Statistical Analysis Plan: Mock-up Tables

Version 2.0, 10-FEB-2020

Protocol Number: V203-AD-EXT

An Extension Study of a Phase IIa study in Patients with Mild Alzheimer's Disease to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of UBITh® AD Immunotherapeutic Vaccine (UB-311)

Protocol version: 1.1, 22JAN2018
Sponsor: United Neuroscience Ltd., Taiwan Branch (UNS Taiwan)

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1 Statistical Changes from Study Protocol

The statistical analysis methods will follow study protocol version 1.1 (22JAN2018). Due to incorrect treatment assignment (detailed in Section 1.2), the study was terminated earlier than the planned schedule. Exceptions and clarifications are described below:

1.1 Incorrect Treatment Group Assignment

There are 3 treatment groups in main study V203-AD, corresponding dosing regimen is listed as table below.

Clinical schematic diagram in main study - V203-AD

Treatment Group in V203-AD	Screening	Treatment											Follow-up	
Visit	S1 S2	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13
Week	-6 ~ -1	1	5	13	17	25	29	37	41	49	53	61	65	79
UB-311 7 doses		↑	↑	↑		↑		↑		↑		↑		
UB-311 5 doses		↑	↑	↑		↑P		↑		↑P		↑		
Placebo		↑P	↑P	↑P		↑P		↑P		↑P		↑P		

↑: UB-311 ↑P: placebo
†: In V203-AD study, the week no. counts from 0, yet counts from 1 in V203-AD-EXT study. In order to be consistent with V203-AD-EXT, week no. in V203-AD study here are added 1.

According to protocol, the dosing regimen in extension study V203-AD-EXT should follow table below.

Clinical schematic diagram in extension study - V203-AD-EXT

Treatment Group in V203-AD	Planned Treatment Group in V203-AD-EXT	Screening	Treatment							Follow-up
Visit		S1	V1	V2	V3	V4	V5	V6	V7	V8
Week		-6 ~ -1	1	5	13	25	49	73	97	109
UB-311 7 doses	UB-311 3 doses		↑	↑P	↑P		↑		↑	
UB-311 5 doses	UB-311 3 doses		↑	↑P	↑P		↑		↑	
Placebo	UB-311 5 doses		↑	↑	↑		↑		↑	

↑: UB-311 ↑P: placebo (no injection after treatment unblinding of main study V203-AD)

However, incorrect treatment group assignment occurred during V203-AD-EXT study, and summary is given as below.

Subject Number		Actual Treatment Group in V203-AD-EXT		
		UB-311 1 dose	UB-311 3 doses	Total
Treatment Group in V203-AD	UB-311 7 doses	10	2*	12
	UB-311 5 doses	7	5*	12
	Placebo	8*	2	10
	Total	25	9	34

*: incorrect treatment group assignment

There are 15 subjects who administered wrong treatment. From sponsor's judgment, the wrong treatment assignment is significantly impacting the primary endpoint. Consequently, the project is decided to be terminated and all subjects should finish all assessments at early termination visit.

As the study was early terminated by sponsor, there will be some visits or some measurement in the mock table(s) without data and will not be presented in the final table(s).

1.2 Analysis Populations

Per-protocol (PP) defined in protocol is listed below.

Section 9.2.1 "Efficacy populations" of study protocol
Per-protocol (PP) population: subjects who receive all planned doses of the study drug, complete the treatment period, fulfil all entry criteria, and have no key protocol deviation.

According to protocol section 9.2 "Efficacy populations" that one condition of Per-protocol (PP) population is "***complete the treatment period***", however, there will be no PP subjects due to early termination of the study. All efficacy analyses will be analyzed based on Modified Intent-to-Treat population and the conclusion will be made on Modified Intent-to-Treat population.

1.3 Primary Endpoints - Response Rate

Response rate defined in protocol is provided below.

Section 9.1.2 "Immunogenicity variables" of study protocol
The level of anti-Aβ antibodies is one of the primary endpoints and is assessed at Week 1 (V1), Week 5 (V2), Week 13 (V3), Week 49 (V5), Week 97 (V7) and Week 109 (V8). **The one-sided 95% confidence interval (CI, right side) from all visits (V1 to V13) for subjects in Arm 3 (placebo group) of V203-AD study will be calculated as the threshold of response. Antibody responders will be defined as the subjects with serum antibody titer > response threshold at any visit after first injection of UB-311.**

Since there was randomization error in this study and there are only 2 valid placebo subjects, the analysis of response rate will be omitted.

1.4 Primary Endpoints - Analysis of Immunogenicity Variable

Analysis of immunogenicity variable defined in protocol is listed below.

Section 9.3.3 "Analysis of immunogenicity variable" of study protocol
Immunogenicity analyses will be performed on the mITT and PP populations. The change in antibody level will be analyzed by a repeated-measures mixed-effects model.
Section 9.3.4 "Analysis of efficacy variables" of study protocol
Efficacy analyses will be performed on the mITT and PP populations. Descriptive statistics will be provided for all continuous variables at the scheduled visits. Continuous variables with repeated measures will be analyzed using a mixed-effects model.

Due to incorrect assignment and early termination resulting in more treatment groups and fewer visits than planned in the protocol, the Repeated-Measures Mixed-Effects Model is no longer appropriate. Change from baseline of each post-treatment visit will be presented in descriptive statistics instead.

