Certain information within this clinical study report has been redacted (ie, specific content is masked irreversibly from view with a black bar) to protect either personally identifiable information or company confidential information.

This may include, but is not limited to, redaction of the following:

- Named persons or organizations associated with the study.
- Patient identifiers within the text, tables, or figures or in by-patient data listings.
- Proprietary information, such as scales or coding systems, which are considered confidential information under prior agreements with license holder.
- Other information as needed to protect confidentiality of Takeda or partners, personal information, or to otherwise protect the integrity of the clinical study.

If needed, certain appendices that contain a large volume of personally identifiable information or company confidential information may be removed in their entirety if it is considered that they do not add substantially to the interpretation of the data (eg, appendix of investigator's curriculum vitae).

Note; This document was translated into English and the language in original document was Japanese.

Statistical Analysis Plan

Title of Study	:	A Multicenter, Open-label, Long-term, Extension, Phase 3 Study to Evaluate the Safety and Efficacy of TVP-1012 at 1 mg in Early Parkinson's Disease Patients Not Treated with Levodopa
Study Number:	:	TVP-1012/OCT-001
Sponsor:	:	Takeda Pharmaceutical Company Limited

[redacted]

Second Version: Created on 11 April 2017

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Considerations

This is a multicenter, open-label, long-term, extension, phase 3 study that evaluates the safety and efficacy of long-term administration of TVP-1012 at 1 mg for another 26 weeks in patients with early Parkinson's disease who have completed the 26-week treatment period in the preceding TVP-1012/CCT-001 study.

The analyses for this study will be performed using pooled data from the preceding study and this study based on data obtained after administration of TVP-1012, unless otherwise specified.

Glossary

- Descriptive statistics:

  Number of subjects, mean, standard deviation, maximum, minimum, and quartiles

- MAV:

  Markedly Abnormal Value

- Treatment groups in the preceding study:

  TVP-1012 1 mg and placebo groups in the preceding study. However, they are shown as "1 mg ->1 mg group" and "P ->1 mg group" respectively in this statistical analysis plan.

- Study drugs for treatment period in both studies:

  Study drug for treatment period in the previous study and study drug in this study

- Number of days after administration (days):

  A) For the analyses based on the data after administration of TVP-1012

  The day before the day of first TVP-1012 administration is shown as Day -1 and the day of first TVP-1012 administration as Day 1. That is, shown as follows:

  [If the treatment group in the preceding study is 1 mg ->1 mg group]

Day before the day of first study drug administration for the treatment period in the preceding study:	Day -1
Day of first study drug administration for the treatment period in the preceding study:	Day 1

  [If the treatment group in the preceding study is P ->1 mg group]

Day before the day of first study drug administration in this study:	Day -1
Day of first study drug administration in this study:	Day 1

  B) For the analyses based on the data after study drug administration for the treatment period in the preceding study

  The day before the day of the first study drug administration for the treatment period in the preceding study is shown as Day -1 and the day of the first study drug administration for the treatment period in the preceding study as Day 1.

- Number of days after the end of administration (days):

  Day 1 is defined as the day following the later of "day of the last study drug administration for the treatment period in the preceding study" or the "day of the last study drug administration in this study."

- Protocol Deviations:

  Protocol deviations in this study, unless otherwise specified.

Definition of Visit Window

A) For the analyses based on the data after administration of TVP-1012

For each test, observation, and evaluation items, evaluable data (i.e., non-missing and acceptable according to the Handling Rules for Analysis Data) will be handled according to the following rules. However, the number of days after administration and number of days after the end of administration will be the contents of "For the analyses based on the data after administration of TVP-1012" in the Glossary.

Among the evaluation points, at points other than at the end of administration, evaluable data within the visit window will be used. If more than one evaluable data lies within the same visit window, the examinations, observation, and assessments with the Study Time closest to the scheduled Study Time will be used. If there are two observations equidistant to the scheduled Study Time, the later observation will be used. The size of difference from the Study Time will be determined based on the number of days after administration.

Among the evaluation points, at the end of administration, the data with the largest number of days after administration will be used among the evaluable data within the visit window.

MDS-UPDRS Part I, II, III, and IV Total Scores, MDS-UPDRS Part II + Part III Total Score, MDS-UPDRS Tremor, Muscle Rigidity, and Akinesia/Bradykinesia Scores, and MDS-UPDRS Individual Scores

Visit	Scheduled Study Time	Visit Windows	
		Number of days after administration	Number of days after the end of administration
Baseline (prior to TVP-1012 administration)	Number of days after administration: -1	-22 ~ -1	
Week 6	Number of days after administration: 42	1 ~ 55	< 8
Week 10	Number of days after administration: 70	56 ~ 83	< 8
Week 14	Number of days after administration: 98	84 ~ 118	< 8
Week 20	Number of days after administration: 140	119 ~ 160	< 8
Week 26	Number of days after administration: 182	161 ~ 202	< 8
Week 32	Number of days after administration: 224	203 ~ 237	< 8
Week 36	Number of days after administration: 252	238 ~ 265	< 8
Week 40	Number of days after administration: 280	266 ~ 300	< 8
Week 46	Number of days after administration: 322	301 ~ 342	< 8
Week 52	Number of days after administration: 364	343 ~ 385	< 8
At end of administration		1 ~ 385	< 8

PDQ-39 Summary Index and Score by Domain

Visit	Scheduled Study Time	Visit Windows	
		Number of days after administration	Number of days after the end of administration
Baseline (prior to TVP-1012 administration)	Number of days after administration: -1	-22 ~ -1	
Week 14	Number of days after administration: 98	1 ~ 139	< 8
Week 26	Number of days after administration: 182	140 ~ 230	< 8
Week 40	Number of days after administration: 280	231 ~ 321	< 8
Week 52	Number of days after administration: 364	322 ~ 385	< 8
At end of administration		1 ~ 385	< 8

Clinical Laboratory Tests

Visit	Scheduled Study Time	Visit Windows	
		Number of days after administration	Number of days after the end of administration
Baseline (prior to TVP-1012 administration)	Number of days after administration: -1	-22 ~ -1	
Week 3	Number of days after administration: 21	1 ~ 31	< 8
Week 6	Number of days after administration: 42	32 ~ 69	< 8
Week 14	Number of days after administration: 98	70 ~ 118	< 8
Week 20	Number of days after administration: 140	119 ~ 160	< 8
Week 26	Number of days after administration: 182	161 ~ 192	< 8
Week 29	Number of days after administration: 203	193 ~ 213	< 8
Week 32	Number of days after administration: 224	214 ~ 251	< 8
Week 40	Number of days after administration: 280	252 ~ 300	< 8
Week 46	Number of days after administration: 322	301 ~ 342	< 8
Week 52	Number of days after administration: 364	343 ~ 385	< 8

