirements

- For subjects who have not received the anti-PD drug at study entry, the MDS-UPDRS assessment time points and corresponding assessment parts are as follows:

Visit	**MDS-UPDRS assessment part**	**Assessment time points**
V1	Part I	No special requirements
	Part III	No special requirements
V2	Part III	No special requirements
	Parts I, II, and IV	No special requirements
V3～V6	Part III	Before administration of the investigational product (≥ 12 hours from the most recent administration of the investigational product)
		After administration of the investigational product (to be performed at 2 ± 1 hours after the administration of the investigational product at this visit)

Visit	MDS-UPDRS assessment part	Assessment time points
	Parts I, II, and IV	No special requirements
Early Withdrawal Visit (if applicable)	Part III	≥ 12 hours from the most recent administration of the investigational product
	Parts I, II, and IV	No special requirements

3.3. Safety Endpoints

3.3.1. AEs

Adverse Event (AE)

The definition of adverse events collected in this study will be detailed in Section 9 of the protocol. Specific information such as the start date, end date, and severity of adverse events will be recorded in detail on the adverse event page of the eCRF.

Treatment-Emergent Adverse Event (TEAE)

TEAE will be defined as any adverse event that newly occurs (not present before treatment) or worsens relative to pretreatment after the first administration of the investigational product.

Treatment-related Adverse Event (TRAE)

TRAE will be defined as a TEAE assessed by the investigator as related to the investigational product, including "definitely related," "probably related," or "possibly related." The relationship to the investigational product will be recorded in the eCRF adverse event page.

Serious Adverse Event (SAE)

The definition of serious adverse events (SAEs) will be detailed in Section 9.1.4 of the protocol. Investigators will determine whether an event qualifies as an SAE. Information such as the occurrence date of the SAE and the criteria met will be recorded in the adverse event page of the eCRF.

Adverse Event Grading

The severity of AEs will be recorded according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. The CTCAE grade of adverse events will be determined by the investigator and recorded in the eCRF.

Adverse Events Leading to Dose Interruption, Dose Reduction, or Discontinuation

The actions taken for adverse events that will be recorded in the eCRF adverse event page include dose suspension, dose reduction, and discontinuation.

Death

Any death due to adverse events will be recorded in the adverse event page of the eCRF. In addition, detailed information on deaths will be recorded in the death page of the eCRF, including the date of death and cause of death.

3.3.2. Laboratory Tests

Including hematology , blood biochemistry, urinalysis, coagulation function, serum pregnancy test, urine pregnancy test, etc. The laboratory tests collected in the eCRF are listed in Table 1.

Table 1 Laboratory Test Items

Items	Examination Indicators
Hematology (CBC)	White blood cell count, absolute neutrophil count, neutrophil percentage, absolute lymphocyte count, lymphocyte percentage, absolute monocyte count, monocyte percentage, absolute eosinophil count, eosinophil percentage, absolute basophil count, basophil percentage, red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, red cell distribution width, platelet count, mean platelet volume, plateletcrit, and platelet distribution width
Blood Biochemistry	Fasting blood glucose, bile acid, total protein, albumin, globulin, albumin/globulin ratio, TBIL, direct bilirubin, indirect bilirubin, ALT, AST, γ-glutamyl transferase, alkaline phosphatase, lactate dehydrogenase, creatine kinase, creatine kinase-MB , urea/urea nitrogen, serum uric acid, creatinine, potassium, sodium, chloride, calcium, magnesium, inorganic phosphorus, triglycerides, total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol.
Creatinine clearance rate (Ccr)	Calculate Ccr based on body weight measurements and serum creatinine levels in blood biochemistry tests.
Urinalysis	Glucose urine, bilirubin urine, urine ketone body, urine pH, protein urine, urine urobilinogen, nitrite urine, occult blood urine, white blood cells urine, red blood cells urine, microscopic examination of urine sediment (red blood cells, white blood cells), and specific gravity urine.
Coagulation function	Prothrombin time, activated partial thromboplastin time, thrombin time, international normalized ratio, and fibrinogen
Pregnancy Test	Serum pregnancy and urine pregnancy

3.3.3. Vital Signs

Including respiration, pulse, body temperature, systolic blood pressure, and diastolic blood pressure.

3.3.4. Physical Examination

It includes skin and mucous membranes, lymph nodes, head, neck, chest, abdomen, spine and limbs, nervous system and mental state.

3.3.5. 12-lead ECG

The parameters include: heart rate, PR interval, QRS complex duration, uncorrected QT interval, and Fridericia-corrected QTc (QTcF). Two measurements will be taken within 20 minutes, and the average value is calculated and rounded to the nearest integer.

3.4. Exploratory Endpoints

3.4.1. Inflammatory Markers

The exploratory inflammatory indicators of this study include interleukin (IL)-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12p70, IL-17A, interferon (IFN)-α, IFN-γ, and tumor necrosis factor (TNF)-α. The specific testing indicators should be determined based on the actual implementation at each center.

3.4.2. PD Biomarkers

The exploratory PD biomarker measures in this trial include α-synuclein and GFAP.

3.4.3. Assessment of Skeletal Muscle Mass and Function

The exploratory skeletal muscle mass and function assessment indicators in this trial include ASMI, muscle strength (handgrip strength), and the 6-meter walk test. The specific testing indicators should be determined based on the actual operations of each center.

