Title: Study of the QOL evaluation of Trelagliptin in patient with type 2 Diabetes mellitus (TRENDS)

NCT Number: NCT03014479

Statistical analysis plan Approve Date: 28-Dec-2017

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

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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 as the language on original version was Japanese. This file is Statistical Analysis Plan Version 2.0 as the latest version and the initial version of SAP is not included in this file because the amendment was occurred for just only minor updates to correct expression/ misspellings.

Statistical Analysis Plan

Study Name	Study of the QOL evaluation of Trelagliptin in patient with type 2 diabetes mellitus
Protocol number	Trelagliptin-4002
Sponsor	Takeda Pharmaceutical Company Limited

Authorizer:

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Version.2.0: 28 Dec 2017

Contents

DEFINITIONS of TERMS

- Treatment -emergent adverse event (TEAE) : The AE which occurs after taking the first dose of trial medication.
- Summary Statistics: Number of subjects, mean, SDs, maximum values, minimum values, and quartiles
- BMI: Body Mass Index
- MedDRA: Medical Dictionary for Regulatory Activities
- QOL: Quality Of Life
- WHO: World Health Organization
- DTSQ: Diabetes Treatment Satisfaction Questionnaire
- DTR -QOL: Diabetes Therapy -Related QOL
- Subject with hypoglycemia: The subject with AE related to hypoglycemia
- Non Serious TEAE: Non -Serious TEAE is defined as Non -Serious TEAEs of at least 5% in any treatment group by SOC and PT. (if no event exceeds the 5% frequency, cutoff is lowered to 2%).

ANALYSIS SET

- Full Analysis Set
  The subjects who were randomized and received at least one dose of the Trelagliptin or Daily DPP-4 inhibitor
- Safety Analysis Set
  The subjects who received at least one dose of the Trelagliptin or Daily DPP-4 inhibitor

TIME WINDOW

For each assessment, observation and evaluation item, evaluable data is selected according to the following table. When there are multiple data exist within a time window, the one with the closest date to the reference date is adopted, and if the differences from the reference date are the same for multiple data, the later one is adopted.

1) DTR -QOL Questionnaire, The Basic Information on Study Subject, Laboratory Test (HbA1c)

Analysis Visit	Reference Date	Time Allowance (Number of Study Days)
Week -4	-30	-30～-15
Week 0	-1	-14～-1
Week 4	28	21～35
Week 12	84	70～97

Analysis Visit	Reference Date	Time Allowance (Number of Study Days)
End of Study	The latest date in treatment period	21～97

2) DTSQ, Laboratory Test (except HbA1c)

Analysis Visit	Reference Day	Time Allowance (Number of Study Days)
Week -4	-30	-30～-2
Week 0	-1	-1
Week 4	28	21～35
Week 12	84	70～97
End of Study	The latest date in treatment period	21～97

OTHER DATA HANDLING

Items	Method	Conditions
DTR -QOL Questionnaire Factor1: Burden on Social Activities and Daily Activities	The sum total of questions number 1 -13 was converted into a 0 -100 score [the best (91) = 100 and worst (13) = 0].	For a factor with <50% missing data, the mean value (round off 2 digits) calculated from available answers is applied to cover the missing data.
DTR -QOL Questionnaire Factor 2: Anxiety and Dissatisfaction with Treatment	The sum total of questions number 14 and 19 -25 is converted into a 0 -100 score [the best (56) = 100 and worst (8) = 0].	For a factor with <50% missing data, the mean value (round off 2 digits) calculated from available answers is applied to cover the missing data.
DTR -QOL Questionnaire Factor 3: Hypoglycemia	The sum total of questions number 15 -18, and is converted into a 0 -100 score [the best (28) = 100 and worst (4) = 0].	For a factor with <50% missing data, the mean value (round off 2 digits) calculated from available answers is applied to cover the missing data.
DTR -QOL Questionnaire Factor 4: Treatment Satisfaction	Each score of question number 26 -29 is reversed (i.e., 1 converted to 7, 7 converted to 1, and so on; the converted scores, where 7 is the best	For a factor with <50% missing data, the mean value calculated from available answers is applied to cover the missing data.