Vital Signs

Visit	Scheduled Study Time		Visit Windows	
			Number of days after administration	Number of days after the end of administration
Baseline (prior to TVP-1012 administration)	Number of days after administration:	-1	-22 ~ -1	
Week 3	Number of days after administration:	21	1 ~ 31	< 8
Week 6	Number of days after administration:	42	32 ~ 55	< 8
Week 10	Number of days after administration:	70	56 ~ 83	< 8
Week 14	Number of days after administration:	98	84 ~ 118	< 8
Week 20	Number of days after administration:	140	119 ~ 160	< 8
Week 26	Number of days after administration:	182	161 ~ 192	< 8
Week 29	Number of days after administration:	203	193 ~ 213	< 8
Week 32	Number of days after administration:	224	214 ~ 237	< 8
Week 36	Number of days after administration:	252	238 ~ 265	< 8
Week 40	Number of days after administration:	280	266 ~ 300	< 8
Week 46	Number of days after administration:	322	301 ~ 342	< 8
Week 52	Number of days after administration:	364	343 ~ 385	< 8

12-lead ECG, Weight

Visit	Scheduled Study Time		Visit Windows	
			Number of days after administration	Number of days after the end of administration
Baseline (prior to TVP-1012 administration)	Number of days after administration:	-1	-22 ~ -1	
Week 14	Number of days after administration:	98	1 ~ 139	< 8
Week 26	Number of days after administration:	182	140 ~ 230	< 8
Week 40	Number of days after administration:	280	231 ~ 321	< 8
Week 52	Number of days after administration:	364	322 ~ 385	< 8

B) For the analyses based on the data after study drug administration for the treatment period in the preceding study

For MDS-UPDRS Part II + Part III total score among each test, observation, and evaluation items, evaluable data will be handled according to the following rules. The number of days after administration and number of days after the end of administration is defined in "For the analyses based on the data after study drug administration for the treatment period in the preceding study" in Glossary.

Among the visits, at visits other than baseline (at end of observation period) and Week 52 of the Treatment Period (LOCF), evaluable data within the visit window will be used. If more than one evaluable data lies within the same visit window, the examinations, observation, and assessments with the Study Time closest to the scheduled Study Time will be used. If there are two observations equidistant to the scheduled Study Time, the later observation will be used. The size of difference from the Study Time will be determined based on the number of days after administration.

Among the visits, at baseline (at end of observation period) and Week 52 of Treatment Period (LOCF), the data with the largest number of days after administration will be used among the evaluable data within the visit window.

MDS-UPDRS Part II + Part III total score

Visit	Scheduled Study Time	Visit Windows	
		Number of days after administration	Number of days after the end of administration
Baseline (end of observation period)	Number of days after administration: -1	-22 ~ -1	
Week 6 (Treatment Period)	Number of days after administration: 42	1 ~ 55	< 8
Week 10 (Treatment Period)	Number of days after administration: 70	56 ~ 83	< 8
Week 14 (Treatment Period)	Number of days after administration: 98	84 ~ 118	< 8
Week 20 (Treatment Period)	Number of days after administration: 140	119 ~ 160	< 8
Week 26 (Treatment Period)	Number of days after administration: 182	161 ~ 202	< 8
Week 32 (Treatment Period)	Number of days after administration: 224	203 ~ 237	< 8
Week 36 (Treatment Period)	Number of days after administration: 252	238 ~ 265	< 8
Week 40 (Treatment Period)	Number of days after administration: 280	266 ~ 300	< 8
Week 46 (Treatment Period)	Number of days after administration: 322	301 ~ 342	< 8
Week 52 (Treatment Period)	Number of days after administration: 364	343 ~ 385	< 8
Week 52 (Treatment Period) (LOCF)		1 ~ 385	< 8

Others

- Causality of AEs with study drug:

  Cases where the causality with the study drug cannot be ruled out, that is, "Unlikely," "Possibly," or "Probably" are handled as "Related," and cases where the causality with the study drug are "Unrelated" are handled as "Not related."

- Smoking history:

  When the smoking history is "Current smoker," it is handled as "Yes." When the smoking history is "Never smoked" or "Ex-smoker," it is handled as "No."

  * If the category is set as [Yes or No], it is handled with the aforementioned contents.

- Entry to this study:

  If the subject is considered eligible to enter to this study, it is handled as "Yes" and other cases are handled as "No."

- Duration of study drug administration in this study (days):

  Day of last study drug administration in this study - Day of first study drug administration in this study +1

- Duration of study drug administration for the treatment period in both studies (days):

  "Day of last study drug administration for the treatment period in the preceding study" or "Day of last study drug administration in this study," whichever the latest - Day of first study drug administration for the treatment period in the preceding study +1

- Duration of Exposure to TVP-1012 (days):

  Day of last TVP-1012 administration - Day of first TVP-1012 administration +1

- Compliance of TVP-1012 (%):

  (Prescribed quantity of TVP-1012 - Retrieved quantity of TVP-1012) / Duration of TVP-1012 administration × 100 (rounded to the first decimal place)

- Duration of Parkinson's disease (years):

  ([Year when the consent was obtained × 12 + Month when the consent was obtained] – [Onset year of Parkinson's disease × 12 + Onset month of Parkinson's disease]) / 12 (rounded to the first decimal place)

  * If the onset month of Parkinson's disease is missing, the onset month will be imputed as January.

- MDS-UPDRS score:

  See Appendix 3 of this Statistical Analysis Plan

- Modified Hoehn and Yahr Scale:

  See Appendix 4 of this Statistical Analysis Plan

- PDQ-39 score:

  See Appendix 5 of this Statistical Analysis Plan

- QTcF interval (msec):

  QT interval (msec) / ([RR interval (msec) / 1000])$^{0.33}$ (rounded to the nearest integer)

1 Study Subjects, Demographics, and Other Baseline Characteristics

1.1 Disposition of Subjects

1.1.1 Study Information in This Study

Analysis Set: All Subjects Who Signed the Informed Consent Form in This Study

Analysis Variable(s): Date First Subject Signed Informed Consent Form in This Study
Date of Last Subject's Last Visit/Contact in This Study
MedDRA Version in this study
WHO Drug Version in this study
SAS Version Used for Creating the Data Sets in This Study

Analysis Method(s): The following analysis will be performed for the above analysis variables.
(1) Display of analysis variables

1.1.2 All Subjects Who Did Not Enter the Treatment Period

Analysis Set: All Subjects Who Did Not Enter the Treatment Period Among the Subjects Who Signed the Informed Consent Form in This Study

Analysis Variable(s): Categories in parentheses (hereinafter the same)