4. Sample Size

The sample size of this study is not determined based on the formal statistical assumptions and it is expected to include approximately 150 subjects with early-stage PD, who will be randomized in a 1:1 ratio into two cohorts (Cohort 1: 200 mg dose group; Cohort 2: 400 mg dose group). Within each cohort, the subjects will be randomized into the TJ0113 capsules group and the placebo group in a ratio of 2:1, with approximately 50 subjects receiving TJ0113 capsules and approximately 25 subjects receiving the placebo. In this study, there will be approximately 50 subjects in each of the TJ0113 capsules 200 mg group, TJ0113 capsules 400 mg group and the placebo group.

5. Analysis Sets

Full analysis set (FAS): including all randomized subjects who have received at least one dose of investigational product.

Per-protocol set (PPS): including subjects in the FAS who have not experienced major protocol deviations that affect the primary efficacy endpoint.

Safety Set (SS): Includes all subjects who received at least one dose of the investigational product and underwent at least one post-dose safety assessment.

Demographics and baseline characteristics will be analyzed based on FAS, the efficacy analyses will be performed based on both FAS and PPS, and the safety analyses will be performed based on SS.

6. Statistical Analysis Methods

6.1. Statistical Considerations

Statistical analyses will be performed using SAS 9.4 or higher, with results reported in summary tables or subject listings. In the subject list, the subject screening number serves as the universal unique identifier for subjects in this study, and the default sorting will be based on the subject screening number.

Continuous Variables

For continuous variables, unless otherwise specified, the following descriptive statistics will be used for summarization: number of subjects, mean (Mean), standard deviation (SD), median (Median), first quartile (Q1), third quartile (Q3), minimum (Min), and maximum (Max). The measurement precision of each continuous variable will be used to determine the number of decimal places displayed in tables, charts, and listings. The decimal places for minimum and maximum will remain consistent with the original data recorded in the database; means and quantiles will retain one additional decimal place compared to the original data in the database; standard deviations will retain two additional decimal places compared to the original data in the database. Any values requiring conversion to standard units should adhere to the aforementioned principles after being converted to the corresponding precision values. When determining the number of decimal places to display, both the validity of precision and the practicality of presentation will be considered. For example, if there are too many decimal places to accommodate additional information, the reported data will retain an appropriate number of decimal places, up to a maximum of four.

Categorical Variable

For categorical variables, the number and percentage of subjects will be summarized. Unless otherwise specified, percentages will be calculated based on all subjects in the respective analysis population. Percentages will be rounded to one decimal place. When the percentage is 100%, it will be reported as 100%. If the number of subjects is 0, the percentage will not be reported.

General Principles of Statistical Inference

A Mixed Model for Repeated Measures (MMRM) will be used to calculate nominal P values for between-group comparisons of primary and secondary endpoints; where applicable, analysis of covariance (ANCOVA) will be employed to calculate nominal P values for between-group comparisons of primary endpoints. For exploratory endpoints with normally distributed variables, analysis of variance (ANOVA) will be used to calculate nominal P-values for between-group comparisons; otherwise, the Wilcoxon rank-sum test will be employed for between-group comparisons to calculate nominal P-values.

Confidence Interval (CI)

Unless otherwise specified, the CI refers to a two-sided 95% CI, with one more decimal place than the derived data or parameters.

P-value

This study does not conduct formal hypothesis testing, and the summarized P-values will be nominal P-values. P-values should be retained to 4 decimal places. If the P-value is less than 0.0001, it should be presented as "<.0001"; if the P-value will be greater than 0.9999, it should be presented as ">.9999".

Treatment Group

Unless otherwise specified, it will be summarized by the TJ0113 capsules 200 mg group, TJ0113 capsules 400 mg group, and the placebo group.

Study Day 1

Study Day 1 is defined as the day of the first dose of the investigational product. All safety and efficacy assessments will be calculated based on Study Day 1.

- If the visit date ≥ the first dose date, then: Study day = Visit date - First dose date + 1
- If the visit date < the first dose date, then: Study day = Visit date - First dose date.

There is no definition of Study Day 0 in this study.

Repeated Measurements or Assessments

If more than one measurement or assessment of a certain parameter is conducted at the same time point during the same visit according to the study protocol, it will be defined as a repeated measurement or assessment. The mean value of repeated measurements or evaluations will be used as the analytical value. In this study, all 12-lead electrocardiogram (ECG) parameters will be measured twice, and clinical evaluations will be performed with duplicate assessments.

Baseline Value

Unless otherwise specified, baseline is defined as the last valid measurement or assessment result prior to the first dose (including scheduled or unscheduled visits). If an unscheduled visit date coincides with the scheduled visit date and the exact time is unknown, the results from the scheduled visit should be used as the baseline.

For repeated measurements (e.g., duplicate ECG measurements), the mean of the repeated measurements will be used as the baseline value in the analysis.

For the MDS-UPDRS Part III (Motor Examination) score, if the assessment time point is ≥12 hours after the last dose of anti-PD medication, the last valid assessment result corresponding to the "≥12 hours after the last dose of anti-PD medication" time point prior to the first dose will be used as the baseline value in the analysis. If the assessment time point is 2±1 hours after the last dose of anti-PD medication, the last valid assessment result corresponding to the "2±1 hours after the last dose of anti-PD medication" time point prior to the first dose will be used as the baseline value in the analysis.