1.5 Treatment Tolerability and Compliance

According to protocol section 9.3.2, treatment tolerability and compliance will be derived by formulas below:

Section 9.3.2 "Treatment tolerability and compliance" of study protocol

The overall treatment tolerability of UB-311 is defined as the percentage of number of administered doses divided by number of administered doses plus number of missed doses of subject(s) who drops out due to drug-related AE(s). It is calculated according to the following formula:

$100\% \times (A+B_1+C+D) / (A+B_1+B_2+C+D)$

where
A: number of administered doses of completers
B_1: number of administered doses of subject(s) who drops out due to drug-related AE(s)
B_2: number of missed doses of subject(s) who drops out due to drug-related AE(s)
C: number of administered doses of subject(s) who drops out due to drug-unrelated AE(s)
D: number of administered doses of subject(s) who drops out not due to AE(s)

The overall compliance is defined as the actual dose (UB-311 or placebo) of injection compared to the prescribed dose of treatment during the study. It is calculated according to the following formula:

100% x (Actual injection dose/Prescribed injection dose)

Due to study early termination, the description of treatment tolerability and compliance is modified as below:

The overall treatment tolerability of UB-311 is defined as the percentage of number of administered doses divided by number of administered doses plus number of missed doses of subject(s) who drops out due to drug-related AE(s). Due to early termination of this study, for the purpose of calculating tolerability, the completers are defined as the subjects who finished all required doses before study termination by sponsor or treatment unblinding of V203-AD for placebo. It is calculated according to the following formula:

$100\% \times (A+B_1+C+D) / (A+B_1+B_2+C+D)$

where
A: number of administered doses of completers
B_1: number of administered doses of subject(s) who drops out due to drug-related AE(s)
B_2: number of missed doses (up to treatment unblinding of main study for placebo or study termination by sponsor) of subject(s) who drops out due to drug-related AE(s)
C: number of administered doses of subject(s) who drops out due to drug-unrelated AE(s)
D: number of administered doses of subject(s) who drops out not due to AE(s)

The overall compliance is defined as the actual dose (UB-311 or placebo) of injection compared to the prescribed dose of treatment during the study. It is calculated according to the following formula:

100% x (Actual injection dose/Prescribed injection dose)
$=100\% \times$ (actual injected doses of $(A+B_1+C+D)$) / (prescribed injection doses of $(A+B_1+B_3+C+D)$)

where
B_3: number of missed doses (up to treatment unblinding of main study for placebo or study termination by sponsor) with visit date

1.6 Secondary and Exploratory Endpoints

Secondary endpoints described in the protocol is provided below.

The secondary endpoints are to measure the treatment effects of UB-311 on:
- The change in cognitive and global assessments, including:
  - Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog)
  - Mini-Mental State Exam (MMSE)
  - Clinical Dementia Rating-Sum of Boxes (CDR-SB)
  - Computerized cognitive tests
- The change from baseline of V203-AD study in amyloid deposition by 18F-AV-45 PET imaging;

Due to the incorrect treatment assignment and study early termination, this study is underpowered for analyses with secondary endpoints. Therefore, all secondary endpoints will be considered as exploratory and the definition of Modified Intent-to-Treat Population will be revised as "Have both baseline and at least one post-baseline assessment in any of the primary variables, irrespective of compliance with the study protocol and procedures".

Exploratory analysis described in protocol is provided below.

The changes in anti-Aβ antibody levels, cognitive and global assessments, PET, qEEG, brain volume and cortical thickness and neurodegenerative biomarkers in blood will be compared **between the 3 treatment groups from V203-AD study**. If subjects agree to provide his/her remaining specimens from V203-AD for neurodegenerative biomarkers analysis, the data will be also compared from baseline in V203-AD study between 3 treatment groups.

Due to the incorrect treatment assignment and early termination, it is not appropriate to perform statistical tests on the change in anti-Aβ antibody levels, cognitive and global assessments, PET, qEEG, brain volume and cortical thickness and neurodegenerative biomarkers in blood compared between treatment groups. Hence these analyses will be omitted but descriptive statistics will be presented.

Exploratory endpoints (qEEG and cortical thickness) with substantial amount of missing data/visit due to study early termination or data quality issue cannot provide longitudinal evaluations so they will be omitted from analyses. No data listing or statistical analysis will be included in the SAP except what collected in EDC for these two exploratory endpoints.

1.7 Exploratory Endpoints - Correlation between Titers of anti-Aβ antibody with anti-measles or anti-HBV antibodies and Memory T cell responses for UBITh® 1 and UBITh® 2.

The correlation between titers of anti-Aβ antibody and anti-measles or anti-HBV antibodies as well as memory T cell response for UBITh® 1 and UBITh® 2 described in protocol is given as below.

Section 6.3.1.6 "The correlation between titers of anti-Aβ antibody and anti-measles or anti-HBV antibodies as well as memory T cell response for UBITh® 1 and UBITh® 2"

The titers of anti-measles and anti-HBV antibodies will be compared to the maximum titer of anti-Aβ antibody in subjects to evaluate the possible correlation between the titers of anti-Aβ antibody elicited by UB-311 and anti-measles or anti-HBV antibodies in subjects.