Age (years)	[Min<= - <65, 65<= - <=Max]
Gender	[Male, Female]

Analysis Method(s): The following analysis will be performed for the above analysis variables.
(1) Frequency distributions for categorical variables and descriptive statistics for continuous variables

1.1.3 Subject Eligibility in This Study

Analysis Set: All Subjects Who Signed the Informed Consent Form in This Study

Analysis Variable(s):

Status of Entrance into This Study	[Yes, No]
Reason for Not Entering to This Study	[Pretreatment Event/Adverse Event, Significant Protocol Deviation, Lost to Follow-up, Voluntary Withdrawal, Study Termination, Did Not Meet Entrance Criteria or Violation of Exclusion Criteria, Other]

Analysis Method(s): The following analysis will be performed for the above analysis variables. When calculating percentages for the primary reasons for subject not entering to this study, the total number of subjects who did not enter this study will be used as the denominator.
(1) Frequency distributions

1.1.4 Number of Subjects Who Entered This Study in Each Site

Analysis Set: All Subjects Who Entered This Study

Analysis Variable(s):	Status of Entrance into This Study	[Yes]
Stratified Variable(s):	Site	[Site numbers will be used as categories]

Analysis Method(s): The following analysis will be performed for the above analysis variables by treatment group in the preceding study for each stratified item and by combining the treatment groups in the preceding study.
(1) Frequency distributions

1.1.5 Disposition of Subjects

Analysis Set:	All Subjects Who Entered This Study	
Analysis Variable(s):	Study Drug Administration Status in This Study	[No]
	Reason for Not Being Treated	[Pretreatment Event/Adverse Event, Significant Protocol Deviation, Lost to Follow-up, Voluntary Withdrawal, Study Termination, Did Not Meet Entrance Criteria or Violation of Exclusion Criteria, Other]
	Study Drug Completion Status in This Study	[Completed Study Drug, Prematurely Discontinued Study Drug]
	Reason for Discontinuation of Study Drug	[Pretreatment Event/Adverse Event, Significant Protocol Deviation, Lost to Follow-up, Voluntary Withdrawal, Study Termination, Pregnancy, Lack of Efficacy, Other]
Analysis Method(s):	The following analysis will be performed for the above analysis variables by treatment group in the preceding study and by combining the treatment groups in the preceding study. When calculating percentages for the primary reasons for not being treated, the total number of subjects who did not receive TVP-1012 will be used as the denominator and when calculating percentages for the primary reasons for prematurely discontinued study drug, the total number of subjects who did complete the study drug administration will be used as the denominator. (1) Frequency distributions	

1.1.6 Study Drug Completion Status

1.1.6.1 Assessment of This Study

Analysis Set:	All Subjects Who Entered This Study	
Analysis Variable(s):	Study Drug Completion Status in This Study	[Completed Study Drug, Prematurely Discontinued Study Drug]
	Reason for Discontinuation of Study Drug	[Pretreatment Event/Adverse Event, Significant Protocol Deviation, Lost to Follow-up, Voluntary Withdrawal, Study Termination, Pregnancy, Lack of Efficacy, Other]
Categories:	Duration of study drug administration in this study (days)	[0, 1<= - <28, 28<= - <56, 56<= - <84, 84<= - <112, 112<= - <140, 140<= - <168, 168<= - <=Max]
Analysis Method(s):	The following analysis will be performed for the above analysis variables by treatment group in the preceding study and by combining the treatment groups in the preceding study. (1) Frequency distributions by treatment period of study drug in this study	

1.1.6.2 Assessment of Preceding Study and This Study

Analysis Set:	All Subjects Who Were Randomized in the Preceding Study	
Analysis Variable(s):	Study Drug Completion Status for the Treatment Period in Both Studies	[Completed Study Drug, Prematurely Discontinued Study Drug]
	Reason for Discontinuation of Study Drug	[Pretreatment Event/Adverse Event, Significant Protocol Deviation, Lost to Follow-up, Voluntary Withdrawal, Study Termination, Pregnancy, Lack of Efficacy, Other]
Categories:	Duration of study drug administration for the treatment period in both studies (days)	[0, 1<= - <84, 84<= - <168, 168<= - <252, 252<= - <336, 336<= - <=Max]

Analysis Method(s): The following analysis will be performed for the above analysis variables by treatment group in the preceding study and by combining the treatment groups in the preceding study.

(1) Frequency distributions by treatment period of study drug administration for the treatment period in both studies

1.1.7 Protocol Deviations and Analysis Data Set

1.1.7.1 Protocol Deviations

Analysis Set:	All Subjects Who Entered This Study	
Analysis Variable(s):	Protocol Deviations	[Major GCP Violations, Deviations of Protocol Entry Criteria, Deviations of Discontinuation Criteria, Deviations Related to Treatment Procedure or Dose, Deviations Concerning Excluded Medication or Therapy, Deviations to Avoid Emergency Risk, Other Deviation]

Analysis Method(s): The following analysis will be performed for the above analysis variables by treatment group in the preceding study and by combining the treatment groups in the preceding study.

The number of subjects with protocol deviations will be calculated and the details of deviations will be shown after classifying the contents of deviations into the above categories. A subject who has several categories will be counted once in each appropriate category.

(1) Frequency distributions

1.1.7.2 Analysis Sets

Analysis Set:	All Subjects Who Were Randomized in the Preceding Study	
Analysis Variable(s):	Handling of Cases in Analysis Sets and Case Data	[Categories are based on the specifications in “Handling Rules for Analysis Data”]
	Inclusion/Exclusion of Analysis Set	

Full Analysis Set	[Included]
Full Analysis Set 2	[Included]
Safety Analysis Set	[Included]

Analysis Method(s): The following analyses (1) and (2) will be performed for the above analysis variables by treatment group in the preceding study and the following analysis (3) will be performed by treatment group in the preceding study and by combining the treatment groups in the preceding study.
For (1) and (2), a subject who has several categories will be counted once in each appropriate category.

(1) Frequency distributions for handling of cases in each analysis set
(2) Frequency distributions for handling of case data in each analysis set
(3) Frequency distributions for number of cases included in each analysis set

1.2 Demographic and Other Baseline Characteristics

1.2.1 Summary of Demographics and Other Baseline Characteristic

Analysis Set: Safety Analysis Set

Analysis Variable(s):

Age (years)	[Min<= - <65, 65<= - <=Max]
Gender	[Male, Female]
Height (cm)	
Weight (kg) (Baseline (prior to TVP-1012 administration))	
BMI(kg/m^2)	
Smoking history	[The subject has never smoked, The subject is a current smoker, The subject is an ex-smoker]
Timing of Study Drug Administration	[Before breakfast, After breakfast]
Duration of Parkinson's disease (years)	[Min<= - <1.5, 1.5<= - <=Max]
Modified Hoehn and Yahr Scale	[Min<= - <2.0, 2.0<= - <3.0, 3.0<= - <=Max]
MDS-UPDRS Part II + Part III total score (Baseline (prior to TVP-1012 administration))	

Analysis Method(s): The following analysis will be performed for the above analysis variables by treatment group in the preceding study and by combining the treatment groups in the preceding study.