For the MDS-UPDRS Parts I, II, and IV scores, the last valid assessment result prior to the first dose will be used as the baseline value for analysis.

Change from Baseline

Change from baseline = Post-baseline measurement - Baseline value.

Analysis Visit

Analysis visits include: Baseline, V3 (Week 1 of treatment), V4 (Week 4 of treatment), V5 (Week 8 of treatment), V6 (Week 12 of treatment).

Unscheduled Visit

For safety analysis tables summarized by visit, only scheduled visits are included. Unless otherwise specified, data from unscheduled visits will be included in the following analyses:

- Calculate baseline values
- Analyses involving abnormalities and clinically significant findings
- Listing

6.2. Data Handling Methods

6.2.1. Missing Data

Missing Data Handling

1) Multiple Imputation (MI) Method

The MI method will be applied for the sensitivity analysis of the primary endpoint. For all subjects in the FAS, missing data of the primary endpoint—the score of Part III (Motor Examination) of the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) at 12 weeks post-dose (evaluation time point: ≥12 hours after the last dose of anti-PD drug)—will be imputed. The imputation rules are detailed in Section 11.1 of the Appendix in SAP.

2) Last Observation Carried Forward (LOCF) Method

The LOCF method will be applied for sensitivity analysis of the primary endpoint. For all subjects in the FAS, missing data of the primary endpoint—the score of Part III (Motor Examination) of the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) at Week 12 (assessment time point: ≥12 hours after the last dose of anti-PD drug)—will be imputed. Missing data will be imputed using the last non-missing observation prior to the visit after baseline (excluding baseline).

3) Missing Date:

For incomplete date data, the dates in the list will be presented according to the actual circumstances. The missing date imputation rules are as follows:

Missing AE Onset Date

- Only day missing: If the year and month of the AE onset date are the same as the year and month

of the first dose date, and the AE end date is confirmed to be no earlier than the first dose date or missing, then the first dose date will be used as the AE onset date. Otherwise, impute as the 1st day of the month.

- Month and day missing: If the year of the AE onset date is the same as the year of the first dose date, and the AE end date is confirmed to be no earlier than the first dose date or missing, then the first dose date will be used as the AE onset date. Otherwise, impute as January 1 of that year;
- Year, month, and day missing: Impute with the subject's first dose date.

Missing AE End Date

- Only day missing: impute as the date of the last day of the month;
- Month and day missing: imputed as December 31 of that year;
- Year, month, and day missing: no imputation.

The imputation of the end date should not be earlier than the onset date.

Missing Or Incomplete Start Dates Of Previous And Concomitant Medications/Non-Drug Therapies

- Only day missing: impute as the first day of the month;
- Month and day missing: impute as January 1 of that year;
- Year, month, and day missing: no imputation.

Missing Or Incomplete End Dates Of Previous And Concomitant Medications/Non-Drug Therapies

- Only day missing: Impute as the last day of that month;
- Month and day missing: impute as December 31 of that year;
- Year, month, and day missing: no imputation.

The imputation of the end date should not be earlier than the onset date.

6.2.2. Derived and Transformed Data

No derivation or transformation of other data will be performed, except for the calculation of certain study endpoints based on collected data.

Definitions and calculation methods for drug exposure and compliance are as follows:

Drug exposure will be calculated based on the eCRF page "Administration of Investigational Product":

- Actual total exposure (mg):
    - For placebo, the actual total exposure (mg) = 0 mg;
    - For the TJ0113 capsule group, the actual total exposure (mg) = actual cumulative number of doses administered (capsules) × 100 mg.

- Total actual exposure days (days) = Sum of actual dosing days, calculated by accumulating the interval days between the start and end dates of actual dosing collected in the eCRF to determine the subject's actual dosing duration. If a dose is missed, it will be recorded as a separate line in the eCRF, with the "Actual Daily Dose" recorded as "0 capsules." When calculating the total exposure days, the corresponding number of missed days should be deducted based on the start and end dates of the missed doses.
- Actual dose level (mg/day) = Total actual exposure / Total exposure days.

Medication compliance (%) will be calculated based on the eCRF pages "Investigational Product Dispensing" and "Investigational Product Accountability ":

- Total cumulative number of drug dispensed (capsules) = Sum of the number of drug dispensed.
- Total number of recovered drug (capsules) = Sum of recovered drug.
- Cumulative lost/contaminated drug count (capsules) = Sum of lost/contaminated capsules.
- Actual cumulative administered dose (capsules) = Actual cumulative total dispensed dose (capsules) - Actual cumulative total recovered dose (capsules) - Actual cumulative lost/damaged dose (capsules)
- Planned cumulative dose (capsules):
    - For the 200 mg cohort: Planned cumulative dose (capsules) = Planned dosing days (days) × 2;
    - For the 400 mg cohort: Planned cumulative dose (capsules) = Planned dosing days (days) × 4;

Planned dosing days (days) = Date of last drug recovery – Date of first dose dispensing. If the last drug recovery visit is the withdrawal visit and the last drug recovery date > (first dose dispensing date + 84 days), replace it with (first dose dispensing date + 84 days). If the last drug recovery visit is an unscheduled visit and the date of last drug recovery is > the date of study completion/withdrawal, then the date of study completion/withdrawal should be used instead. If there is no record of drug recovery after the last dose dispensing and the study has ended, the date of the next visit after the last dose dispensing or the study completion/withdrawal date, whichever is earlier, should be used. If the date of the next visit after the last dose dispensing or the study completion/withdrawal date exceeds (the first dose dispensing date + 84 days), then (the first dose dispensing date + 84 days) should be used instead.