Memory T cell response for UBITh® 1 and UBITh® 2 will be compared with titers of anti-measles or anti-HBV antibodies and anti-Aβ antibody.

All planned exploratory analyses described above will be omitted due to insufficient data causing by early termination.

2 Protocol Version

The first subject was screened on 10-AUG-2018, and the last subject was dismissed on 30-OCT-2019 due to early termination of the study. All applied protocol and CRF versions are listed as below.

No.	Protocol Version	CRF Version	IRB Approval	TFDA Approval
1	1.1, 22JAN2018	2.1, 26JAN2018	TVGH: 05FEB2018 NTUH: 08MAY2018 LK-CGMH: 03APR2018 KS-CGMH: 03APR2018	14MAR2018

3 Statistical Methodology

3.1 Data Handling

Unless specially defined in corresponding sections, the data handling will follow tips below.

3.1.1 Definition of baseline values

The baseline value of each assessment will be the value assessed closest and prior to UB-311/Placebo injection at Visit 1.

3.1.2 Data handling for outliers

No data handling on outliers will be done.

3.1.3 Data handling for missing data

Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog): ADAS-Cog-13 Total Score

- The calculation of ADAS-Cog-13 from ADAS manual 2015 includes ADAS-Cog-11 total items and 2 subscale (Maze and Cancellation Tasks).
- If more than one of 13 items of ADAS-Cog are missing/NA, ADAS-Cog-13 total score will be set to missing.
- The imputed total score of ADAS-Cog-13 when there is only one item is missing due to non-cognitive reasons is presented in:

Missing Question	Imputed Total formula
Word Recall	Observed Total*(1+10/75)
Orientation	Observed total*(1+8/77)
Word Recognition	Observed total*(1+12/73)
Delayed Word Recall	Observed Total*(1+10/75)

Memory T Cell Response Test

Negative control:

- If negative control has a too numerous too count (TNTC) value, also called "Off scale well", it means the data has a quality control issue and the data is set as missing.
- For missing data at Visit 3 and Visit 8(ET), Screening Visit(S1) data will be used for imputation.
- Assume the negative control 0 as 1 in the analysis of fold change from negative control for Antigen - 10 ug/ml, Antigen - 5 ug/ml, Antigen- 2.5 ug/ml.

Other condition (Positive Control, Antigen - 10 ug/ml, Antigen - 5 ug/ml, Antigen- 2.5 ug/ml):

- For the value is "Off scale well" or "Out well value", using the max from each cytokine including all concentrations and positive control across all subjects and all visits for imputation in the analysis of fold change from negative control.

3.1.4 Data handling for retest data

For the Laboratory Assessment, the retest result will be used for analysis instead of the first result, even if the collection date of retest data is after the injection date. For subject 02013E, the retest LB data (item: Potassium (K+)) that the date of retest is after the injection date will be used for analysis instead of the first result and the retest reason is due to hemolysis.

3.1.5 Data handling for protocol deviation

Protocol deviations will be identified through programmatic checks of study data, as well as manual methods including clinical and monitoring reports. Statistician will examine the data by program in at least following aspects to confirm the protocol deviation list. The final protocol deviation list and population definition will be logged using TWDM-F17 "Protocol Violation & Population" form.

- Non-mITT population criteria
- Procedures/visits not done
- Procedures/visits out of time window
- Other protocol non-compliance.

3.1.6 Data handling for withdrawals, dropouts, lost to follow-up

No data handling on withdrawals, dropouts, loss to follow-up will be done.

Visit 8 is an early termination visit since no subject completed all treatment visits due to study early termination. Measurements of visit 8 not in its visit window will not be adjusted.

3.1.7 Data handling for early termination reason

There are 32 early termination subjects due to the study was early terminated by sponsor, therefore the reasons for early termination will be consolidated as below.

Original reason	Recoded reason
by sponsor decided to terminate the long - term extension study with UB-311 <study v203-AD-EXT	Early Termination by Sponsor.
Based on review of V203-AD-EXT study baseline data on disease severity, and the treatment assignment error issue significantly impacting a primary endpoint, Sponsor (United Neuroscience Ltd.) executive team has evaluated the UB-311 clinical development pipeline and decided to terminate the long-term extension study with UB-311 (Study V203-AD-EXT).	
Early Termination by Sponsor.	

The original reason will be presented in Listing and recoded reason will presented in Table.

3.1.8 Data handling for Laboratory category

Neurodegenerative Biomarkers

"Not detectable" and "not tested" values will be set as missing for descriptive analysis.

Virology

Original results with both numerical value and categorical value (Positive/ Negative/ Equivocal), only categorical values will be presented for descriptive analysis.

Others (Biochemistry/ Inflammatory/ Hematology)

Original results with both numerical value and string value "<" or ">" will be transformed to exact numeric value with standard unit for descriptive analysis.

3.1.9 Data handling for Computerized Cognitive Test

1. If completion = 1, excluding the data from all descriptive statistics
2. If the baseline is missing, exclude the subject from descriptive statistics of change from baseline
3. If data missing with completion = 0 and integrity = 1, add footnote in listing and indicate these data are "no correct response".

