STATISTICAL ANALYSIS PLAN
FOR PROTOCOL DA-9805-PD-001

Sponsor:		
	Dong-A ST Co., Ltd 64, Cheonho-daero Dongdaemun-gu Seoul, Korea	E-mail: treadwheel@donga.co.kr
Protocol Number:	DA-9805-PD-001	
Protocol Title:	A PHASE IIa, RANDOMIZED, MULTICENTER, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE SAFETY, TOLERABILITY AND EFFICACY OF DA-9805 IN SUBJECTS WITH PARKINSON'S DISEASE	
Protocol Date / Version:	Version 3.0 / 12 July 2017	

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Plan Version:	SAP –Version 1.0		
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Protocol Number:	DA-9805-PD-001
Protocol Version/Date:	Version 3.0 / 12 July 2017
Protocol Name:	A Phase IIa, Randomized, Multicenter, Double-blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability and Efficacy of DA-9805 in Subjects with Parkinson's Disease
Sponsor:	**Dong-A ST Co., Ltd.** 64, Cheonho-daero Dongdaemun-gu Seoul, Korea
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SAP Version:	SAP –Version 1.0
SAP Date:	27 April 2018

I have read and approve the Statistical Analysis Plan specified above and agree with its content:

Statistician, Amarex — Date: 30 Apr 2018

Dong-A ST Co., Ltd. Representative — Date: 2018. 4. 30

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LIST OF ABBREVIATIONS

Abbreviation	Term
%	Percent
AE	Adverse Event
Amarex	Amarex Clinical Research, LLC.
ANCOVA	Analysis of Covariance
ASA	American Statistical Association
BMI	Body Mass Index
CGI-I	Clinical Global Impression-Improvement
CGI-S	Clinical Global Impression-Severity
CI	Confidence Interval
CM	Concomitant Medications
CRF	Case Report Form
CRO	Contract Research Organization
C-SSRS	Columbia-Suicide Severity Rating Scale
ECG	Electrocardiogram
EOS	End of study
EOT	End of Treatment
FDA	Food and Drug Administration
g/dL	grams/deciliter
H&Y	Hoehn and Yahr
IA	Interim Analysis
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
ITT	Intent-to-Treat
IWRS	Interactive Web Based Response System
Kg	Kilograms
MAPK	Mitogen-activated protein serine/threonine kinase
MDS-UPDRS	Movement Disorder Society - Unified Parkinson Disease Rating Scale
MedDRA	Medical Dictionary for Regulatory Activities
Mg	Milligrams
mg/dL	Milligram/deciliter

MMSE	Mini-Mental State Examination
N	Number in sample
PD	Parkinson’s Disease
PDQ	Parkinson's Disease Questionnaire
PE	Physical Examination
PP	Per Protocol
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS®	Statistical Analysis System
SD	Standard Deviation
SOC	MedDRA system organ class
SOP	Standard Operating Procedures
S&E	Schwab and England
TEAE	Treatment Emergent Adverse Event
TID	ter in die (Three times daily)
TV	Treatment Visit
U/L	Units/Liter
USA	United States of America
WHO	World Health Organization
μL	Microliter

1. INTRODUCTION

This Statistical Analysis Plan describes the planned analyses and reporting for the clinical trial protocol DA-9805-PD-001, sponsored by Dong-A ST Co., Ltd.. The reader of this Statistical Analysis Plan (SAP) is encouraged to review the complete protocol as this plan contains only a limited overview of protocol information. The main objective of this plan is to provide details pertaining to statistical methodology, data conventions, and processes used for the analysis of data from this trial.

The format and content of this Statistical Analysis Plan are structured to provide sufficient detail to meet the requirements specified by the International Conference on Harmonization (ICH) E9: Guidance on Statistical Principles in Clinical Trials. All work planned and presented in this Statistical Analysis Plan will follow the ethical guidelines published by the American Statistical Association (ASA).