- Medication compliance (%) = Actual Cumulative Dose Administered (tablets) / Planned Cumulative Dose (tablets) × 100.

For subjects who were randomized but did not receive any investigational product, or who were randomized but received different dose groups, the compliance will be 0.

6.3. Subject Distribution Analysis

Based on all subjects who signed the informed consent form, the number and percentage of subjects in the following categories will be summarized:

- Successfully screened subjects
- Screen failures (reasons for screen failure)
- All randomized subjects (including those randomized at each center)

Based on all randomized subjects, the number and percentage of subjects in the following categories will be summarized:

- Randomized subjects who did not receive any investigational product
- Randomized subjects who received any dose of the investigational product
- Ongoing
- Completion of the study
- Early withdrawal of study (Reasons for early withdrawal of study)

List the reasons for screen failure and early withdrawal of study in detail.

6.4. Subject Analysis Set Classification

Based on all randomized subjects, calculate the number and percentage of subjects included in the FAS, PPS, and SS. Additionally, provide a detailed list of reasons for subjects excluded from each analysis set.

6.5. Protocol Deviations

Based on the FAS, categorize and summarize significant protocol deviations, and provide a detailed listing of all subjects with protocol deviations.

6.6. Demographic Data and Baseline Characteristics Analysis

Based on the FAS, summarize and tabulate the demographic data and baseline characteristics of the subjects.

Demographic data of subjects include:

- Age (years)
- Age groups (<18 years, 18-65 years, 66-75 years, >75 years)
- Gender (Male, Female)
- For females, is the subject of childbearing potential (yes, no (postmenopausal, sterilization surgery, ovarian failure, other), uncertain if menopausal)
- Ethnicity (Han, Others)
- Height (cm)
- Weight (kg)
- Body Mass Index (kg/m^2)

The baseline characteristics of subjects include:

- Random stratification factors:
    - Is the subject currently on stable levodopa-based anti-PD therapy (Yes, No)
- Medications for Anti-Parkinson's Disease:
    - No prior anti-PD therapy
    - Previous anti-PD therapy but no anti-PD therapy within 4 weeks prior to enrollment
    - Patients must have received stable anti-PD drug therapy for at least 4 weeks prior to enrollment and agree to maintain the original treatment regimen unchanged during the trial.
- Age at initial diagnosis (years) = (Initial diagnosis date - Birth date + 1) / 365.25, rounded to 1 decimal place. If the initial diagnosis date is missing, impute according to the following principles before calculation: if the day is missing, impute as the 1st day; if both the month and day are missing, impute as January 1st; if the year, month, and day are all missing, treat as missing.
- Age group at initial diagnosis (≤50 years, >50 years)
- Past and Present Medical History (excluding Parkinson's disease) (Yes, No)
- Previous surgical history (Yes, No)
- Allergy history (Yes, No)
- Modified Hoehn-Yahr Scale (Stage 0, Stage 1.0, Stage 1.5, Stage 2.0, Stage 2.5, Stage 3.0, Stage 4.0, Stage 5.0)
- Disease duration (years) = (Date of informed consent signing - Initial diagnosis date + 1) / 365.25, with results rounded to 1 decimal place. If the initial diagnosis date is missing, impute according to the following principles before calculation: if the day is missing, impute as the 1st day; if both the month and day are missing, impute as January 1st; if the year, month, and day are all missing, treat as missing.
- Type of Parkinson's Disease History (Clinically Confirmed Parkinson's Disease, Probable Parkinson's Disease, Other)

6.7. Past and Current Medical History

Code past and current medical history using the Medical Dictionary for Regulatory Activities (MedDRA; version 27.0 or above). Based on the FAS, summaries will be conducted according to the System Organ Class (SOC) and Preferred Term (PT), with detailed listings provided.

6.8. Prior and Concomitant Medications/Non-Pharmacological Therapies

Prior and Concomitant Medications

This study includes prior and concomitant medications, excluding medication for anti-Parkinson's disease, as well as anti-Parkinson's disease medications (excluding the investigational product). The World Health Organization Drug Dictionary (WHODrug, Global B3, Sep2024 or later version) will be used for coding.

Prior medication is defined as drugs with both start and end dates occurring before the first dose of study drug.

Concomitant medication is defined as any drug initiated on or after the date of the first dose of study drug, or any drug initiated before the date of the first dose of study drug and still in use on the date of the first dose of study drug.

Based on the FAS, the prior and concomitant medications of subjects, excluding medications for anti-Parkinson's disease, as well as the prior and concomitant medications for anti-Parkinson's disease (excluding investigational products), will be summarized by Anatomical Therapeutic Chemical (ATC) classification level 2 (ATC2) and Preferred Name (PN). List the subjects' prior and concomitant medications in detail.