3.1.10 Data handling for Disease Duration

For subjects (03001E, 03005E and 03007E) without Alzheimer's Disease record in this study, PET scan date of The Second Stage Screening from V203-AD study will be used to impute the missing onset date of Alzheimer's Disease diagnosis and derive their disease durations. Therefore, the onset date of Alzheimer's Disease diagnosis of these three subjects will be missing in Listing but their disease durations will be derived in Listing and Table.

3.2 General Statistical Methodology

Descriptive statistics will be provided for all endpoints.

Continuous variables will be summarized by reporting the number of observations, mean, standard deviation, median, interquartile range (IQR = third quartile (Q3) - first quartile (Q1)), Q1, Q3, minimum and maximum, by group and overall.

Categorical variables will be summarized using frequency tables showing the number and percentage of subjects within a particular category, by group and overall.

Number of subjects at each visit will be based on the data with visit date.

4 Mock-up Tables and Figures

The Mock-up "TABLES and FIGURES" is planned according to ICH E3, in which relevant CSR section is 14. The words shadowed below are to be adjusted or repeated upon real data, or just for notification.

Columns {Label, Treatment Groups, Total, Difference (if necessary)} will be included in the table with the analyzed population specified. In the mock table below, only the Label with one treatment column were presented to show the descriptive statistics to be displayed in the final tabulation. Column 'Difference' denotes pairwise comparison statistics.

For column Treatment Groups:

- **It will be treatment group in V203-AD main study and actual treatment group in V203-AD-EXT extension study for tabulation.**
- **Treatment group in V203-AD main study will be added, respectively, for some section of 14.2 tabulation.**

Note:

(1) Site ID CC:

Site ID	Full Name
01	Taipei Veterans General Hospital (TVGH)
02	National Taiwan University Hospital (NTUH)
03	Linkou Chang Gung Memorial Hospital (LK-CGMH)
04	Kaohsiung Chang Gung Memorial Hospital (KS-CGMH)

(2) Treatment group in V203-AD main study (unblinded on 01-NOV-2018) and actual treatment group in V203-AD-EXT extension study:
M7E1: 7 UB-311 injections in main study and 1 UB-311 injections in extension study
M7E3: 7 UB-311 injections in main study and 3 UB-311 injections in extension study
M5E1: 5 UB-311 injections + 2 Placebo injections in main study and 1 UB-311 injections in extension study
M5E3: 5 UB-311 injections + 2 Placebo injections in main study and 3 UB-311 injections in extension study
M0E1: 7 Placebo injections in main study and 1 UB-311 injections in extension study
M0E3: 7 Placebo injections in main study and 3 UB-311 injections in extension study

(3) Treatment group in V203-AD main study and regardless of the treatment group in extension study:
M7: 7 UB-311 injections in main study
M5: 5 UB-311 injections + 2 Placebo injections in main study
M7+M5: Once receiving UB-311 injection in main study
M0: 7 Placebo injections in main study

(4) Population
- Safety population:
  (1) All subjects exposed to at least one dose of the study drug, regardless of the amount of treatment administered.
- Modified Intent-to-Treat Population (mITT):
  (1) All subjects who receive at least one dose of the study drug
  (2) Have both baseline and at least one post-baseline assessment in any of the primary variables, irrespective of compliance with the study protocol and procedures

(5) For Visit Name (in Tables and Figures) and Visit Code (in Subject Data Listing):In the study, no Visits 5~7 data is collected and V8(ET) means early termination only since there is no Visit 8.

Visit No.	Visit Description	Visit Day	Visit Name	Visit Code
0	Screen (Day -42 to -1)	-42	Visit 0 (Screening)	V0 (S)

Visit No.	Visit Description	Visit Day	Visit Name	Visit Code
1	Day 1	1	Visit 1 (Day 1)	V1 D01
2	Week 5 ± 3 Days	29	Visit 2 (Week 5)	V2 W05
3	Week 13 ± 3 Days	85	Visit 3 (Week 13)	V3 W13
4	Week 25 ± 14 Days	169	Visit 4 (Week 25)	V4 W25
5	Week 49 ± 14 Days	337	Visit 5 (Week 49)	V5 W49
6	Week 73 ± 14 Days	505	Visit 6 (Week 73)	V6 W73
7	Week 97 ± 14 Days	673	Visit 7 (Week 97)	V7 W97
8	Early Termination (ET)	Varied	Visit 8 (ET)	V8 ET

(6) Treatment Tolerability and Treatment Compliance

The overall treatment tolerability of UB-311 is defined as the percentage of number of administered doses divided by number of administered doses plus number of missed doses of subject(s) who drops out due to drug-related AE(s). It is calculated according to the following formula:

$100\% \times (A+B_1+C+D) / (A+B_1+B_2+C+D)$

where

A: number of administered doses of completers

B_1: number of administered doses of subject(s) who drops out due to drug-related AE(s)

B_2: number of missed doses (up to treatment unblinding of main study for placebo or study termination by sponsor) of subject(s) who drops out due to drug-related AE(s)

C: number of administered doses of subject(s) who drops out due to drug-unrelated AE(s)

D: number of administered doses of subject(s) who drops out not due to AE(s)

The overall compliance is defined as the actual dose (UB-311 or placebo) of injection compared to the prescribed dose of treatment during the study. It is calculated according to the following formula:

$100\% \times$ (Actual injection dose/Prescribed injection dose)