Items	Method	Conditions
	and 1 is the worst, had the opposite sequence of the original scores). The converted scores are then added up, and the total is converted into a 0 -100 score [the best (28) = 100 and worst (4) = 0].	
DTR -QOL Questionnaire Total Score of all Questions	1) Each score of question number 26 -29 was reversed.((i.e., 1 converted to 7, 7 converted to 1, and so on;). Factor1 – Factor 4 are calculated as described above.(Not converted) 2) Factor 1 - Factor 4, which calculated by the method described above, are subsequently added up, and converted into a 0 -100 score [the best (203) = 100 and worst (29) = 0].	The total score of whole questions is not calculated if a total score of any of the four factors was unavailable.
DTSQ Total Score	Item 1, 4, 5, 6, 7, 8 scores are added up,	All data must not be missing.
Planned Number of Dosage of Trelagliptin (tablets)	(The last administration date - the first administration date) / 7) +1. * Cut off to the whole number	All data must not be missing.
Planned Number of Dosage of Daily DPP -4 Inhibitor (tablets)	(The last administration date - the first administration date)) ×number of daily dose×number of tablets at the first administration date	All data must not be missing.
Study Medication Compliance (%)	Actual number of dosage / Planned number of dosage ×100 (tablets)	All data must not be missing.
Days after Administration (Days)	Examination/observation/evaluation date - the first administration date +1	All data must not be missing.

Items	Method	Conditions
Duration of Diabetes (year)	{ (The first administration date (year) ×12+The first administration date (month)) - (Onset Date of Diabetes (year) ×12 + Onset Date of Diabetes (month)) } / 12 (rounded off two decimal places)	All data must not be missing. If only the month of the onset of diabetes is unknown, the month of the onset of diabetes is regarded as "January".
8 -OHdG/Creatinine (ng/mg CRE)	8 -OHdG (ng/mL) / Urine creatinine (mg/dL) ×100	All data must not be missing.

Display digit

Item	Defitintion
Mean, Confidence interval, Quartiles	Round statistics down to the 1 digits lower than significant digits of the data.
Standard Deviation	Round to the 2 digits lower than significant digits of the data.
Minimum and Maximum Values	Display the data at the significant digits.
Proportion, Percentage	Round to the one decimal place.
P-value	Round down to four decimal places. If p-value is less than 0.0001, display "p<0.0001"

AE related to Hypoglycaemia

AE related to Hypoglycaemia is defined as below.

PT Code	PT Name (Japanese)	PT Name (English)
10020993	低血糖	Hypoglycaemia
10040576	低血糖ショック	Shock hypoglycaemic
10065981	低血糖性意識消失	Hypoglycaemic unconsciousness
10048803	低血糖性痙攣	Hypoglycaemic seizure
10021002	低血糖性脳症	Hypoglycaemic encephalopathy
10021000	低血糖昏睡	Hypoglycaemic coma
10020997	無自覚性低血糖	Hypoglycaemia unawareness
10054998	神経低糖症	Neuroglycopenia

1 SUBJECTS, DEMOGRAPHIC and OTHER BASELINE CHARACTERISTICS

1.1 Subject Disposition

1.1.1 **Study Information**

Analysis Set: All subjects who are obtained informed consent

Items: Date of First Subject Signed Informed Consent Form
Date of Last Subject's Last Dose/Last Observation/Last Examination
MedDRA Version
SAS Version

Method : For the above analysis items, the following analysis will be performed.
(1) Display the above items

1.1.2 **Eligibility of Subjects**

Analysis Set: All subjects who are obtained informed consent

Items: Randomization into the Treatment Period of the Study [Yes, No]
Reason for Not randomized [Major Protocol Deviation, Lost to Follow-Up, Voluntary Withdrawal, Study Termination, Pregnancy, Did not meet entrance criteria, Other]

Method : For the above analysis items, the following analysis will be performed.
The denominator for the reasons is the number of subjects of Not randomized.
(1) Frequency distribution

1.1.3 **Disposition of Subjects**

Analysis Set: All Randomized subjects

Items: Status at the End of Study [Completed, Not Completed]
Reason for Not Completed [Adverse Event, Major Protocol Deviation, Lost to Follow-Up, Voluntary Withdrawal, Study Termination, Pregnancy, Lack of Efficacy, Other]

Method : For the above analysis items, the following analysis will be performed for each treatment group and total.
The denominator for the reasons is the number of subjects of Not completed.