The following documents and references [1-6], were reviewed in preparation of this Statistical Analysis Plan:

- Version 3.0, protocol 12 July 2017
- ASA Ethical Guidelines for Statistical Practice (2016)
- The Royal Statistical Society: Code of Conduct (2014)
- ICH Guidance on the Structure and Content of Clinical Study Reports (ICH E3, 1996)
- ICH Guideline on General Considerations for Clinical Trials (ICH E8, 1997)
- ICH Guidance on the Statistical Principles for Clinical Trials (ICH E9, 1998)

2. PROTOCOL DESIGN AND OBJECTIVES

2.1 Study Objectives

The **primary** objective of this study is:

- To evaluate the safety and tolerability of DA-9805 at 45mg, 90mg compared to Placebo (0 mg) in subjects with Parkinson's Disease.

The **secondary** objective of this study is:

- To evaluate DA-9805 at 45mg, 90mg compared to Placebo (0 mg), in terms of efficacy in subjects with Parkinson's Disease.

2.2 Design Overview

This is a phase IIa, first in human, randomized, double-blind, multicenter study to evaluate the safety, tolerability and efficacy of DA-9805 at 45mg, 90mg versus placebo in subjects with early diagnosed Parkinson's disease.

The study will include three parts: a 2-week Screening part, a 12-week Double-Blind Treatment part, and a 4-week Follow-up part. The detailed study schedule and assessments in each visit are provided in Appendix I of this SAP. For a schematic of the study design, see Figure 2-1.

Study Visits:

- **Screening Visit** (Day -14 to Day -1), up to 14 days:

  Screening part is designed to determine subject's eligibility to proceed to Randomization and the Treatment Phase of the study. During this part, a series of assessments will be performed to determine subject eligibility as per inclusion and exclusion criteria.

  At the Screening Visit, prior to any study-related procedures, a written informed consent will be obtained from the subject by the Investigator or suitable qualified personnel. Subjects who meet eligibility criteria, but have some abnormal laboratory values, based on PI review a repeat laboratory sample may be collected. The repeat laboratory reports should be reviewed by the PI to confirm eligibility prior to randomization.

  Subjects who fail to meet eligibility criteria during the Screening part will be considered screen failures and will be exited from the study. Subjects who have successfully completed the Screening part will enter the Double-Blind treatment part of the study. Treatment part followed by randomization will last for 12 weeks. Subjects will take the randomized treatment, DA-9805 at 45mg, 90mg or placebo for 12 weeks.

- **Visit 0: Randomization/Baseline Visit (Day 0) (TV0):**

  On Day 0 prior to randomization, the subject's continued eligibility will be evaluated. Subjects who continue to be eligible will be randomized in a 1:1:1 ratio to one of the following treatment groups and assigned the study treatment kit:

  - Group 1: DA-9805 45mg tablet
  - Group 2: DA-9805 90mg tablet

- Group 3: placebo (0 mg DA-9805) tablet

DA-9805 and matching placebo are oral tablets that will be taken three times daily during this study.