$=100\% \times$ (actual injected doses of $(A+B_1+C+D)$) / (prescribed injection doses of $(A+B_1+B_3+C+D)$)

where

B_3: number of missed doses (up to treatment unblinding of main study for placebo or study termination by sponsor) with visit date

(7) Full term for 'Protocol Deviation Code':

Code	Full Term
	<To be added upon real data in final tabulation>

(8) Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog): ADAS-Cog-13 Total Score

- The calculation of ADAS-Cog-13 from ADAS manual 2015 includes ADAS-Cog-11 total items and 2 subscale (Maze and Cancellation Tasks).
- If more than one of 13 items of ADAS-Cog are missing/NA, ADAS-Cog-13 total score will be set to missing.
- The imputed total score of ADAS-Cog-13 when there is only one item is missing due to non-cognitive reasons is presented in:

Missing Question	Imputed Total formula
Word Recall	Observed Total*(1+10/75)
Orientation	Observed total*(1+8/77)
Word Recognition	Observed total*(1+12/73)
Delayed Word Recall	Observed Total*(1+10/75)

(9) MMSE and CDR-SB

No imputation will be performed if there is a missing point in MMSE or CDR-SB and the total score of MMSE or CDR-SB will be treated as missing.

(10) Neurodegenerative Biomarkers

"Not detectable" and "not tested" values will be set as missing for descriptive analysis.

(11) Virology

Original results with both numerical value and categorical value (Positive/ Negative/ Equivocal), only categorical values will be presented for descriptive analysis.

(12) Others Laboratory (Biochemistry/ Inflammatory/ Hematology)
Original results with both numerical value and string value "<" or ">" will be transformed to exact numeric value with standard unit for descriptive analysis.

(13) Memory T Cell Response Test – Missing data estimation
Negative control:

- If negative control has TNTC value (off scale well), it means the data has quality control issue and set as missing.
- For missing data at Visit 3 and Visit 8(ET), Screening Visit(S1) data will be used for imputation in the analysis of fold change.
- Assume the negative control 0 as 1 in the analysis of fold change from negative control for Antigen - 10 ug/ml, Antigen - 5 ug/ml, Antigen- 2.5 ug/ml.

Other condition (Positive Control, Antigen - 10 ug/ml, Antigen - 5 ug/ml, Antigen- 2.5 ug/ml):

- For the value is Off scale well or Out well value (too numerous to count, TNTC), using the max from each cytokine including all concentrations and positive control across all subjects and all visits for imputation.

(14) Memory T Cell Response Test - Fold change values for each test and concentration (Antigen-2.5 ug/ml, Antigen - 5 ug/ml, or Antigen - 10 ug/ml)

- Fold change values at each visit:

$$\text{Fold change value at visit} = \frac{\text{value at visit}}{\text{Negative Control value at visit}}$$

- Fold change values for change from baseline:

$$\text{Fold change value for change from baseline (visit} - \text{baseline)} = \text{Fold change value at visit} - \text{Fold change value at baseline}$$

(15) Structural MRI defined in protocol used for safety endpoints will be named as safety MRI and used for efficacy endpoints will be named as volumetric MRI.

(16) For clinical relevant

CS: abnormal and clinically significant	LLN: lower limit of normal range
NCS: abnormal but not clinically significant	ULN: upper limit of normal range

(17) Abbreviations of statistics

N: number of non-missing values	Median: median of values
Missing: number of missing values	IQR: inter-quartile-range (IQR=Q3-Q1)
Mean: mean of values	Min: minimum of values
SD: standard deviation of values	Max: maximum of values
Q1: 25% quartile of values	CI: confidence interval
Q3: 75% quartile of values	

(18) Full term for Amyloid-related Imaging Abnormalities (ARIA):

Code	Full Term
ARIA-E	Vasogenic Edema and/or Sulcal Effusion
ARIA-H	Hemosiderin Deposits
ADE	Acute Disseminated Encephalomyelitis
ARWMC	Age-Related White Matter Changes
Non-ARIA	Other Significant Non-ARIA Abnormal Finding

14 TABLES AND FIGURES

14.1 DEMOGRAPHIC DATA AND BASELINE CHARACTERISTICS

14.1.1 Screen Failures and Subject Disposition by Study Site

Population: All Screened Subjects / Enrolled Subjects

Characteristics	Study Site
.All Screened Subjects	
N	XXX
~Enrolled Subjects	XXX (XXX.X%)
~Screening Failures	XXX (XXX.X%)
~INC1	XXX (XXX.X%)
~INC2	XXX (XXX.X%)
~INC3	XXX (XXX.X%)
~EXC1	XXX (XXX.X%)
~EXC2	XXX (XXX.X%)
~EXC3	XXX (XXX.X%)
.Enrolled Subjects	
N	XXX
Safety	XXX (XXX.X%)
~mITT	XXX (XXX.X%)
~ <Reason 1>	XXX (XXX.X%)
~ <Reason 2>	XXX (XXX.X%)
...	XXX (XXX.X%)
~Non-mITT	XXX (XXX.X%)
Non-Safety	XXX (XXX.X%)
.Treatment group in V203-AD main study of Enrolled Subjects	
N	XXX
M7	XXX (XXX.X%)
M5	XXX (XXX.X%)
M0	XXX (XXX.X%)
.Actual Treatment group in V203-AD-EXT extension study of Enrolled Subjects	
N	XXX
E1	XXX (XXX.X%)
E3	XXX (XXX.X%)
.Treatment group in V203-AD main study and Actual Treatment group in V203-AD-EXT extension study of Enrolled Subjects	
N	XXX
M7E1	XXX (XXX.X%)
M7E3	XXX (XXX.X%)
M5E1	XXX (XXX.X%)
M5E3	XXX (XXX.X%)
M0E1	XXX (XXX.X%)
M0E3	XXX (XXX.X%)
.Protocol Deviation of Enrolled Subjects	
N	XXX
~ Major	XXX (XXX.X%)
~ <Reason 1>	XXX (XXX.X%)
~ <Reason 2>	XXX (XXX.X%)
...	XXX (XXX.X%)
~ Minor	XXX (XXX.X%)