Previous and Concomitant Non-Pharmacological Therapies

Code prior and concomitant non-drug therapies using the Medical Dictionary for Regulatory Activities (MedDRA) version 27.0 or higher.

Previous non-pharmacological therapy is defined as non-pharmacological therapy with both start and end dates occurring before the first dose of the study.

Concomitant non-drug therapy is defined as any non-drug therapy initiated on or after the date of the first dose of study drug, or initiated before the date of the first dose of study drug and still ongoing on the date of the first dose of study drug.

Based on the FAS, a detailed listing of subjects' prior and concomitant non-drug therapies will be provided.

6.9. Compliance

Based on the FAS, analyze and tabulate the compliance of the subjects. For subjects who were randomized but did not receive any investigational product, or who were randomized but received different dose groups, the compliance will be 0. Summarize descriptively the continuous and categorical (<80%, 80% - 120%, >120%) outcomes for the following indicators: total cumulative number of drugs dispensed (capsules), total cumulative number of drugs recovered (capsules), total cumulative number of drugs lost/damaged (capsules), actual cumulative number of drugs administered (capsules), planned duration of drug administration (days), planned cumulative number of drugs administered (capsules), and medication compliance (%). For specific definitions and calculation methods, please refer to Section 6.2.2.

6.10. Efficacy Analysis

The primary efficacy endpoint analysis will be conducted based on both the FAS and PPS, while the secondary efficacy endpoint analysis will be performed based on the FAS.

Descriptive statistics will be performed for changes from baseline in MDS-UPDRS part scores and total scores at each visit.

6.10.1. Primary Efficacy Endpoint Analysis

The primary efficacy endpoint of this study is the change from baseline in the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III (Motor Examination) score after 12 weeks of treatment. Evaluation time point: ≥ 12 hours from the most recent dose of anti-PD drug. The statistical methods, strategies for concomitant events, and handling of missing values are summarized in the following table:

Analysis	Analysis Population	Statistical Analysis Methods	Strategies and Missing Data Handling
Primary Analysis	FAS	Mixed Model for Repeated Measures (MMRM)	Treatment strategy, no imputation for missing values
Sensitivity Analysis 1	FAS	Analysis of Covariance (ANCOVA)	Treatment strategy, LOCF for missing value imputation
Sensitivity Analysis 2	FAS	Mixed Model for Repeated Measures (MMRM)	Treatment strategy, MI for missing value imputation
Supplementary Analysis 1	PPS	Mixed Model for Repeated Measures (MMRM)	Treatment strategy, no imputation for missing values
Supplementary Analysis 2	FAS	Mixed Model for Repeated Measures (MMRM)	A hypothetical strategy of employing MI to impute missing data.

6.10.1.1. Primary Analysis

The analysis will be performed using a mixed models for repeated measures (MMRM) with the changes from baseline in the MDS-UPDRS Part III scores after 12 weeks of treatment as the dependent variable, whether subjects have been receiving levodopa, the background medication for PD (yes vs. no) at a stable dose at baseline and the baseline MDS-UPDRS Part III score as the covariates, and the treatment group, visit, and the treatment group-by-visit interaction as the fixed effects. The covariance matrix prioritizes an unstructured (UN) covariance matrix. If the results do not converge, the following covariance structures will be tested sequentially: heterogeneous Toeplitz (TOEP), first-order autoregressive (AR1), and compound symmetry (CS). The first covariance structure that achieves convergence will be used. Based on the model, calculate the least squares mean of the change from baseline in MDS-UPDRS Part III score at 12 weeks of treatment, along with its 95% CI, the between-group difference in least squares means with its two-sided 95% CI, and the nominal P-value.

6.10.1.2. Sensitivity Analysis Methods

The sensitivity analysis of the primary endpoint will be conducted based on the FAS.

Sensitivity Analysis 1: For missing data in the primary endpoint, a Last Observation Carried Forward (LOCF) imputation will be applied, followed by a sensitivity analysis using Analysis of Covariance (ANCOVA). The imputation rules are detailed in Section 6.2.1. The model used the change from

baseline in the MDS-UPDRS Part III score at 12 weeks of treatment as the dependent variable, with baseline stable use of levodopa as anti-PD background medication (yes vs. no), baseline MDS-UPDRS Part III score, and treatment group as covariates. Based on the model, calculate the least squares mean of the change from baseline in MDS-UPDRS Part III score at 12 weeks of treatment, along with its 95% CI, the between-group difference in least squares means with its two-sided 95% CI, and the nominal P-value. The reference procedure is as follows:

```
ODS OUTPUT lsmeancl=lsmeans lsmeandiffcl=lsmeansdiff;

PROC GLM data=dataset;

    CLASS trtpn pd;

    MODEL chg = trtpn pd base/SOLUTION;

    LSMEANS trtpn/CL STDERR PDIFF COV;

run;
```

Sensitivity Analysis 2: Assuming the missing data mechanism is missing at random (MAR), a sensitivity analysis will be conducted using the same method as the primary analysis after performing multiple imputation for missing values. For imputation rules, refer to Section 11.1 of the SAP Appendix.

6.10.1.3. Supplementary Analysis Methods

Supplemental Analysis 1: Based on PPS, summarize using the same statistical methods described in the primary analysis in Section 6.10.1.1.