(1) Frequency distribution

1.1.4 **Protocol Deviations**

Analysis Set: All Randomized subjects

Items: Protocol Deviations [Major GCP Violation, Deviations of Protocol Entry Criteria, Deviations Related to Treatment Procedure or Dose, Deviations Concerning Excluded Medication or Therapy,Deviation to Avoid Emergency Risk , Other]

Method: For the above analysis items, the following analysis will be performed for each treatment group and total. Summarize the number of subjects who have deviated from the protocol, classify the deviations into the above category, and show the breakdown of deviations. Subjects applicable for multiple categories will be counted once in each category.

(1) Frequency distribution

1.1.5 **Datasets Analyzed**

Analysis Set: All Randomized subjects

Items: Subjects Included/Excluded from Analysis Sets

Full Analysis Set [Inclusion]

Safety Analysis Set [Inclusion]

Method: For the above analysis items, the following analysis will be performed.

(1) Frequency distribution

1.2 Demographics and Other Baseline Characteristics

1.2.1 **Distribution of Demographics Items**

Analysis Set: Full Analysis Set

Items: Age (years) [Min<= - <65, 65<= - <75, 75<= - <=Max]

Gender [Male, Female]

Height (cm) [Min<= - <150, 150<= - <160, 160<= - <170, 170<= - <=Max]

Weight (kg) [Min<= - <50.0, 50.0<= - <60.0, 60.0<= - <70.0, 70.0<= - <80.0, 80.0<= - <=Max]

BMI (kg/m2) [Min<= - <18.5, 18.5<= - <25.0,

	25.0<= - <=Max]
Smoking Classification	[Never smoked, Current smoker, Ex-smoker]
Drink Alcohol Almost Every Day?	[Yes, No]
Duration of type 2 Diabetes Mellitus (years)	[Min<= - < 5, 5<= - <10, 10<= - <=Max]
Any Medication for Concurrent Condition?(Week 0)	[Yes, No]
Number of Daily Doses of Drugs (Concurrent Condition Medicine.)	[Less than 2 Times, 2 Times or More]
Total Number of Daily Tablets (Concurrent Condition Medicine.)	[Less than 2 Tablets, 2 Tablets or More]
Number of Doses of Drugs (Study drug.)	[Once a Week, Once daily, Twice daily]
HbA1c (Week -4)	[Less than 8.0%, 8.0% or more]
DTR -QOL Total Score (Week -4)	[Less than 80, 80 or more]
DTR -QOL Total Score (Week 0)	
DTR -QOL Total Score of "Factor 1: Burden on Social Activities and Daily Activities" (Week 0)	
DTR -QOL Total Score of "Factor 2: Anxiety and Dissatisfaction with Treatment" (Week 0)	
DTR -QOL Total Score of "Factor 3: Hypoglycemia" (Week 0)	
DTR -QOL Total Score of "Factor 4: Satisfaction with Treatment" (Week 0)	
DTSQ Total Score (Week 0)	

Method: For the above analysis items, the following analysis will be performed for each treatment group and total.

(1) Summary of frequency distribution for discrete variables and summary statistics for continuous variables.

1.2.2.**Medical History and Concurrent Disease**

Analysis Set: Full Analysis Set

Items: Medical History

Concurrent Medical Conditions

Method: For the above analysis items, the following analysis will be performed for each treatment group and total.

Analysis variables will be coded using the MedDRA dictionary and be summarized into SOC and PT. SOCs will be sorted in alphabetical order, then PTs will be sorted in frequency order.

(1) Medical history: Summary of frequency distribution by SOC/PT

(2) Concurrent medical conditions: Summary of frequency distribution by SOC/PT

The method of accounting for the frequency is as follows.