- **Treatment Visits 1 (TV1) through Treatment Visit 3 (TV3):**

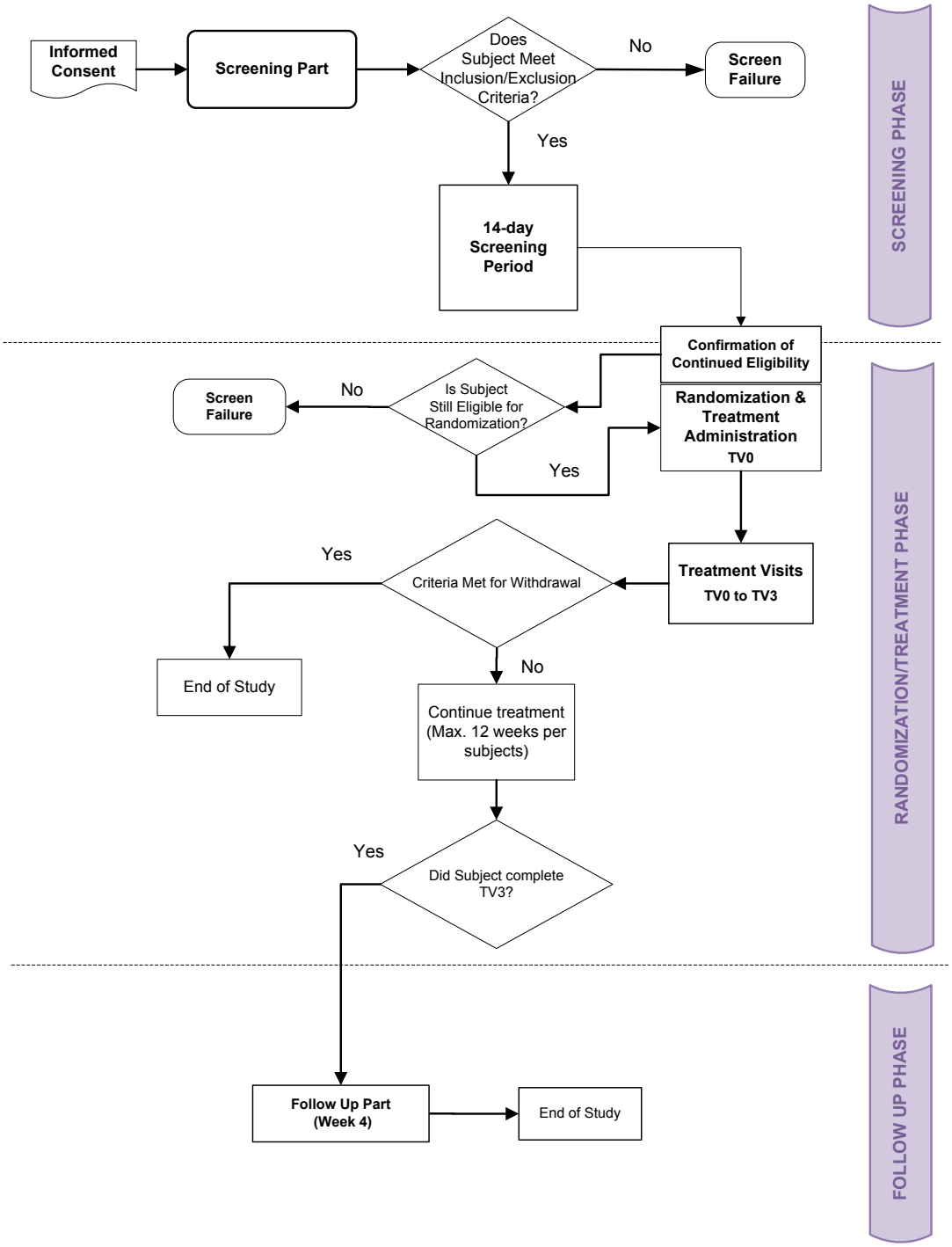
Clinic treatment visits TV1 through TV3 will be conducted every four (4) week (± 3 days). During each of these visits, study evaluations will be conducted per the study schedule of events (Refer to section 4.1.3), and sufficient supply of DA-9805 or placebo till the next treatment visit will be dispensed.

Treatment Visit 3 (TV3) will be considered the end of treatment (EOT) clinic visit. Study evaluations, review of the adverse events and concomitant medications and final study treatment accountability will be conducted.

- **Follow-up Part** (4 weeks ± 3 days)

The follow-up part will consist of a follow-up visit at the end of the Double-Blind Treatment part.

Figure 2-1: Study Flow Diagram



2.3 Study Treatments and treatment assignments

2.3.1 Treatment Groups

The three treatment groups to be assessed in this trial are described below

Table 2-1: Treatment Groups

Group	Description
1	DA-9805 (45 mg/day – 15mg TID) for 12 weeks
2	DA-9805 (90 mg/day – 30mg TID) for 12 weeks
3	Placebo (0 mg/day) for 12 weeks

2.3.2 Method of Treatment Assignment, Randomization Ratio, and Stratification

The randomization in this multi-center study will be applied centrally across the sites and will use a mixed block size of 3 and 6 with a 1:1:1 ratio of DA-9805 (45mg/day), DA-9805 (90mg/day) and Placebo Treatment groups.

Subjects who have provided written informed consent and have met all the inclusion criteria and none of the exclusion criteria will be randomized to one of the treatment groups mentioned in Table 2-1 based on a randomization schedule. An individual, independent of the clinical trial team, will develop the randomization schedules.