(1) Frequency distributions for categorical variables and descriptive statistics for continuous variables

1.2.2 Medical History and Concurrent Medical Conditions

Analysis Set: Safety Analysis Set

Analysis Variable(s):

Medical History in the Preceding Study	
Concurrent Medical Conditions in the Preceding Study	

Analysis Method(s): The following analysis will be performed for the above analysis variables by treatment group in the preceding study and by combining the treatment

groups in the preceding study.
MedDRA dictionary will be used for coding. Summaries will be provided using SOC and PT, where SOC will be sorted alphabetically and PT will be sorted in decreasing frequency.

(1) Frequency distributions for medical history in the preceding study (by SOC/PT)
(2) Frequency distributions for concurrent medical conditions in the preceding study (by SOC/PT)

The method of counting events when conducting each frequency distribution will be as follows:
[Number of subjects with medical history and/or concurrent medical conditions]
A subject with multiple occurrences of medical history or concurrent medical conditions within a SOC will be counted only once in that SOC.
A subject with multiple occurrences of medical history or concurrent medical conditions within a PT will be counted only once in that PT.

1.2.3 Medication History and Concomitant Medications

Analysis Set: Safety Analysis Set

Analysis Variable(s): Medication History in the Preceding Study
Concomitant Medications in the Preceding Study and This Study

Analysis Method(s): The following analysis will be performed for the above analysis variables by treatment group in the preceding study and by combining the treatment groups in the preceding study.
The WHO Drug dictionary will be used for coding. Summaries will be provided using Preferred Names and sorted in decreasing frequency based on the number of reports.
A subject who has been administered multiple doses of the same medication (Preferred Name) will be counted only once for that medication (Preferred Name).

(1) Frequency distributions for medication history in the preceding study
(2) Frequency distributions for concomitant medications that the subject started to use prior to study drug administration for the treatment period in the preceding study and also used during the treatment period, and concomitant medications that the subject started to use after study drug administration for the treatment period in the preceding study

1.3 Measurements of Treatment Compliance

1.3.1 Exposure and Compliance of TVP-1012

Analysis Set: Safety Analysis Set

Analysis Variable(s):	Duration of Exposure to TVP-1012 (days)	[1<= - <84, 84<= - <168, 168<= - <252, 252<= - <336, 336<= - <=Max]
	Compliance of TVP-1012 (%)	[Min<= - <50.0, 50.0<= - <70.0, 70.0<= - <90.0, 90.0<= - <=Max]

Analysis Method(s): The following analysis will be performed for the above analysis variables

by treatment group in the preceding study and by combining the treatment groups in the preceding study.

(1) Frequency distributions for categorical variables and descriptive statistics for continuous variables

2 Efficacy Analysis

2.1 Secondary Endpoint and Analytical Method

2.1.1 MDS-UPDRS Part II + Part III Total Score

2.1.1.1 Analysis based on the data after administration of TVP-1012

Analysis Set: Full Analysis Set

Analysis Variable(s): MDS-UPDRS Part II + Part III total score

Visit: Baseline (prior to TVP-1012 administration), Week 6, Week 10, Week 14, Week 20, Week 26, Week 32, Week 36, Week 40, Week 46, Week 52, End of Treatment

Analysis Method(s): Descriptive statistics and two-sided 95% confidence intervals of means at each visit by treatment group in the preceding study will be provided for the MDS-UPDRS Part II + Part III total score at each visit and the change from baseline (prior to TVP-1012 administration) in the MDS-UPDRS Part II + Part III total score at each visit of the treatment period (at each visit during the treatment period (Week 6 to End of Treatment)-Baseline (prior to TVP-1012 administration)). Furthermore, the means and standard deviations by treatment group in the preceding study will be shown in graphical display for the MDS-UPDRS Part II + Part III total score at each visit, and the change from baseline (prior to TVP-1012 administration) in the MDS-UPDRS Part II + Part III total score at each visit of the treatment period.

2.1.1.2 Analysis based on the data after study drug administration for the treatment period in the preceding study

Analysis Set: Full Analysis Set 2

Analysis Variable(s): MDS-UPDRS Part II + Part III total score

Visit: Baseline (at end of observation period), Week 6, Week 10, Week 14, Week 20, Week 26, Week 32, Week 36, Week 40, Week 46, Week 52 of Treatment Period, Week 52 of Treatment Period (LOCF)

Analysis Method(s): The same analysis as 2.1.1.1 will be performed for the above analysis variables.
Furthermore, the point estimates of the mean differences between treatment groups (1 mg -> 1 mg group-P -> 1 mg group) and the two-sided 95% confidence intervals at each visit by treatment group in the preceding study will be provided for the change from baseline (at end of observation period) in the MDS-UPDRS Part II + Part III total score at each visit during the treatment period (at each visit during the treatment period (Week 6 to Week 52 of Treatment Period (LOCF))-Baseline (at end of observation period)).

2.2 Other Endpoints and Analytical Methods

2.2.1 MDS-UPDRS Total Scores and Individual Scores

Analysis Set: Full Analysis Set

Analysis Variable(s): MDS-UPDRS Part I total score
MDS-UPDRS Part II total score
MDS-UPDRS Part III total score
MDS-UPDRS Part IV total score

	MDS-UPDRS tremor score MDS-UPDRS bradykinesia score MDS-UPDRS muscle rigidity score MDS-UPDRS individual scores
Visit:	Baseline (prior to TVP-1012 administration), Week 6, Week 10, Week 14, Week 20, Week 26, Week 32, Week 36, Week 40, Week 46, Week 52, End of Treatment
Analysis Method(s):	The same analysis as 2.1.1.1 will be performed for the above analysis variables. However, the graphical display of the mean and standard deviation is excluded.

2.2.2 PDQ-39 Summary Index and Domain Scores

Analysis Set:	Full Analysis Set
Analysis Variable(s):	PDQ-39 Summary Index PDQ-39 domain scores
Visit:	Baseline (prior to TVP-1012 administration), Week 14, Week 26, Week 40, Week 52, End of Treatment
Analysis Method(s):	The same analysis as 2.1.1.1 will be performed for the above analysis variables. However, the graphical display of the mean and standard deviation is excluded.

2.3 Statistical/Analytical Issues

2.3.1 Adjustments for Covariates

Not applied in this study.