[Number of subjects]

For each summary, subjects with one or more events within a level of SOC term is counted only once in that level. Similarly, subjects with one or more events within a level of PT term is counted only once in that level.

1.2.3 **Concomitant Medications**

Analysis Set: Full Analysis Set

Items: Concomitant Medication

Method: For the above analysis items, the following analysis will be performed for each treatment group and total. Analysis variables will be coded using the WHO (World Health Organization) Drug. Coded medications will be sorted in frequency order. Medications used more than once within a subject will be counted only once for the subject.

(1) Frequency distribution

1.2.4 **Dosing conditions of Study drug**

Analysis Set: Full Analysis Set

Items:	Trelagliptin (mg/week)	[50, 100, Other]
	Control Drugs	[Sitagliptin, Vildagliptin, Alogliptin, Linagliptin, Teneligliptin, Anagliptin, Saxagliptin]
	Control Drug(mg/day)	
	Sitagliptin	[25, 50, 100, Other]
	Vildagliptin	[50, 100, Other]

Alogliptin	[25, Other]
Linagliptin	[5, Other]
Teneligliptin	[20, 40, Other]
Anagliptin	[200, 400, Other]
Saxagliptin	[2.5, 5, Other]

Method: (1) Frequency distribution at Week 0.

2 EFFICACY EVALUATIONS

2.1 Primary Endpoint and the Analytical Methods

Analysis Set: Full Analysis Set

Items: Change from Baseline in DTR-QOL Total Score at End of Study (Week 12)

Method: Analysis of covariance (ANCOVA) is conducted to compare between the treatment groups using "Change from baseline in DTR-QOL total score by the end of treatment [the End of Study (Week 12) - baseline (Week 0)]" as a dependent variable; DTR-QOL Total Score at the start of the screening period(<80 or ≥80) and HbA1c (<8.0% or ≥8.0%) at the start of the screening period as covariates; and "treatment group" as an independent variable. The level of significance is defined as 5% (two-sided).

2.2 Secondary Endpoints and the Analytical Methods

Analysis Set: Full Analysis Set

Items:
1) DTR -QOL Total Score
2) DTR -QOL Total Score of Factor1 to Factor 4
"Factor 1: Burden on Social Activities and Daily Activities" (13 questions)
"Factor 2: Anxiety and Dissatisfaction with Treatment" (8 questions)
"Factor 3: Hypoglycemia" (4 questions)
"Factor 4: Satisfaction with Treatment" (4 questions)
3) DTSQ Total Score
4) DTR -QOL Total Score of Each Items
5) DTSQ Total Score of Each Items

Analysis Visit: Week 0, Week 4, Week 12, End of Study

Method: (1) The following analysis will be performed for the Items 1 to 3 described above.

Summary statistics of observed value and 95% confidence interval for the mean will be calculated by treatment groups and Analysis Visit. In addition, Mean (+/-SD) plots will be made by treatment group and Analysis Visit. Adjusted mean differences and the 95% confidence interval (two-sided) will also be provided. The same analyses described above will be performed on change from baseline at each analysis visit.

(2) The following analysis will be performed for the Items 2 to 3 described above.

Analysis of covariance (ANCOVA) will be conducted to compare between the treatment groups using "the change from baseline in the total score by the end of treatment [the End of Study(Week 12) - baseline (Week 0)]" as a dependent variable; the total score of "the DTR-QOL Total score (<80 or ≥80)" at the baseline (Week 0) and "HbA1c (<8.0% or ≥8.0%)" at the baseline (Week 0) as covariates; and "a treatment group" as an independent variable.

(3) The following analysis will be performed for the Items 1, 3 described above.

The summary statistics and two-sided 95% CI for means of change from baseline by treatment group will be calculated, with stratification by the following factors at the start of the treatment period (Week 0):

- Use of medication for treatment of comorbidities;
- Number of daily doses of medication for treatment of comorbidities (<2 times or ≥2 times);
- total number of daily tablets of medication for treatment of comorbidities (<2 tablets or ≥2 tablets);
- Number of doses of the study drug or comparative drug (once weekly, once daily or twice daily).

(4) The following analysis will be performed for the Items 4 -5 described above.