The actual randomization assignment will be made through an Interactive Web Based System (IWRS) called WebView (Amarex Clinical Research, Germantown MD). WebView is a Secure Socket Layer (SSL) web portal that allows 24/7 access to clinical trial information. Authorization is based on approved access control list (ACL) that determines a user's access to the site. The Amarex Technology department, who is not otherwise involved with the study, is responsible for the implementation and maintenance of WebView. Each user will be trained in how to use the website. A WebView user manual will be supplied to all study personnel with instructions on using the website.

The Randomization/Supply module of WebView allows authorized users to request randomization (Site Personnel only) into the trial. The detailed description and instructions are included in the

WebView user manual. Amarex Clinical Research has further documentation and validation of WebView specifically with regards to preserving the blinding of this study.

2.4 Blinding

As this is a double-blind trial, the subjects, investigators and their staff, and all Sponsor/CRO personnel involved in the management, and data collection in this study will be blinded to the treatment assignments.

Treatment unblinding for the study will only occur:

1. at the time of final analysis after all clinical data have been received, data inconsistencies/queries have been resolved, and the database is locked
2. for emergency unblinding in the event of safety concerns for individual subjects; these special cases will be documented and reported.

The process for unblinding will be outlined in the Randomization Plan. In addition, any subject with emergency unblinding for any reason will be identified and discussed in the final clinical study report.

3. STUDY ASSESSMENTS/ OUTCOME

3.1 Efficacy Assessments

3.1.1 Primary Efficacy Outcome Measure

The primary efficacy outcome measure for this study is Change in motor MDS-Unified Parkinson Disease Rating Scale (MDS-UPDRS) total score from baseline at week 12.

3.1.2 Secondary Efficacy Outcome Measures:

There are multiple secondary outcomes in this trial as follows:

- Change in total MDS- UPDRS total score from baseline at week 12.
- Change in MDS-UPDRS subscale scores from baseline at week 12.
- Change in Schwab and England (S&E) Scale total score from baseline at week 12.
- Change in Parkinson's Disease Questionnaire (PDQ-39) total score from baseline at week

12.

- Change in Hoehn and Yahr (H&Y) scale total score from baseline at week 12.
- Change in Clinical Global Impression-Severity (CGI-S) and Clinical Global Impression-Improvement (CGI-I) scale score from baseline at week 12.

3.2 Safety Assessments

- Incidence of Treatment-Emergent Adverse Events (AEs).
- Incidence of withdrawals due to AEs.
- Change/shifts in laboratory values.
- Change in vital signs.
- Change in Electrocardiogram (ECG) parameters.
- Change in Columbia- Suicide Severity Rating Scale from baseline at week 12.

4. SAMPLE SIZE DETERMINATION AND RATIONALE

It is planned to randomize a total of 60 subjects (20 subjects per group) with early Parkinson's disease in this trial. This sample size is selected on the basis of clinical judgment and not based on statistical power calculation; it is deemed adequate to provide clinically meaningful descriptive results consistent with the study objectives.

5. INTERIM ANALYSIS

There is no interim analysis planned for this study.

6. ANALYSIS POPULATIONS

6.1 Intent-to-Treat (ITT) population

The Intent-to-Treat (ITT) population is defined as all randomized subjects who have received at least one dose of study treatment and undergone at least one post-randomization efficacy assessment.

6.2 Per Protocol (PP) Population

The Per Protocol (PP) population is defined as the set of subjects who meet the ITT population

requirements, and were not associated with a major protocol violation. This population will be identified before the database lock, and before the treatment assignments are revealed.

The primary analysis of the primary and secondary outcomes will be conducted using the PP population.

6.3 Safety Population

The Safety population is defined as all subjects receiving at least one dose of the treatment after randomization. This population will be used for the analyses of safety parameters.

7. DATA CONVENTION AND RELATED DEFINITIONS

7.1 Baseline Definition

For all parameters, baseline will be defined as the last available value before the randomized treatment.

7.2 Duplicate Data

For unplanned duplicate data within a protocol-specified visit, the last measured value will be used for the analysis. If it is not possible to identify the "last measured value" the average of the duplicate values will be used.

No data will be excluded. All collected data will be listed.

7.3 Handling of Missing Data

7.3.1 Handling of Missing Data for Efficacy Evaluations

There is no imputation of missing data planned for efficacy evaluations.