Supplementary Analysis 2: Based on the FAS, summarize concomitant events using the hypothetical strategy with the same statistical methods described in Section 6.10.1.1 for the primary analysis.

Concomitant Events and Handling Strategy: Any concomitant medications (excluding the investigational product and stable anti-PD medications at the time of enrollment) or treatments that may impact the PD progression will be addressed using the hypothetical strategy, wherein data following the concomitant event will be excluded and treated as missing data. Assuming the missing mechanism is missing at random (MAR), multiple imputation will be performed for missing values prior to analysis. For imputation rules, refer to Section 11.1 of the SAP Appendix.

6.10.2. Secondary Efficacy Endpoint Analysis

Secondary efficacy endpoint analyses will be based on the FAS.

The secondary efficacy endpoints of this study include:

- Changes from baseline in scores of MDS-UPDRS Part III (motor examination) in subjects after 1, 4, 8 weeks of treatment. Evaluation time point at each visit: ≥ 12 hours from the most recent dose of anti-PD drug;
- Changes from baseline in scores of MDS-UPDRS Part III (motor examination) in subjects after 1, 4, 8, 12 weeks of treatment. Evaluation time point at each visit: 2 ± 1 hours from the most recent

dose of anti-PD drug;

- Changes from baseline in scores of MDS-UPDRS Part I, II and IV in subjects after 1, 4, 8 and 12 weeks of treatment;
- Changes from baseline in the total scores of MDS-UPDRS in subjects after 1, 4, 8, 12 weeks of treatment, including:

- Total score 1: II+III; wherein, the evaluation time point for MDS-UPDRS Part III (motor examination) is ≥ 12 hours from the most recent dose of anti-PD drug;

- Total score 2: II+III; wherein, the evaluation time point for MDS-UPDRS Part III (motor examination) is 2 ± 1 hours from the most recent dose of anti-PD drug;

- Total score 3: I+II+III; wherein, the evaluation time point for MDS-UPDRS Part III (motor examination) is ≥ 12 hours from the most recent dose of anti-PD drug;

- Total score 4: I+II+III; wherein, the evaluation time point for MDS-UPDRS Part III (motor examination) is 2 ± 1 hours from the most recent dose of anti-PD drug;

- Total score 5: I+II+III+IV; wherein, the evaluation time point for MDS-UPDRS Part III (motor examination) is ≥ 12 hours from the most recent dose of anti-PD drug;

- Total score 6: I+II+III+IV; wherein, the evaluation time point for MDS-UPDRS Part III (motor examination) is 2 ± 1 hours from the most recent dose of anti-PD drug.

The analysis of secondary efficacy endpoints will be summarized using the same statistical methods as described in Section 6.10.1.1 for the primary analysis. Based on the model, the least squares means (LSM) of the change from baseline in MDS-UPDRS-related scores at each endpoint visit, along with their 95% CIs, will be derived. Additionally, the between-group differences in LSM, their two-sided 95% CIs, and nominal P-values will be calculated.

Additionally, line graphs will be plotted to display the least squares mean changes from baseline in MDS-UPDRS Part III (Motor Examination) scores at each visit (assessed at ≥12 hours and 2±1 hours after the last dose of anti-PD medication), along with their corresponding 95% CIs.

The MDS-UPDRS Part III (Motor Examination) scores at each visit (assessed at ≥12 hours and 2±1 hours after the last dose of anti-PD medication) will be plotted as line graphs showing the arithmetic mean change from baseline and its standard error.

6.11. Exploratory Analysis

Exploratory analyses will be performed based on the FAS.

6.11.1. Exploratory Analysis of Inflammatory Markers

The exploratory inflammatory endpoints are the changes in inflammatory markers from baseline at 4, 8, and 12 weeks of treatment. The exploratory inflammatory biomarkers in this trial include: interleukin (IL)-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12p70, IL-17A, interferon (IFN)-α, IFN-γ, and tumor necrosis factor (TNF)-α. The specific testing indicators should be determined based on the actual

implementation at each center. Descriptive statistics will be performed for inflammatory marker results at each visit and their changes from baseline.

Exploratory inflammatory endpoints will be analyzed using analysis of variance (ANOVA) or nonparametric tests: if the variables followed a normal distribution, ANOVA will be used for between-visit group comparisons; otherwise, the Wilcoxon rank-sum test will be employed for between-visit group comparisons.

List the inflammatory indicators of the subjects.

6.11.2. Exploratory PD Biomarker Analysis

The exploratory PD biomarker endpoints are the changes from baseline in α-synuclein and GFAP after 12 weeks of treatment. Descriptive statistics will be performed on the results of α-synuclein and GFAP indicators at 12 weeks post-treatment and their percentage changes from baseline.

Analyze α-synuclein and GFAP using analysis of variance (ANOVA) or nonparametric tests: if the variables follow a normal distribution, employ ANOVA for between-visit group comparisons; otherwise, use the Wilcoxon rank-sum test for between-visit group comparisons.

List the PD biomarker indicators for subjects.