Summary statistics for measurements and the change from baseline (Week 0) will be calculated by treatment group per question at each analysis visit.

2.3 Other Analysis

Analysis Set: Full Analysis Set

Items: 1) Laboratory Tests

Serum Chemistry:

HbA1c

Fasting Blood Glucose

Fasting Insulin

Fasting Glucagon

Fasting Glycoalbumin

1.5 -AG

Serum creatinine

Urinalysis:

Urinary 8-OHdG (using a correction value of uric creatinine)

Urinary creatinine

2) Treatment Compliance

3) The Basic Information on Study Subject

How was Blood Glucose level in the previous a month?	[1: Well-Controlled, 2, 3: Not Sure, 4, 5: Poorly-Controlled]
Which diabetes Med do you like to use? If efficacy, side effect, cost are equivalent	[3 Times Daily, Twice Daily, Once Daily, Once a Week, Any Will be OK]
Have you experienced hypoglycemia in the previous a month?	[Yes, No]
How many times have you experienced hypoglycemia in the previous a month?	[0, 1, 2, 3, 4, 5<= - <=Max]
When do you take other medicine (ex. hyperpiesia) in the previous a month? [multiple answers are allowed]	[Breakfast, Lunch, Dinner, Bedtime, No Rules, Not Taking]
How often do you forget to take other medicine (ex. hyperpiesia) in the previous a month?	[Never, Rarely, 1-3 Times per Month, Once a Week, A Few Times a Week, >4 Times a Week, Not Taking]
What kind Job are you with?	[Full Time Job, Part Time Job, No Job, Other]
How many Days Go to Work or go outside from Morning?	[Rarely, 1-2 Days per Week, 3-4 Days per Week, 5-6 Days per Week, 7 Days per Week]

Hours taken from wake up to leave Home	[Less than 1 hr, More than 1 hr Less than 2 hr, More than 2 hr Less than 3 hr, More than 3 hr]
How often do you have to take medicine during busy hours in the previous one month ?	[Always, Sometimes, Occasionally, Rarely, Never]
When do you take diabetes medicine? [multiple]	[Breakfast, Lunch, Dinner, Bedtime, No Rules, Not Taking]
How Often do you forget to take diabetes medicine in the previous one month ?	[Never, Rarely, 1-3 Times per Month, Once a Week, A Few Times a Week, >4 Times a Week, Not Taking,]
Felt guilty when forgot to take DM medicine	[Exactly, Somewhat, Not Sure, Not Exactly, Never]
Burdensome to take diabetes medicine outside	[Exactly, Somewhat, Not Sure, Not Exactly, Never]

Analysis Visit: Item 1: Week 0, Week 4, Week 12, End of Study
Item 3: Week 0, Week 4, Week 12, End of Study

Method:

(1) The following analysis will be performed for the Items 1 described above.

Summary statistics of observed value and change from baseline (week 0) will be calculated by treatment groups. Mean differences and the 95% confidence interval (two-sided) will also be provided. In addition, Mean (+/-SD) plots will be made by treatment group.

(2) The following analysis will be performed for the Items 2 described above.

Treatment compliance of each subject will be calculated and summary statistics of compliance by treatment group will also be provided.

(3) The following analysis will be performed for the Items 3described above.

Frequency distribution to each question will be analyzed byper treatment group.

2.4 CONSIDERATIONS on STATISTICAL ANALYSIS

2.4.1 **Adjustments for Covariates**

ANCOVA will be performed on primary and secondary endpoints using treatment group as independent variables. Details are described in 2.1 and 2.2

2.4.2 **Handling of Dropouts or Missing Data**

Data which are not adopted as a result of data missing of each analysis item or data handling in accordance with this statistical analysis plan item will be excluded from the analysis target for the statistical test or estimation of the evaluation.

2.4.3 **Interim Analysis and Early Discontinuation**

Interim analysis will not be performed.

2.4.4 **Multicenter Studies**

Analyses for consideration of centers will not be performed.

2.4.5 **Multiple Comparisons/Multiplicity**

It does not adjust multiplicity.

2.4.6 **Use of an Efficacy Subset of Subjects**

Not applicable in this study.