7.3.2 Handling of Missing Data for Safety Evaluations

Adverse Event (AE) Summaries

With respect to summaries of AEs, only AEs that were treatment emergent will be tabulated. Treatment–emergent is defined as AEs with start date ≥ date of first treatment administration.

1) If AE start date is completely missing, the date of first treatment administration will be taken as the start date of the event.
2) If AE start date is partially missing:

a. If the day part of the start date is missing, the start date will be estimated to be equal to the date of first treatment administration, provided the start month and year are the same as the date of first treatment administration and the stop date either after the date of first treatment administration or completely missing. Otherwise, the AE will be assumed to have started on the first day of the month (01/MMM/YYYY)

b. If the month part of the start date is missing, the start month will be estimated to be equal to the month of the date of first treatment administration or the following month after the month of the date of first treatment administration depending on the day part of the start date provided that the start year is the same as the year of date of first treatment administration and the stop date is either after date of first treatment administration or completely missing. Otherwise, the AE will be assumed to have started on the first month of the year (DD/Jan/YYYY)

c. If both the day and month parts of the start date are missing, the start date will be estimated to be equal to the date of first treatment administration, provided the start year is the same as year of date of first treatment administration and the stop date is either after the date of first treatment administration or completely missing. Otherwise, the AE will be assumed to have started on first day and first month of the year (01/Jan/YYYY)

d. If all day, month and year parts of the start date are missing, the start date will be estimated to be equal to the date of first treatment administration (and thus treatment emergent) provided that the stop date is either after the date of first treatment administration or completely missing. Otherwise, the start date will be estimated to be the first day of the same year as the stop date.

3) If AE stop date is partially or completely missing:

a. If only the day portion of the stop date is unknown, the day will be assumed to be last date of the month (e.g., ??-Jan-2004 will be treated as 31-Jan-2004).

b. If both the day and month of stop date are unknown, the event will be assumed to have ceased on the last day of the year (e.g., ??-???-2004 will be treated as 31-Dec-2004).

c. If the stop date is completely missing, the event will be assumed to be "Ongoing".

Concomitant medications (CM) Summaries

1) If CM start date is completely missing then the date of first treatment administration will be taken as the start date of the medication
2) If CM start date is partially missing:
    a. If the Day part of the start date is missing, the CM will be assumed to have started on the first day of the month (01/MMM/ YYYY)
    b. If the month part of the start date is missing, the CM will be assumed to have started on the first month of the year (dd/Jan/YYYY)
    c. If both the day and month parts of the start date are missing, the CM will be assumed to have started on first day and first month of the year (01/Jan/YYYY)

7.4 Multiplicity

No Multiplicity adjustment will be implemented for this Phase 2 clinical trial.

7.5 Covariates

Baseline values will be used as covariates for efficacy analysis.

7.6 Stratification Factors

There are no stratification factors for this study.

7.7 Subgroups

There are no pre-planned subgroup analyses, however subgroup analyses will be done as needed.

7.8 Multicenter Clinical Trials

This is a randomized study with multiple centers.

7.9 Standard Calculations

7.9.1 Age

Age will be calculated as the number of completed years between the date of informed consent and the subject's birth date.

Age (years) = integer of [(date of informed consent – date of birth)/ 365.25+ 0.5]

7.9.2 Height

For summary purposes height will be expressed in centimeters. Entries made in inches will be converted to centimeters using the formula noted below.

Height (cm) = Height (in)*2.54

7.9.3 Weight

For summary purposes weight will be expressed in kilograms. Entries made in pounds will be converted to kilograms using the formula noted below.

Weight (kg) = Weight (lb)/ 2.2046

7.9.4 Body Mass Index (BMI)

BMI will be calculated using height (in cm) and weight (in kg) according to the formula noted below.

BMI (kg/m^2) = weight (kg) / [height (cm)/100]^2

7.9.5 Change from Baseline

For any of the effectiveness measurements change from baseline will be calculated using the formula noted below.

Change from baseline = Post Baseline Measurement – Baseline Measurement

8. STATISTICAL METHODS

All data collected during this study will be presented in subject data listings.

All statistical analyses will be performed using SAS® for Windows, version 9.4 or later. For

continuous variables, descriptive statistics (n, mean, standard deviation, median, minimum and maximum) will be presented by treatment group. For categorical variables both frequencies and percentages will be presented by treatment group.