6.11.3. Exploratory Analysis of Skeletal Muscle Mass and Function Assessment

Exploratory endpoints for skeletal muscle mass and function assessment include:

- Change in ASMI from baseline measured by dual-energy X-ray absorptiometry (DXA) after 12 weeks of treatment.
- Changes from baseline in muscle strength (grip strength) after 12 weeks of treatment;
- Changes from baseline in 6-meter walking speed test after 12 weeks of treatment.

The specific testing indicators should be determined based on the actual implementation at each center. Descriptive statistics will be performed on the results of skeletal muscle mass and functional assessment indicators after 12 weeks of treatment, as well as their changes from baseline.

Analysis of ASMI, muscle strength (grip strength), and 6-meter walk speed test will be performed using analysis of variance (ANOVA) or nonparametric tests: if the variables followed a normal distribution, ANOVA will be used for inter-visit group comparisons; otherwise, the Wilcoxon rank-sum test will be employed for inter-visit group comparisons.

List the indicators for assessing skeletal muscle mass and function in subjects.

6.12. Safety Analysis

Safety endpoints include: AEs, laboratory tests, vital signs, physical examinations, and 12-lead ECG. Safety analyses will be based on the SS.

6.12.1. Drug Exposure

Based on SS, analyze and tabulate drug exposure in subjects. A descriptive summary of the total actual drug exposure (mg), total exposure duration (days), and actual dose level (mg/day) for the subjects will be provided. For specific definitions and calculation methods, please refer to Section 6.2.2.

6.12.2. AEs

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 27.0 or higher. The severity of AEs will be classified according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

Summarize and tabulate adverse events, with the summary including only TEAEs and the tabulation encompassing all AEs.

The summary table of adverse events will include the number of AE occurrences, the number and percentage of subjects. When calculating the incidence of adverse events, multiple occurrences will be counted if the same subject experiences different adverse events multiple times. When calculating the number of subjects with adverse events, each subject will be counted only once, even if they experience multiple different adverse events. The percentage of adverse events will be calculated based on the number of subjects who experienced adverse events, not the number of adverse event occurrences. When counting the severity of adverse events, if the same subject experiences multiple adverse events under the same SOC or PT, the number of instances will be counted multiple times, while the number of cases will be only counted for the most severe occurrence.

The overall summary table of AEs will include the following TEAE categories:

- All TEAEs
- All TRAEs
- Treatment-emergent SAEs
- Treatment-emergent drug-related SAEs
- CTCAE ≥ Grade 3 TEAE
- CTCAE ≥ Grade 3 TRAE
- TEAE leading to death
- TEAE leading to dose suspension
- TEAEs leading to dose reduction
- TEAE leading to dose discontinuation
- TEAEs leading to early withdrawal

Summarize the above TEAE categories by SOC and PT. All TEAEs and SAEs during treatment will also be summarized by SOC, PT, and the highest CTCAE grade.

List all adverse events in detail.

Summarize the number and percentage of deceased subjects, along with the causes of death. List the causes of death.

6.12.3. Laboratory Tests

Descriptive statistics will be performed for the results of hematology, blood biochemistry, coagulation function, and Ccr measurements at each visit, as well as their changes from baseline.

For the clinical significance assessment of hematology, blood biochemistry, urinalysis, and coagulation function, cross-tabulation will be used to summarize the changes in subjects' clinical assessment categories from baseline to the worst post-baseline clinical assessment category (clinically significant abnormality > abnormality without clinical significance > normal > not examined). Analyze the "urine white blood cells" and "urine sediment microscopic white blood cells" results in the clinical significance of urinalysis collectively, and analyze the "urine red blood cells" and "urine sediment microscopic red blood cells" results collectively.

List the hematology, blood biochemistry, urinalysis, coagulation function, and Ccr of the subjects. Tabulate all abnormal test results.

For laboratory tests, if the original result contains an equal sign(e.g., <=, ≤, >=, ≥), the numeric value will be directly used. If the original result contains only a less-than symbol, subtract 0.0001 from the numeric value. If the original result contains only a greater-than symbol, add 0.0001 to the numeric value.

6.12.4. Vital Signs

Descriptive summaries will be provided for vital signs (respiration, pulse, temperature, systolic blood pressure, diastolic blood pressure) measured at each visit and time point, as well as their changes from baseline.

To evaluate the clinical significance of vital sign indicators, a cross-tabulation will be used to summarize the changes in subjects' clinical assessment categories from baseline to the worst post-baseline clinical assessment category (abnormal with clinical significance > abnormal without clinical significance > normal > not examined).

List the vital signs of the subjects in detail.

6.12.5. Physical Examination

For the clinical significance evaluation of each body part or system in physical examinations, a cross-tabulation will be used to summarize the changes in subjects' clinical assessment categories from baseline to the worst post-baseline clinical assessment category (clinically significant abnormality > abnormality without clinical significance > normal > not examined).

List the physical examination results of the subjects.

6.12.6. 12-lead ECG

Descriptive statistics will be performed on the ECG parameters (heart rate, PR interval, QRS duration, uncorrected QT interval, and QTcF corrected by Fridericia's formula) measured at each visit and time point, as well as their changes from baseline.

For the assessment of clinical significance of electrocardiograms, a cross-tabulation will be used to summarize the changes in subjects' clinical assessment categories from baseline to the worst post-baseline clinical assessment category (abnormal with clinical significance > abnormal without clinical significance > normal > not performed).