2.4.7 **Active-Control Studies Intended to Show Equivalence**

This is not an active-control study intended to show equivalence.

2.4.8 **Subgroup Analysis**

Subgroup analysis will be performed in 2.2.

3 SAFETY EVALUATION

3.1 Treatment -Emergent Adverse Event

3.1.1 Brief Summary of Adverse Events

Analysis Set: Safety Analysis Set

Items: TEAE

Classification: Causal relationship with treatment/control drug [Related, Not related]

Severity [Mild, Moderate, Severe]

Method: For the above analysis items, the following analyses of frequency distribution will be performed

(1) Brief Summary of TEAE (events, subject, percent)

1) All TEAEs
2) TEAEs by causality
3) All TEAEs by severity
4) TEAEs leading to discontinuation
5) Serious TEAEs
6) Serious TEAEs by causality
7) Serious TEAEs leading to study drug discontinuation
8) TEAEs leading to death

Incidence rates will be calculated as following on each analysis

[Number of Subjects]

- Frequency by Causality

  In case of the analysis by causality, subjects with one or more adverse events within a level of MedDRA term is counted only once as related AE.

- Frequency by Severity

  Subjects with one or more adverse events within a level of MedDRA term will be counted only once in that level using the most severe incident.

- Others

  Subjects with one or more adverse events within a level of MedDRA term will be counted only once for that MedDRA term. The denominator when calculating the incidence of adverse events is the number of subjects of safety analysis set.

[Number of Events]

Number of events will be allowed multiple counts for the subject with one or more adverse events within a level of MedDRA term.

3.1.2 **Display of TEAE**

Analysis Set: Safety Analysis Set

Items: TEAE

Classification: Severity [Mild, Moderate, Severe]

Method: For the above analysis items, the following analysis will be performed for each treatment group. Analysis variables will be coded using the MedDRA dictionary and be summarized into SOC and PT. SOCs will be sorted in alphabetical order, then PTs will be sorted in frequency order.

(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) All TEAEs by severity by SOC and PT

(6) Drug-related TEAEs by severity by SOC and PT

(7) TEAEs leading to discontinuation by SOC and PT

(8) Serious TEAEs by SOC and PT

(9) Non-serious TEAEs of by SOC and PT

Incidence rates will be calculated as following on each analysis.

[Number of Subjects]

- Frequency distribution (by SOC/PT, SOC, PT)
  Within each summary, subjects with one or more adverse events within a level of SOC term is counted only once in that level. Similarly, subjects with one or more adverse events within a level of PT term is counted only once in that level. The denominator when calculating the incidence of adverse events is the number of subjects of safety analysis set.
- Frequency by Severity (by SOC/PT)
  Subjects with one or more adverse events within a level of SOC/PT term is counted only once in that level using the most severe incident. The denominator when calculating the incidence of adverse events is the number of subjects of safety analysis set.

3.2 Frequency of Hypoglycemia

Analysis Set:	Safety Analysis Set	
Items:	Hypoglycemia During Study	[Yes, No]
	Incidence of Hypoglycemia (times)	[0, 1, 2, 3, 4, 5<= - <=Max]
Method:	Incidence rates will be calculated as following on each analysis.	
	(1) Frequency distribution	

3.3 Hospitalization related to type 2 diabetes mellitus

Analysis Set:	Safety Analysis Set	
Items:	Hospitalization Related to Type 2 Diabetes Mellitus	[Yes, No]
	Period (Days)	[Min<= - <7, 7<= - < 14, 14<= - <=Max]
	Frequency (Times)	[1, 2, 3, 4, 5<= - <=Max]
Method:	Incidence rates will be calculated as following on each analysis.	
	(1) Frequency distribution	
	For subjects who hospitalized for type 2 diabetes, duration and number of times will be counted. For subjects who remain hospitalized at the end of this study, duration will be calculated by using the last examination date.	