8.1 Disposition and Baseline Characteristics

8.1.1 Subject Disposition and Withdrawals

There will be a detailed accounting of all subjects that signed the informed consent to participate in this trial. The following will be summarized by treatment group:

- The number of subjects who signed the informed consent
- The number of subjects who are screen failures
- The number of subjects who are randomized
- The number of subjects who received at least one study drug administration
- The number of subjects who completed the study
- The number of subjects who discontinued

Reasons for discontinuation will also be summarized.

In addition, there will also be a listing of all discontinued subjects, which will provide the clinical trial center, treatment group and the specific reason for discontinuation.

8.1.2 Major Protocol Deviations

The deviations occurring during the clinical trial will be summarized descriptively according to the following categories:

- Entrance criteria deviation
- Withdrawal criteria deviation
- Received wrong treatment or incorrect dose
- Received an excluded medication
- All other major protocol deviations

Additionally a by-subject listing of all deviations will also be prepared.

8.1.3 Demographics and Baseline Characteristics

Demographic (age, race, gender, ethnicity) and other basic baseline characteristics will be summarized and/or listed, descriptively, by treatment groups for the Safety population.

Medical history results will be provided as by-subject listings.

8.1.4 Prior and Concomitant Medications/Therapies

Prior and concomitant medications/therapies will be summarized for the Safety population.

All prior and concomitant medications recorded in the case report form will be coded to all matching Anatomic Therapeutic Classification codes using the most recent version of WHO Drug.

Descriptive summaries, by treatment group, will be prepared using the coded generic term. All prior and concomitant medications recorded in the case report form will be listed.

8.1.5 Medical History

The medical history will be summarized and/or listed descriptively.

8.1.6 Treatment Compliance

All treatment compliance data will be summarized and/or listed descriptively for the Safety population.

8.2 Analysis of Efficacy Outcome

The primary analysis of the primary and secondary outcomes will be conducted using the PP population.

To assess the consistency of the Primary Analysis results, a supportive analysis will be conducted using the ITT population. Statistical methodology for the supportive analyses will be the same as that of the primary analysis, with the exception of the analysis population.

All statistical tests for efficacy will be two-sided tests, with α=0.05.

8.2.1 Primary Efficacy Outcome

The primary efficacy outcome for this study is change in motor MDS-Unified Parkinson Disease Rating Scale (MDS-UPDRS) total score from baseline at week 12.

Change in motor MDS-UPDRS total score from baseline at week 12 will be calculated for each subject using the formula in Section 7.9.5. Both Treatment Group 1 and 2 will be compared with Group 3 using Analysis of Covariance (ANCOVA) with baseline value as a covariate to compare the change in motor MDS-UPDRS total score from baseline at week 12. 95% confidence interval

around the difference and P value for the treatment effect will be reported.

8.2.2 Secondary Efficacy Outcome

The secondary efficacy outcome measures will be analyzed as follows:

8.2.2.1 Change in total MDS-UPDRS total score from baseline at week 12.

Change in total MDS-UPDRS total score from baseline at week 12 will be calculated for each subject using the formula in Section 7.9.5, similar statistical methods as the primary outcome will be used for inferential statistics.

8.2.2.2 Change in MDS-UPDRS subscale scores from baseline at week 12.

Change in total MDS-UPDRS subscale scores from baseline at week 12 will be calculated for each subject using the formula in Section 7.9.5, similar statistical methods as the primary outcome will be used for inferential statistics.

8.2.2.3 Change in Schwab and England (S&E) Scale total score from baseline at week 12.

Change in Schwab and England (S&E) Scale total score from baseline at week 12 will be calculated for each subject using the formula in Section 7.9.5, similar statistical methods as the primary outcome will be used for inferential statistics.

8.2.2.4 Change in Parkinson's Disease Questionnaire (PDQ-39) total score from baseline at week 12.

Change in Parkinson's Disease Questionnaire (PDQ-39) total score from baseline at week 12 will be calculated for each subject using the formula in Section 7.9.5, similar statistical methods as the primary outcome will be used for inferential statistics.