Characteristics	Study Site
~ <Reason 1>	XXX (XXX.X%)
~ <Reason 2>	XXX (XXX.X%)
...	XXX (XXX.X%)

Enrolled subjects: subjects who are enrolled in the extension study.

14.1.2 Study Visits, Study Termination, Subject Disposition and Protocol Deviation

Population: Safety Population

Characteristics	Treatment Group
. Study Termination	
N	XXX
Study Completed	XXX (XXX.X%)
Not Completed	XXX (XXX.X%)
~ Withdrew consent	XXX (XXX.X%)
~ Protocol issue	XXX (XXX.X%)
…	XXX (XXX.X%)
. Study Duration [days]	
N (Missing)	XXX
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
.Population	
N	XXX
~mITT	XXX (XXX.X%)
~ <Reason 1>	XXX (XXX.X%)
~ <Reason 2>	XXX (XXX.X%)
...	XXX (XXX.X%)
~Non-mITT	XXX (XXX.X%)
.Protocol Deviation (Multi-Selection)	
N	XXX
~ Major	XXX (XXX.X%)
~ <Reason 1>	XXX (XXX.X%)
~ <Reason 2>	XXX (XXX.X%)
...	XXX (XXX.X%)
~ Minor	XXX (XXX.X%)
~ <Reason 1>	XXX (XXX.X%)
~ <Reason 2>	XXX (XXX.X%)
...	XXX (XXX.X%)
. Study Visits Completed (Multi-Selection by Status & mITT)	
N	XXX
Visit 0 (Screening)	XXX (XXX.X%)
~ mITT	XXX (XXX.X%)
Visit 1 (Day 1)	XXX (XXX.X%)
~ mITT	XXX (XXX.X%)
Visit 2 (Week 5)	XXX (XXX.X%)
~ mITT	XXX (XXX.X%)
Visit 3 (Week 13)	XXX (XXX.X%)
~ mITT	XXX (XXX.X%)

Characteristics	Treatment Group
Visit 4 (Week 25)	XXX (XXX.X%)
~ mITT	XXX (XXX.X%)
Visit 5 (Week 49)	XXX (XXX.X%)
~ mITT	XXX (XXX.X%)
Visit 6 (Week 73)	XXX (XXX.X%)
~ mITT	XXX (XXX.X%)
Visit 7 (Week 97)	XXX (XXX.X%)
~ mITT	XXX (XXX.X%)
Visit 8 (ET)	XXX (XXX.X%)
~ mITT	XXX (XXX.X%)

Study Duration [days] = Date of Termination – Visit 0, or alternatively as the last visit date - Visit 0

14.1.3 Demographic Data

Population: Safety Population

Characteristics	Treatment Group
Study Sites	
N (Missing)	XXX (XXX)
Site 01 TVGH	XXX (XXX.X%)
Site 02 NTUH	XXX (XXX.X%)
Site 03 LK-CGMH	XXX (XXX.X%)
Site 04 KS-CGMH	XXX (XXX.X%)
Variable, including Age [Y/O], Body Weight [kg], Body Height [cm], BMI [kg/m^2]	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
Gender	
N (Missing)	XXX (XXX)
Male	XXX (XXX.X%)
Female	XXX (XXX.X%)

Age [Y/O] = int((date of informed consent – year/month/01 of birth)/365.25)
BMI [Kg/m^2]= body weight [kg] / body height [m]^2

14.1.4 Study Disease History

Population: Safety Population

Characteristics	Treatment Group
Disease Duration [years],	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX

Disease Duration [years] =(date of informed consent – onset date of Alzheimer's Disease diagnosis)/365.25, missing day is estimated as 15, missing month is estimated as Jul-01
For missing Alzheimer's Disease onset date, the PET scan date of The Second Stage Screening from V203-AD study will be used

14.1.5 Previous Medical and Surgery /Procedure History and Concurrent Disease

Population: Safety Population

Characteristics	Treatment Group
.Previous Medical History (Multi-Selection)	
. By MedDRA SOC, Preferred Term	
N	XXX
At least one below [Event#:Subj#]	XXX: XXX (XXX.X%)
<MedDRA Body System1>	XXX: XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX: XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX: XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX: XXX (XXX.X%)
<MedDRA Body System2>	XXX: XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX: XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX: XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX: XXX (XXX.X%)
.Current Condition (Multi-Selection)	
. By MedDRA SOC, Preferred Term	
N	XXX
At least one below [Event#:Subj#]	XXX: XXX (XXX.X%)
<MedDRA Body System1>	XXX: XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX: XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX: XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX: XXX (XXX.X%)
<MedDRA Body System2>	XXX: XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX: XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX: XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX: XXX (XXX.X%)