2.3.2 Handling of Dropouts or Missing Data

Missing test results and data determined to be non-evaluable according to the Handling Rules for Analysis Data and this statistical analysis plan will not be used for hypothesis testing and estimations. Values below/less than or equal to the lower limit of quantification will be treated as zero when calculating the descriptive statistics. Values above/greater than or equal to the upper limit of quantification will be treated as the upper limit of quantification when calculating the descriptive statistics.

2.3.3 Interim Analyses and Data Monitoring

No interim analysis is planned.

2.3.4 Multicentre Studies

Not applied in this study.

2.3.5 Multiple Comparison/Multiplicity

Not applied in this study.

2.3.6 Use of an "Efficacy Subset" of Subject

Not applicable in this study.

2.3.7 Active-Control Studies Intended to Show Equivalence or Non-inferiority

Not applicable in this study.

2.3.8 Examination of Subgroups

2.3.8.1 Examination of Subgroups for Secondary Endpoint

Analysis Set:	Full Analysis Set	
Analysis Variable(s):	Change from baseline (prior to TVP-1012 administration) in the MDS-UPDRS Part II + Part III total score at end of treatment (at end of treatment-baseline (prior to TVP-1012 administration))	
Subgroup(s):	Age (years)	[Min<= - <65, 65<= - <=Max]
	Gender	[Male, Female]
	Smoking history	[Yes, No]
	Timing of Study Drug Administration	[Before breakfast, After breakfast]
	Duration of Parkinson's disease (years)	[Min<= - <1.5, 1.5<= - <=Max]
	Modified Hoehn and Yahr Scale	[Min<= - <2.0, 2.0<= - <3.0, 3.0<= - <=Max]
Analysis Method(s):	Descriptive statistics and two-sided 95% confidence intervals of means will be provided for the above each subgroup by treatment group in the preceding study.	

3 Safety Analysis

Of the safety evaluation variables in this study, the frequency of adverse events (AEs) will be used as the primary endpoint, and clinical laboratory test results, vital signs, ECGs, and weight will be used for the assessment of secondary endpoints.

3.1 Treatment-Emergent Adverse Event

3.1.1 Overview of Treatment-Emergent Adverse Events

Analysis Set: Safety Analysis Set

Analysis Variable(s): TEAEs that occurred after administration of TVP-1012

Categories: Relationship to Study Drug [Related, Not Related]
Intensity [Mild, Moderate, Severe]

Analysis Method(s): The following summaries will be provided for each treatment group in the preceding study.

(1) Overview of TEAEs
   1) All TEAEs (number of events, number and percentage of subjects)
   2) Relationship of TEAEs to study drug (number of events, number and percentage of subjects)
   3) Intensity of TEAEs (number of events, number and percentage of subjects)
   4) TEAEs leading to study drug discontinuation (number of events, number and percentage of subjects)
   5) Serious TEAEs (number of events, number and percentage of subjects)
   6) Relationship of serious TEAEs to study drug (number of events, number and percentage of subjects)
   7) Serious TEAEs leading to study drug discontinuation (number of events, number and percentage of subjects)
   8) TEAEs resulting in death (number of events, number and percentage of subjects)

TEAEs will be counted according to the rules below.

[Number of subjects with TEAEs]

- In case of "frequency distributions by relationship to study drug"
  A subject with occurrences of a TEAE in both categories (i.e., Related and Not Related) will be counted once in the Related category.
- In case of "frequency distributions by intensity"
  A subject with multiple occurrences of a TEAE will be counted once for the TEAE with the maximum intensity.
- In case of distributions other than the above
  A subject with multiple occurrences of a TEAE will be counted only once.

[Number of events]

For each summary, the total number of events will be calculated.

3.1.2 Displays of Treatment-Emergent Adverse Events

Analysis Set: Safety Analysis Set

Analysis Variable(s): TEAEs that occurred after administration of TVP-1012

Categories:
- Intensity [Mild, Moderate, Severe]
- Time of Onset (days) [1<= - <84, 84<= - <168, 168<= - <252, 252<= - <336, 336<= - <=Max]

Analysis Method(s): The following summaries will be provided for each treatment group in the preceding study.

TEAEs will be coded using MedDRA and will be summarized using SOC and PT. SOC will be sorted alphabetically and PT will be sorted in decreasing frequency for tables provided by SOC and PT. SOC and PT will be sorted in decreasing frequency for tables provided by SOC only or PT only.

(1) All TEAEs by SOC and PT
(2) All TEAEs by SOC
(3) All TEAEs by PT
(4) Drug-Related TEAEs by SOC and PT
(5) Intensity of All TEAEs by SOC and PT
(6) Intensity of Drug-Related TEAEs by SOC and PT
(7) TEAEs Leading to Study Drug Discontinuation by SOC and PT
(8) Serious TEAEs by SOC and PT
(9) TEAEs by SOC and PT Over Time

The methods of counting events and calculating the percentage of subjects when conducting each frequency distribution will be as follows:

[Number of subjects with TEAEs]

- In case of "frequency distributions by SOC and PT, by SOC only, or PT only"
  A subject with multiple occurrences of TEAE within a SOC will be counted only once in that SOC.
  A subject with multiple occurrences of TEAE within a PT will be counted only once in that PT.
  When calculating percentages for TEAE, the number of subjects in the safety analysis set will be used as the denominator.
- In case of "frequency distributions by SOC and PT"
  A subject with multiple occurrences of a TEAE within a SOC or a PT will be counted only once for the TEAE with the maximum intensity.
  When calculating percentages for TEAE, the number of subjects in the safety analysis set will be used as the denominator.
- In case of "frequency distributions by time of onset by SOC and PT"
  For each time interval, a subject with multiple occurrences of TEAE within a SOC or a PT will be counted only once in that SOC or PT. When calculating the onset rate of TEAEs for each time interval, the number of subjects among the safety analysis set (i.e., subjects who either have an exposure or have an occurrence of a TEAE, during or after the corresponding time interval) will be used as the denominator and the number of subjects whose onset of any one of the TEAEs is within the time interval will be used as the numerator.

3.1.3 Examination of Subgroups for Treatment-Emergent Adverse Event

Analysis Set: Safety Analysis Set

Analysis Variable(s): TEAEs that occurred after administration of TVP-1012

Subgroup(s):

Age (years)	[Min<= - <65, 65<= - <=Max]
Gender	[Male, Female]
Smoking history	[Yes, No]
Timing of Study Drug Administration	[Before breakfast, After breakfast]

Analysis Method(s): The following summaries will be provided for above each subgroup by treatment group in the preceding study.

TEAEs will be coded using MedDRA and will be summarized using SOC and PT, where SOC will be sorted alphabetically and PT will be sorted in decreasing frequency.