8.2.2.5 Change in Hoehn and Yahr (H&Y) scale total score from baseline at week 12.

Change in Hoehn and Yahr (H&Y) scale total score from baseline at week 12 will be calculated for each subject using the formula in Section 7.9.5, similar statistical methods as the primary outcome will be used for inferential statistics.

8.2.2.6 Change in Clinical Global Impression-Severity (CGI-S) and Clinical Global Impression-Improvement (CGI-I) scale score from baseline at week 12.

Change in Clinical Global Impression-Severity (CGI-S) and Clinical Global Impression-Improvement (CGI-I) scale score from baseline at week 12 will be calculated for each subject using the formula in Section 7.9.5, similar statistical methods as the primary outcome will be used for inferential statistics.

8.3 Analysis of Safety Data

For continuous variables data will be summarized by treatment using n, mean, SD, minimum and maximum values.

For categorical variables data will be summarized by treatment using frequency and percentage.

8.3.1 Adverse Events

Adverse events will be coded using the most recent version of Medical Dictionary for Regulatory Activities (MedDRA). Treatment Emergent AE's (TEAE) are defined as events with an onset on or after the first randomized treatment. TEAEs will be summarized by treatment group, System Organ Class, and preferred term. The following TEAE summaries will be provided:

- Overall (*i.e.,* regardless of severity or relationship to treatment)
- By severity grade (mild, moderate, severe, life threatening or death for SAEs)
- By relationship to clinical trial treatment according to the mapping scheme below:
    - Potentially related: will include all adverse events with a relationship rating of "definitely", "probably" or "possibly".
    - Unlikely/not related: will include all adverse events with a relationship rating of "unlikely" or "unrelated".

Unless otherwise specified, at each level of subject summarization, a subject will be counted only once. If there is more than one occurrence of an event, the event of the worst severity or the worst-case relationship category will be summarized.

In addition, separate summaries of serious adverse events, and adverse events resulting in discontinuation of study treatment will be presented.

AEs leading to premature discontinuation of clinical trial treatment, AEs that lead to study discontinuation, AEs that lead to death and Serious Adverse Events (SAEs) will also be summarized by treatment group and relationship.

8.3.2 Columbia-Suicide Severity Rating Scale (C-SSRS)

All the data from C-SSRS will be listed and descriptive summaries will be presented for each of the subscales (i.e. Suicidal Ideation and Suicidal Behavior).

8.3.3 Clinical Laboratory Evaluations

The laboratory assessments in this study include Biochemistry, Hematology and Urine analysis. All available data will be summarized or presented as a by-subject listing as follows:

8.3.3.1 Laboratory Values over Time

Summary statistics of raw data and change from baseline values for each laboratory parameter will be presented by treatment group and time point. Data will be summarized as appropriate for the variable type.

- For continuous data, summaries will include the number of observations, mean, SD, median, minimum, and maximum values.
- For categorical data, frequency counts and percentages will be used.

For change from baseline summaries, subjects with an undefined change from baseline, because of missing data, will be excluded.

8.3.3.2 Individual Subject Changes (Shift Tables)

Individual subject changes will be identified through shift tables. Shift tables will be presented for each laboratory parameter with counts and percentages of subjects, by treatment group and time point, for shift (change) from baseline, using the normal ranges from the laboratory.

8.3.3.3 Individual Clinically Significant Abnormalities

Clinically significant laboratory abnormalities (i.e., those laboratory abnormalities recorded as AEs) will be listed.

All results of laboratory evaluations will be presented as by-subject listings

8.3.4 Vital Signs and Weight

Tabulations of raw data and change from baseline values will be presented by time point for each vital sign parameter and weight.

Tabulations will include the number of observations, mean, standard deviation, median, and minimum and maximum values. For change from baseline summaries, subjects with an undefined change from baseline, because of missing data, will be excluded.

8.3.5 ECG

All ECG findings will be listed and/or summarized. Shift tables will also be presented to show any abnormality shifts from baseline to post baseline visits.

8.3.6 Physical Examination

All physical examination findings will be listed and/or summarized by treatment group. Shift tables will also be presented to show any abnormality shifts from baseline to post baseline visits.