Previous Medical History lists the medical histories with start date < date of Visit 1
Current Condition lists the medical histories that are ongoing or with end date ≥ date of screening visit
Based on the Medical Dictionary for Regulatory Activities (MedDRA version 21.1)

14.1.6 Concomitant and Previous Medications

Population: Safety Population

Characteristics	Treatment Group
.Previous Medications (Multi-Selection)	
N	XXX
At least one below	XXX (XXX.X%)
~ <ATC Level 3 Class 1>	XXX (XXX.X%)
~ <ATC Preferred Term 1>	XXX (XXX.X%)
~ <ATC Preferred Term 2>	XXX (XXX.X%)
…	…
~ <ATC Level 3 Class 2>	XXX (XXX.X%)
~ <ATC Preferred Term 1>	XXX (XXX.X%)
~ <ATC Preferred Term 2>	XXX (XXX.X%)
…	…
.Concomitant Medications(Multi-Selection)	
N	XXX

Characteristics	Treatment Group
At least one below	XXX (XXX.X%)
~ <ATC Level 3 Class 1>	XXX (XXX.X%)
~ <ATC Preferred Term 1>	XXX (XXX.X%)
~ <ATC Preferred Term 2>	XXX (XXX.X%)
…	…
~ <ATC Level 3 Class 2>	XXX (XXX.X%)
~ <ATC Preferred Term 1>	XXX (XXX.X%)
~ <ATC Preferred Term 2>	XXX (XXX.X%)
…	…

Previous Medications lists the medications with start date < date of Visit 1
Concomitant Medication lists the medications that are ongoing or with end date ≥ date of Day 1
Medications are classified using the World Health Organization Drug Dictionary (WHODRUG)
Anatomical Therapeutic Chemical (ATC) Level 3 classes and Preferred Terms
(WHODRUG version WHODrug Global B3-format September 1, 2019)

Note: as medication is recorded from 3 months prior to screening visit to end of study, above definition is equivalent with the definition in section 9.3.1.2 in protocol as below.

- ***Previous medications are those that the subject took within 3 months period prior to the Screening visit and prior to the first administration of UB-311 at Week 1 (V1).***
- ***Concomitant medications are those that the subject continued or started on or after the first injection of the study drug up to the end of the study.***

14.1.7 Study Drug Administration, Overall Treatment Tolerability and Compliance

Population: Safety Population

Characteristics	Treatment Group
Gap Period [weeks],	
Total UB-311 + Placebo Dose [injections],	
Total UB-311 Dose [injections],	
Total UB-311 Dose [µg]	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
Overall Treatment Tolerability [%]	XXX.X
Treatment Compliance [%]	XXX.X
Injection Status \\	
Visit 1 (Day 1)	
Visit 2 (Week 5)	
Visit 3 (Week 13)	
Visit 5 (Week 49)	
Visit 7 (Week 97)	
N (Missing)	XXX (XXX)
UB-311 Injection Completed	XXX (XXX.X%)
UB-311 Injection Not Completed	XXX (XXX.X%)
Placebo Injection Completed	XXX (XXX.X%)
Placebo Injection Not Completed	XXX (XXX.X%)
Not Done	XXX (XXX.X%)
UB-311 Dose [µg] for UB-311/Placebo injected subjects \\	
Visit 1 (Day 1)	
Visit 2 (Week 5)	

Characteristics	Treatment Group
Visit 3 (Week 13)	
Visit 5 (Week 49)	
Visit 7 (Week 97)	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX

Gap Period (weeks) = (First Injection Date in V203-AD-EXT study - The Last Injection Date in V203-AD study)/7
UB-311 is 300 µg per 0.5 mL per vial.
Refer to Note of title page for formula of Overall Treatment Tolerability [%] and Treatment Compliance [%]
For group 'M7E1', 'M5E1' and 'M0E1', dosing at V2 and V3 are placebo.
The missing values are due to the IP issue at Site 2 except for the value of M5E1 and M7E1 group at Visits 2 and 3.

14.2 EFFICACY DATA

14.2.1 Immunogenicity

14.2.1.1 Anti-$A\beta_{1-28}$ Antibody [Log 10] - by Visit

14.2.1.2 Anti-$A\beta_{1-42}$ Monomer Antibody [Log 10] - by Visit

14.2.1.3 Anti-$A\beta_{1-42}$ Oligomer Antibody [Log 10] - by Visit

14.2.1.4 Anti-$A\beta_{1-28}$ Antibody [raw scale] - by Visit

14.2.1.5 Anti-$A\beta_{1-42}$ Monomer Antibody [raw scale] - by Visit

14.2.1.6 Anti-$A\beta_{1-42}$ Oligomer Antibody [raw scale] - by Visit

< For 14.2.1.4-14.2.1.6, Log10_Mean will be added, footnote: Log10_Mean = log10 (Mean) >