4 LISTINGS

Analysis Set:	All Randomized subjects	
Items:	Demographics	[Subject No., Site Name, Treatment group, Medication name(control drug), Informed consent date, Age (years) , Sex, Height (cm) , Weight (kg) , BMI (kg / m2) , Smoking Classification, Drink alcohol , Date of DM onset, Medical history(YN), Concurrent Medical Conditions (YN)]
	Protocol Deviation	[Subject No., Site Name, Treatment group, Age(years) , Sex, Contents of Protocol Deviation]
	Excluded from Efficacy	[Subject No., Treatment group, Age(years) , Sex, Reason for exclusion]
	Medical History	[Subject No., Site Name, Treatment group, Age(years) , Sex, Medical history(YN), Reported term for the medical history, SOC name, PT Name]

Concurrent Medical Conditions	[Subject No., Site Name, Treatment group, Age(years) , Sex, Concurrent Medical Conditions (YN), Reported term for the concurrent medical conditions, SOC name, PT name]
Medication for Concurrent Condition	[Subject No., Site Name, Treatment group, Age(years) , Sex, Medication for concurrent Condition (YN), Number of daily doses of drugs, Total number of daily tablets]
Concomitant Medications	[Subject No., Site Name, Treatment group, Age(years) , Sex, Concomitant medication during study(YN), Trade name or Generic medication name, Drug code, Drug code(label), Preferred name, Total daily dose, Dose unit, Total daily dose (as needed), Route, Medication start date, Medication end date, Medication given to treat PTE/AE, Adverse event, Indication]
Basic Information Questionnaire	[Subject No., Site Name, Treatment group, Age(years) , Sex, Analysis visit, Result(No.1-14)]
DTR -QOL Questionnaire	[Subject No., Site Name, Treatment group, Age(years) , Sex, Analysis Visit, Total score (Factor 1-Factor 4), DTR-QOL total score, Each score]
DTSQ	[Subject No., Site Name, Treatment group, Age(years) , Sex, Analysis Visit, DTSQ total score, Each score]
Withdrawal	[Subject No., Site Name, Treatment group, Age(years) , Sex, Reason, Details of reason, Date of last dose , Experience an overdose(YN), PTE/AE During Study(YN), Concomitant Medication(YN)]
Treatment drug / Control drug	[Subject No., Site Name, Treatment group, Age(years) , Sex, Dose date, Dose time (first) , Dose time (second)]
Laboratory Test	[Subject No., Site Name, Treatment group, Age(years) , Sex, Analysis Visit, Sample date, Item, Result, Normal/Abnormal, Specimen abnormal]

	Hospitalization Related to Type 2 Diabetes Mellitus	[Subject No., Site Name, Treatment group, Age(years) , Sex, Date of hospitalization, Date of discharge]
	TEAE	[Subject No., Treatment group, Age(years) , Sex, Adverse event (Verbatim) , SOC name, PT name , AE start date, AE end date, Intensity, Relationship to study drug , Action Concerning Study Drug, Date Dose Stopped, Date Dose Restarted, Outcome, Date of Death, Seriousness]
	Serious TEAE	[Subject No., Site Name, Treatment group, Age(years), Sex, Adverse event (Verbatim) , SOC name, PT name , AE start date, AE end date, Intensity, Relationship to study drug , Action Concerning Study Drug, Date Dose Stopped, Date Dose Restarted, Outcome, Date of Death,]
	Dose Dispensed	[Subject No., Site Name, Treatment group, Age(years) , Sex, Date of dispensed, Quantity of dispensed, Drug unused confirmed date, Quantity of unused]
	Investigational Drug Overdose	[Subject No., Site Name, Treatment group, Age(years) , Sex, overdose start date, overdose end date, maximum daily amount taken, related to study proc./product packaging, nature of overdose, details of overdose, any untoward occurrences?, concomitant medication, procedure, prescribed dose amended, unknown, Other]
Method:	Lists described above will be created for randomized subjects	

Significance level, Confidence coefficient

- Significance level of 5% (2-sided) will be used for analysis.
- Confidence coefficient of 95% (2-sided) will be used for all confidence intervals.

REVISION HISTORY

Version	Date	Author	Revised Content
1.0	2017.1.10	PPD	First Edition
2.0	2017.12.28	PPD	Revision base on revised protocol Ver.1.