(1) All TEAEs by SOC and PT

(2) Drug-Related TEAEs by SOC and PT

The methods of counting events and calculating the percentage of subjects when conducting each frequency distribution will be as follows:

[Number of subjects with TEAEs]

- A subject with multiple occurrences of TEAE within a SOC will be counted only once in that SOC.
  A subject with multiple occurrences of TEAE within a PT will be counted only once in that PT.
  When calculating percentages for TEAE, the number of subjects in each stratified item in the safety analysis set will be used as the denominator.

3.2 Laboratory and Other Safety Data

3.2.1 Laboratory Test Results

3.2.1.1 Hematology and Serum Chemistry

Analysis Set: Safety Analysis Set

Analysis Variable(s): Hematology

RBC	Hemoglobin	Hematocrit
WBC		
WBC Differentials (Neutrophil, Eosinophil, Monocyte, Lymphocyte, and Basophil)		
Platelets		

Serum Chemistry

AST	ALT	γ-GTP
ALP	LDH	Albumin
Total Protein	Total Bilirubin	Total Cholesterol
Triglycerides	Creatinine	
Blood Urea Nitrogen (BUN)		Urine Acid
Creatine Kinase		Sodium
Potassium	Chlorine	Calcium
Phosphorus		

Categories: Results of determination based on reference values
[Below lower limit of reference value, Within the range of reference value, Over upper limit of reference value]

Visit: Baseline (prior to TVP-1012 administration), Week 3, Week 6, Week 14, Week 20, Week 26, Week 29, Week 32, Week 40, Week 46, Week 52

Analysis Method(s): The following summaries will be provided for each treatment group in the preceding study.

(1) Descriptive statistics for observed values for each visit and changes (each visit after administration [Week 3 to Week 52] - baseline [prior to TVP-1012 administration]) will be provided.

(2) Case Plots

(3) A shift table for baseline (prior to TVP-1012 administration) and each visit after administration will be provided for the results of determination based on the reference values.

3.2.1.2 Urinalysis

Analysis Set: Safety Analysis Set

Analysis Variable(s):

Protein	[-, +-, 1+, 2+, 3+, 4+]
Glucose	[-, 1+, 2+, 3+, 4+, 5+]
Blood	[-, +-, 1+, 2+, 3+]
Ketone Body	[-, +-, 1+, 2+, 3+, 4+]

Visit: Baseline (prior to TVP-1012 administration), Week 3, Week 6, Week 14, Week 20, Week 26, Week 29, Week 32, Week 40, Week 46, Week 52

Analysis Method(s): The following summaries will be provided for each treatment group in the preceding study.

(1) A shift table for baseline (prior to TVP-1012 administration) and each visit after administration (Week 3 to Week 52) will be provided.

3.2.2 Vital Signs, Physical Findings, and Other Observations Related to Safety

3.2.2.1 Vital Signs

Analysis Set: Safety Analysis Set

Analysis Variable(s): Body temperature
Systolic blood pressure
Diastolic blood pressure
Pulse rate

Visit: Baseline (prior to TVP-1012 administration), Week 3, Week 6, Week 10, Week 14, Week 20, Week 26, Week 29, Week 32, Week 36, Week 40, Week 46, Week 52

Analysis Method(s): The following summaries will be provided for each treatment group in the preceding study.

If a vital sign parameter has both lower and upper MAV criteria, analysis will be performed for each. Definitions of parameters subject to this analysis and MAV criteria are given in Appendix 2 of this Statistical Analysis Plan.

(1) Descriptive statistics for observed values for each visit and changes (each visit after administration [Week 3 to Week 52] - baseline [prior to TVP-1012 administration]) will be provided.

(2) Case Plots

(3) Overall frequency distributions of MAV after the administration of TVP-1012 will be provided.

3.2.2.2 12-Lead ECG

Analysis Set: Safety Analysis Set

Analysis Variable(s): Heart Rate
RR Interval
PR Interval
QT Interval
QRS Interval
QTcB Interval
QTcF Interval
12-Lead ECG Interpretation [Within Normal Limits, Abnormal but Not Clinically Significant, Abnormal and Clinically Significant]

Visit: Baseline (prior to TVP-1012 administration), Week 14, Week 26, Week 40, Week 52

Analysis Method(s): For each variable other than 12-lead ECG interpretations, summaries (1) and (2) will be provided by treatment group in the preceding study.
For 12-lead ECG interpretation, summary (3) will be provided by treatment group in the preceding study.

(1) Descriptive statistics for observed values for each visit and changes (each visit after administration (Week 14 to Week 52)-baseline (prior to TVP-1012 administration) will be provided.
(2) Case Plots
(3) A shift table for baseline (prior to TVP-1012 administration) and each visit after administration will be provided.

3.2.2.3 Weight

Analysis Set: Safety Analysis Set

Analysis Variable(s): Weight

Visit: Baseline (prior to TVP-1012 administration), Week 14, Week 26, Week 40, Week 52

Analysis Method(s): The following summaries will be provided for each treatment group in the preceding study.

(1) Descriptive statistics for observed values for each visit and changes (each visit after administration (Week 14 to Week 52)-baseline (prior to TVP-1012 administration) will be provided.
(2) Case Plots

4 Significance Level and Confidence Coefficient

- Confidence coefficient: 95% (two-sided)

Creation History (version management)

Version	Date	Created/Modified by	Comments
1	2016.09.30	[redacted]	Creation of first version
2	2017.04.11	[redacted]	Creation of second version

[Appendix 1] A Comparison Table for Changes in TVP-1012/OCT-001

Amendment from First Version (Created on 30 September 2016) to Second Version (Created on 11 April 2017)

Page	Existing Text	Revised Text	Rationale for Amendment
22	3.1.3 Examination of Subgroups for Treatment-Emergent Adverse Event Stratified Variable(s): Smoking history [Yes, No] Timing of Study Drug Administration [Before breakfast, After breakfast]	3.1.3 Examination of Subgroups for Treatment-Emergent Adverse Event Stratified Variable(s): Age (years) [Min<= - <65, 65<= - <=Max] Gender [Male, Female] Smoking history [Yes, No] Timing of Study Drug Administration [Before breakfast, After breakfast]	Modified after examining it with related functional departments.

[Appendix 2] Definition of MAV Criteria

(1) MAV Criteria

1) Vital Signs

For each test item, those obtained until 7 days after the administration of TVP-1012 (including 7 days after the end of TVP-1012 administration and evaluable data [i.e., non-missing and acceptable according to the Handling Rules for Analysis Data]) will be subject and the determination on MAV will be conducted according to the following table. The LLN and ULN in the following table will be the lower limit and upper limit of reference values within the normal range of each test item.