For continuous variables summarized by visit and time point, the average of two replicate measurements will be used as the baseline value and post-baseline analysis value. When summarized by clinical significance assessment, the average of two repeated assessments will be used as the baseline value, and the worst clinical assessment post-baseline will serve as the post-baseline analysis value.

List the ECG examination results of subjects in detail.

6.13. Other Evaluations

Based on the FAS, detailed listings will be provided for infectious disease screening, B-ultrasound, tumor marker testing, serum follicle-stimulating hormone (FSH) testing, blood/urine pregnancy testing, modified Hoehn-Yahr scale assessment, and orthostatic hypotension testing.

6.14. Sub-group Analysis

If the data permit, subgroup analyses of drug exposure will be conducted by age group, with subgroups categorized as:

- Age groups (<18 years, 18-65 years, 66-75 years, >75 years)

If the data permit, subgroup analyses for the primary endpoint will be conducted using the same statistical methods as the primary analysis. Subgroup categories include:

- Whether the subject will be stably receiving levodopa as the basic anti-PD medication (Yes, No)
- Medications for Anti-Parkinson's Disease:
    - No prior anti-PD therapy
    - Previous anti-PD therapy but no anti-PD therapy within 4 weeks prior to enrollment
    - Patients must have received stable anti-PD drug therapy for at least 4 weeks prior to enrollment and agree to maintain the original treatment regimen unchanged during the trial.
- Age group at initial diagnosis (≤50 years, >50 years)

If applicable, subgroup analyses will also be performed for MDS-UPDRS score-related secondary endpoints.

7. Interim Analysis

Not applicable

8. Changes to the Planned Analysis of the Protocol

None

9. References

None

10. Statistical Chart Templates and Dataset Programming Specifications

10.1. Statistical Chart Template

Refer to the separate Statistical Analysis Tables, Figures, and Listings Template file.

10.2. Dataset Programming Specifications

Refer to the separate SDTM/ADAM Spec files.

11. Appendices

11.1. Appendix A Multiple Imputation (MI) Method

MI will adhere to the following steps:

Step 1: For non-monotone missing data, assuming the missing mechanism is missing at random (MAR), the MCMC method will be used with 100 iterations for imputation. The corresponding SAS option will be MCMC IMPUTE = MONOTONE. The number of imputed seeds will be set to 12345. The upper and lower bounds of the MDS-UPDRS Part III (Motor Examination) score will be [0, 132], with imputed scores rounded to the nearest integer. If applicable, covariates include whether stable levodopa-based anti-PD medication was received at screening (yes vs. no), baseline values (base), and scores at post-baseline visits (weeks 1, 4, 8, and 12 of treatment). The order in which these variables enter the procedure step follows the sequence listed above. The imputed data constitutes monotone missing data, and these 100 datasets will be utilized in Step 2. The reference program for the SAS PROC MI procedure is as follows:

```
PROC MI DATA=adeff NIMPUTE=100 OUT=mi_monotone SEED=12345
    ROUND=. .    1    1    1    1
    MIN   =. .   0    0    0    0
    MAX   =. . 132 132 132 132;
    MCMC IMPUTE=MONOTONE;
    VAR pd base week1 week4 week8 week12;
RUN;
```

Step 2: For the monotone missing data imputed in Step 1, assuming the missing mechanism is MAR, use the MONOTONE REG method for imputation. The corresponding SAS PROC MI option is MONOTONE REG. The missing values at post-baseline visits will be imputed using the results from the immediately preceding visit. The seed number for imputation will be set to 23456. The reference program for the SAS PROC MI procedure is as follows:

```
PROC MI DATA=mi_monotone NIMPUTE=1 OUT=mi_complete SEED=23456
    ROUND=. .    1    1    1    1
    MIN   =. .   0    0    0    0
    MAX   =. . 132 132 132 132;
    MINMAXITER=1000;
    BY _imputation_;
    CLASS pd;
    VAR pd base week1 week4 week8 week12;
    MONOTONE REG(pd base week1 week4 week8 week12);
RUN;
```

Step 3: The imputed complete data from Step 2 will be used for statistical analysis. First, the endpoint value will be calculated: the change from baseline in the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III (Motor Examination) score after 12 weeks of treatment (evaluation time point: ≥12 hours since the last dose of anti-PD medication). Then, recalculate the statistical measures for this endpoint (such as least squares mean differences and standard errors) to

obtain the statistical measures for 100 iterations. The reference program for the SAS PROC MIXED procedure is as follows:

```
PROC MIXED DATA=ANA_IMPUT4;
    BY _imputation_;
    CLASS pd trtpn avisitn usubjid;
    MODEL chg = pd base trtpn avisitn avisitn*trtpn /ddfm=kenwardroger htype=3;
    REPEATED avisitn/subject=usubjid type=&type.;
    LSMEANS avisitn*trtpn/cl diff;
    ODS OUTPUT lsmeans=mixedlsmeans1 diffs=diff1;
run;
```

Step 4: Combine the 100 statistics using Rubin's method to obtain the pooled statistic, which serves as the final statistic for analysis. The reference program for the SAS PROC MIANALYZE procedure is as follows:

```
PROC MIANALYZE DATA=formianalyze;
    MODELEFFECTS estimate;
    STDERR stderr;
RUN;
```