9. APPENDIX 1: SCHEDULE OF ASSESSMENTS

Study Parts	**Screening Part** (2 weeks)	**Double-Blind Treatment Part** (12 weeks)					**Follow-up Part Follow-up visit** (4 weeks)
Treatment Visits		**TV0 Randomization**		**TV1**	**TV2**	**TV3**	**FUV**
Weeks from Randomization Date (window period: ± days)	**- 2**	**Day 0**		**+ 4** (± 3)	**+ 8** (± 3)	**+ 12** (± 3)	**+ 16** (± 3)
		Pre-	**Post-**				
Written Informed Consent	X						
Inclusion/Exclusion Criteria	X						
Schedule Randomization Day	X						
Continued Eligibility		X					
Randomization		X					
Demographics	X						
Medical History	X	X					
Physical Examination	X	X		X	X	X	
Vital Signs	X	X	X	X	X	X	
Height[1] and Weight	X	X				X	
ECG	X	X		X		X	
Serum Hematology[2]	X			X	X	X	
Serum Chemistry[2]	X			X	X	X	
Urine Analysis[2]	X			X	X	X	
Urine Pregnancy Test[3]	X	X				X	
MDS-UPDRS		X		X	X	X	
H & Y	X	X		X	X	X	
S & E		X		X	X	X	
PDQ-39		X		X	X	X	
CGI-S and CGI-I[4]	X	X		X	X	X	
C-SSRS	X	X		X	X	X	
MMSE	X	X					
Dispense the DA-9805 or placebo[5]			X	X	X		
DA-9805 or Placebo first dose administration			X				
Study treatment accountability				X	X	X	
Adverse Events			X	X	X	X	X
Concomitant medications	X	X		X	X	X	X

[1] Height only at Screening.

[2] Subjects who meet eligibility criteria, but have some abnormal laboratory values, based on PI review a repeat laboratory sample may be collected. The repeat laboratory reports should be reviewed by the PI to confirm eligibility prior to randomization.

[3] Only for female subjects of childbearing potential.

[4] CGI-I will be done only at Treatment Visit 1 to Treatment Visit 3

[5] Dispense the DA-9805 or placebo at each of the clinic treatment visit, except TV3 which is the End of Treatment visit (EOT).

10. APPENDIX 2 – PLANNED TLG

10.1 Planned by-subject listings

DISPOSITION/WITHDRAWALS (LISTINGS 16.2.1.X)

ELIGIBILTY AND PROTOCOL DEVIATIONS (LISTINGS 16.2.2.X)

EXCLUDED SUBJECTS (LISTINGS 16.2.3.X)

DEMOGRAPHICS, POPULATION, AND BASELINE CHARACTERISTICS (LISTINGS 16.2.4.X)

DRUG COMPLIANCE AND DRUG CONCENTRATION LISTINGS (LISTINGS 16.2.5.X)

EFFICACY RESPONSE (LISTINGS 16.2.6.X)

ADVERSE EVENT DATA (LISTINGS 16.2.7.X)

SAFETY DATA (LISTINGS 16.2.8.1.X)

10.2 Planned Summary Tables

POPULATION DISPOSITION AND PROTOCOL DEVIATIONS

POPULATION DEMOGRAPHICS AND BASELINE CHARACTERISTICS

CONCOMITANT MEDICATION USAGE

EFFICACY SUMMARIES

SAFETY SUMMARIES

- ADVERSE EVENT SUMMARIES
- SERIOUS ADVERSE EVENTS
- LABORATORY
- VITAL SIGNS AND PHISICAL EXAMINATION (PE)
- COLUMBIA-SUICIDE SEVERITY RATING SCALE (C-SSRS)
- OTHER SAFETY

11. VERSION HISTORY

This is the first version.

12. REFERENCES

1. ASA. (2016) Ethical Guidelines for Statistical Practice. Prepared by the Committee on Professional Ethics, April, 2016.
2. The Royal Statistical Society: Code of Conduct (2014).
3. E8 General Considerations for Clinical Trials, ICH Guidance, Federal Register, 1997.
4. E9 Statistical Principles for Clinical Trials, ICH Guideline, Federal Register, 1998
5. Guideline for the Format and Content of the Clinical and Statistical Section of an Application, 1988.
6. Guideline for Industry: Structure and Content of Clinical Study Reports (ICH E3), July 1996.