Vital Signs

Test item	Gender	Age	MAV Criteria	
			Lower	Upper
Body Temperature (°C)	-	-	<35.6	>37.7
Systolic Blood Pressure (mmHg)	-	-	<90	>180
Diastolic Blood Pressure (mmHg)	-	-	<50	>100
Pulse Rate (bpm)	-	-	<45	>120

Overall determination after administration of TVP-1012

The presence or absence of MAV for each subject will be determined for each test item according to the rules (1) to (3). If a test item has both lower and upper MAV criteria, analysis will be performed for each.

[1] If it is determined that at least 1 item among the evaluable data after the administration of TVP-1012 “meets the MAV Criteria,” it will be determined as “Yes.”

[2] If it does not correspond to [1] and it is determined that at least 1 item among the evaluable data after the administration of TVP-1012 “does not meet the MAV Criteria,” it will be determined as “No.”

[3] If it corresponds to neither [1] nor [2], it will be excluded from the analysis for the results of the determination.

[Appendix 3] MDS-UPDRS Score

- MDS-UPDRS individual score

Part I

Number	Variable	Score
1.1	Cognitive impairment	(0, 1, 2, 3, 4, UR)
1.2	Hallucinations and psychosis	(0, 1, 2, 3, 4, UR)
1.3	Depressed mood	(0, 1, 2, 3, 4, UR)
1.4	Anxious mood	(0, 1, 2, 3, 4, UR)
1.5	Apathy	(0, 1, 2, 3, 4, UR)
1.6	Features of DDS	(0, 1, 2, 3, 4, UR)
1.7	Sleep problems	(0, 1, 2, 3, 4)
1.8	Daytime sleepiness	(0, 1, 2, 3, 4)
1.9	Pain and other sensations	(0, 1, 2, 3, 4)
1.10	Urinary problems	(0, 1, 2, 3, 4)
1.11	Constipation problems	(0, 1, 2, 3, 4)
1.12	Light headedness on standing	(0, 1, 2, 3, 4)
1.13	Fatigue	(0, 1, 2, 3, 4)

Part II

Number	Variable	Score
2.1	Speech	(0, 1, 2, 3, 4)
2.2	Saliva and drooling	(0, 1, 2, 3, 4)
2.3	Chewing and swallowing	(0, 1, 2, 3, 4)
2.4	Eating tasks	(0, 1, 2, 3, 4)
2.5	Dressing	(0, 1, 2, 3, 4)
2.6	Hygiene	(0, 1, 2, 3, 4)
2.7	Handwriting	(0, 1, 2, 3, 4)
2.8	Doing hobbies and other activities	(0, 1, 2, 3, 4)
2.9	Turning in bed	(0, 1, 2, 3, 4)
2.10	Tremor	(0, 1, 2, 3, 4)
2.11	Getting out of bed, a car, or a deep chair	(0, 1, 2, 3, 4)
2.12	Walking and balance	(0, 1, 2, 3, 4)
2.13	Freezing	(0, 1, 2, 3, 4)

Part III

Number	Variable	Score
3.1	Speech	(0, 1, 2, 3, 4, UR)
3.2	Facial expression	(0, 1, 2, 3, 4, UR)
3.3a	Rigidity-Neck	(0, 1, 2, 3, 4, UR)
3.3b	Rigidity-RUE	(0, 1, 2, 3, 4, UR)
3.3c	Rigidity-LUE	(0, 1, 2, 3, 4, UR)
3.3d	Rigidity-RLE	(0, 1, 2, 3, 4, UR)
3.3e	Rigidity-LLE	(0, 1, 2, 3, 4, UR)
3.4a	Finger tapping-Right hand	(0, 1, 2, 3, 4, UR)
3.4b	Finger tapping-Left hand	(0, 1, 2, 3, 4, UR)
3.5a	Hand movements-Right hand	(0, 1, 2, 3, 4, UR)
3.5b	Hand movements-Left hand	(0, 1, 2, 3, 4, UR)
3.6a	Pronation-supination movements-Right hand	(0, 1, 2, 3, 4, UR)
3.6b	Pronation-supination movements-Left hand	(0, 1, 2, 3, 4, UR)
3.7a	Toe tapping-Right foot	(0, 1, 2, 3, 4, UR)
3.7b	Toe tapping-Left foot	(0, 1, 2, 3, 4, UR)
3.8a	Leg agility-Right leg	(0, 1, 2, 3, 4, UR)
3.8b	Leg agility-Left leg	(0, 1, 2, 3, 4, UR)
3.9	Arising from chair	(0, 1, 2, 3, 4, UR)
3.10	Gait	(0, 1, 2, 3, 4, UR)
3.11	Freezing of gait	(0, 1, 2, 3, 4, UR)
3.12	Postural stability	(0, 1, 2, 3, 4, UR)
3.13	Posture	(0, 1, 2, 3, 4, UR)
3.14	Global spontaneity of movement	(0, 1, 2, 3, 4, UR)
3.15a	Postural tremor-Right hand	(0, 1, 2, 3, 4, UR)
3.15b	Postural tremor-Left hand	(0, 1, 2, 3, 4, UR)
3.16a	Kinetic tremor-Right hand	(0, 1, 2, 3, 4, UR)
3.16b	Kinetic tremor-Left hand	(0, 1, 2, 3, 4, UR)
3.17a	Rest tremor amplitude-RUE	(0, 1, 2, 3, 4, UR)
3.17b	Rest tremor amplitude-LUE	(0, 1, 2, 3, 4, UR)
3.17c	Rest tremor amplitude-RLE	(0, 1, 2, 3, 4, UR)
3.17d	Rest tremor amplitude-LLE	(0, 1, 2, 3, 4, UR)
3.17e	Rest tremor amplitude-Lip/jaw	(0, 1, 2, 3, 4, UR)
3.18	Constancy of rest tremor	(0, 1, 2, 3, 4, UR)

Part IV

Number	Variable	Score
4.1	Time spent with dyskinesias	(0, 1, 2, 3, 4)
4.2	Functional impact of dyskinesias	(0, 1, 2, 3, 4)
4.3	Time spent in the OFF state	(0, 1, 2, 3, 4)
4.4	Functional impact of fluctuations	(0, 1, 2, 3, 4)
4.5	Complexity of motor fluctuations	(0, 1, 2, 3, 4)
4.6	Painful OFF-state dystonia	(0, 1, 2, 3, 4)

0: Normal, 1: Slight, 2: Mild, 3: Moderate, 4: Severe, UR: Unable to Rate

- Each total score based on scores of each MDS-UPDRS variable

  The score will be calculated according to the following rules for evaluable data (i.e., non-missing and acceptable according to the Handling Rules for Analysis Data).

  MDS-UPDRS Part I total score: Total of variable 1.1 to variable 1.13
  MDS-UPDRS Part II total score: Total of variable 2.1 to variable 2.13
  MDS-UPDRS Part III total score: Total of variable 3.1 to variable 3.18
  MDS-UPDRS Part IV total score: Total of variable 4.1 to variable 4.6
  MDS-UPDRS Part II + Part III total score: Total of variable 2.1 to variable 2.13 and variable 3.1 to variable 3.18
  MDS-UPDRS tremor score: Total of variable 2.10, variable 3.15a to variable 3.18
  MDS-UPDRS muscle rigidity score: Total of variable 3.3a to variable 3.3e
  MDS-UPDRS bradykinesia score: Total of variable 3.4a to variable 3.8b and variable 3.14

  * The score will be calculated using the variable on the same day of the assessment.
  * If a missing or “UR” value is contained in the variable used for calculation, the score will not be calculated.

[Appendix 4] Modified Hoehn and Yahr Scale

- Each Severity Classification of Modified Hoehn and Yahr Scale

  The score that corresponds to each severity classification will be used according to the following table.

Severity Classification	Variable	Score
Stage 0	No Parkinsonism	0
Stage 1	Unilateral Parkinsonism	1
Stage 1.5	Unilateral Parkinsonism and axial involvement	1.5
Stage 2	Bilateral Parkinsonism without impairment of balance	2
Stage 2.5	Mild bilateral Parkinsonism with recovery on retropulsion (pull) test	2.5
Stage 3	Mild to moderate Parkinsonism with impairment of balance but physically independent	3
Stage 4	Severe Parkinsonism; still able to walk or stand unassisted	4
Stage 5	Wheelchair bound or bedridden unless aided	5

[Appendix 5] PDQ-39 Score

- PDQ-39 individual score

Number	Variable	Score
1	Had difficulty doing the leisure activities which you would like to do?	(0, 1, 2, 3, 4)
2	Had difficulty looking after your home, e.g. DIY, housework, cooking?	(0, 1, 2, 3, 4)
3	Had difficulty carrying bags of shopping?	(0, 1, 2, 3, 4)
4	Had problems walking half a mile?	(0, 1, 2, 3, 4)
5	Had problems walking 100 yards?	(0, 1, 2, 3, 4)
6	Had problems getting around the house as easily as you would like?	(0, 1, 2, 3, 4)
7	Had difficulty getting around in public?	(0, 1, 2, 3, 4)
8	Needed someone else to accompany you when you went out?	(0, 1, 2, 3, 4)
9	Felt frightened or worried about falling over in public?	(0, 1, 2, 3, 4)
10	Been confined to the house more than you would like?	(0, 1, 2, 3, 4)
11	Had difficulty washing yourself?	(0, 1, 2, 3, 4)
12	Had difficulty dressing yourself?	(0, 1, 2, 3, 4)
13	Had problems doing up your shoe laces?	(0, 1, 2, 3, 4)
14	Had problems writing clearly?	(0, 1, 2, 3, 4)
15	Had difficulty cutting up your food?	(0, 1, 2, 3, 4)
16	Had difficulty holding a drink without spilling it?	(0, 1, 2, 3, 4)
17	Felt depressed?	(0, 1, 2, 3, 4)
18	Felt isolated and lonely?	(0, 1, 2, 3, 4)
19	Felt weepy or tearful?	(0, 1, 2, 3, 4)
20	Felt angry or bitter?	(0, 1, 2, 3, 4)
21	Felt anxious?	(0, 1, 2, 3, 4)
22	Felt worried about your future?	(0, 1, 2, 3, 4)
23	Felt you had to conceal your Parkinson's from people?	(0, 1, 2, 3, 4)
24	Avoided situations which involve eating or drinking in public?	(0, 1, 2, 3, 4)
25	Felt embarrassed in public due to having Parkinson's disease?	(0, 1, 2, 3, 4)

26	Felt worried by other people's reaction to you?	(0, 1, 2, 3, 4)
27	Had problems with your close personal relationships?	(0, 1, 2, 3, 4)
28	Lacked support in the ways you need from your spouse or partner?	(0, 1, 2, 3, 4, 5)
29	Lacked support in the ways you need from your family or close friends?	(0, 1, 2, 3, 4)
30	Unexpectedly fallen asleep during the day?	(0, 1, 2, 3, 4)
31	Had problems with your concentration, e.g. when reading or watching TV?	(0, 1, 2, 3, 4)
32	Felt your memory was bad?	(0, 1, 2, 3, 4)
33	Had distressing dreams or hallucinations?	(0, 1, 2, 3, 4)
34	Had difficulty with your speech?	(0, 1, 2, 3, 4)
35	Felt unable to communicate with people properly?	(0, 1, 2, 3, 4)
36	Felt ignored by people?	(0, 1, 2, 3, 4)
37	Had painful muscle cramps or spasms?	(0, 1, 2, 3, 4)
38	Had aches and pains in your joints or body?	(0, 1, 2, 3, 4)
39	Felt unpleasantly hot or cold?	(0, 1, 2, 3, 4)

0: Never, 1: Occasionally, 2: Sometimes, 3: Often, 4: Always (or cannot do at all), 5: If you do not have a spouse or partner tick here.

- PDQ-39 score by domain (rounded to the first decimal place)

The score will be calculated according to the following rules for evaluable data (i.e., non-missing and acceptable according to the Handling Rules for Analysis Data).

Mobility: (Total of variable 1 to variable 10) / (4×10) × 100
Activities of daily living: (Total of variable 11 to variable 16) / (4×6) × 100
Emotional well-being: (Total of variable 17 to variable 22) / (4×6) × 100
Stigma: (Total of variable 23 to variable 26) / (4×4)×100
Social support:
[In the case when variable 28 is other than 5 (Total of variable 27 to variable 29) / (4×3)×100
[In the case when variable 28 is 5] (Total of variables 27 and 29) / (4×2) × 100
Cognitions: (Total of variable 30 to variable 33) / (4×4)×100
Communication: (Total of variable 34 to variable 36) / (4×3)×100
Bodily discomfort: (Total of variable 37 to variable 39) / (4×3) × 100

* The score will be calculated using the variable on the same day of the assessment.

* If a missing value is contained in the variable used for calculation, the score will not be calculated.

- PDQ-39 Summary Index (rounded to the first decimal place)

The score will be calculated according to the following rules for evaluable data (i.e., non-missing and acceptable according to the Handling Rules for Analysis Data).

(Total of PDQ-39 Score by Domain Mobility-Bodily discomfort) / 8

* The score will be calculated using the variable on the same day of the assessment.
* If a missing value is contained in the variable used for calculation, the score will not be calculated.