14.2.2 Immunogenicity – By Main Study Treatment Group

14.2.2.1 Anti-$A\beta_{1-28}$ Antibody [Log 10] - by Visit

14.2.2.2 Anti-$A\beta_{1-42}$ Monomer Antibody [Log 10] - by Visit

14.2.2.3 Anti-$A\beta_{1-42}$ Oligomer Antibody [Log 10] - by Visit

14.2.2.4 Anti-$A\beta_{1-28}$ Antibody [raw scale] - by Visit

14.2.2.5 Anti-$A\beta_{1-42}$ Monomer Antibody [raw scale] - by Visit

14.2.2.6 Anti-$A\beta_{1-42}$ Oligomer Antibody [raw scale] - by Visit

< For 14.2.2.4-14.2.2.6, Log10_Mean will be added, footnote: Log10_Mean = log10 (Mean) >

<Layout 1: For Continuous Efficacy Assessment>

Population: Modified Intent-to-Treat Population

Characteristics	Treatment Group
Visit 1 (Day 1), Baseline	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
.Visit: Visit 2 (Week 5), Visit 3 (Week 13), Visit 5 (Week 49), Visit 7 (Week 97), Visit 8 (ET)	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
Visit - Baseline	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX

14.2.3 Rating Scales

14.2.3.1 Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog): ADAS-Cog-13 Total Score

*<**Use Layout 1**; except*
Visits will be Visit 5, Visit 8. Refer to Note in title page for detail instruction>

14.2.3.2 Clinical Dementia Rating (CDR) Sum of Boxes Score

*<**Use Layout 1**; except*
Visits will be Visit 5, Visit 8. >

14.2.3.3 Mini-Mental State Examination (MMSE) Score

*<**Use Layout 1**; except*
Visits will be Visit 5, Visit 8. >

14.2.4 Rating Scales – By Main Study Treatment Group

14.2.4.1 Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog): ADAS-Cog-13 Total Score

14.2.4.2 Clinical Dementia Rating (CDR) Sum of Boxes Score

14.2.4.3 Mini-Mental State Examination (MMSE) Score

14.2.5 Computerized Cognitive Test

14.2.5.1 Computerized Cognitive Test - Detection Test (DET) on Speed of Performance [log10 msec]

14.2.5.2 Cognitive Test - Identification Test (IDN) on Speed of Performance [log10 msec]

14.2.5.3 Computerized Cognitive Test - International Shopping List Test (ISL) on Correct Responses [count]

14.2.5.4 Computerized Cognitive Test - International Shopping List Test – Delayed Recall (ISRL) on Correct Responses [count]

14.2.5.5 Computerized Cognitive Test - Modified Groton Maze Learning Test (GML) on Total Errors [count]

14.2.5.6 Computerized Cognitive Test - One Back Test (ONB) on Speed of Performance [log10 msec]

*<**Use Layout 1**; except*
1. Visits will be Visit 4, Visit 5, Visit6, Visit 8.
2. Practice data will be excluded>

14.2.6 ^{18}F-AV-45 PET - Mean Standard Uptake Value Ratio (SUVR)

14.2.6.1 ^{18}F-AV-45 PET - Mean SUVR

Population: Modified Intent-to-Treat Population

Characteristics	Treatment Group
.By Brain Region	
Baseline from V203-AD study	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX

Characteristics	Treatment Group
.By Brain Region	
Min~Max	XXX~XXX
Visit 7 (Week 97), Visit 8 (ET)	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
Change form baseline	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX

Mean SUVR is calculated using Whole Cerebellum as Reference Region

Brain Region
COMPOSITE_TARGET_WEIGHTED
FRONTAL_LOBE_L
FRONTAL_LOBE_R
TEMPORAL_LOBE_L
TEMPORAL_LOBE_R
PARIETAL_LOBE_PRECUNEUS_L
PARIETAL_LOBE_PRECUNEUS_R
OCCIPITAL_LOBE_L
OCCIPITAL_LOBE_R
CEREBELLAR_GRAY_MATTER
SUBCORTICAL_WHITE_MATTER
PONS

14.2.7 ^{18}F-AV-45 PET - Mean Standard Uptake Value Ratio (SUVR) – By Main Study Treatment Group

14.2.7.1 ^{18}F-AV-45 PET - Mean SUVR

14.2.8 Volumetric Magnetic Resonance Imaging (vMRI)

14.2.8.1 Brain Volume

*<**Use Layout 1**; except*
1. Baseline will be Visit 0 (Screening), Visit will be Visit 3 and Visit 7
2. By Brain Region analyses will be presented>

Brain Region
LEFT_HIPPOCAMPUS
RIGHT_HIPPOCAMPUS
TOTAL_HIPPOCAMPUS
LEFT_LATERAL_VENTRICLE
RIGHT_LATERAL_VENTRICLE
THIRD_VENTRICLE
FOURTH_VENTRICLE

TOTAL_VENTRICLE
WHOLE_BRAIN

14.2.9 Volumetric Magnetic Resonance Imaging (vMRI) – By Main Study Treatment Group

14.2.9.1 Brain Volume

14.2.10 Neurodegenerative Biomarkers

14.2.10.1 Neurodegenerative Biomarker - $A\beta_{1-40}$ Peptide [pg/mL]

14.2.10.2 Neurodegenerative Biomarker - $A\beta_{1-42}$ Peptide [pg/mL]

14.2.10.3 Neurodegenerative Biomarker - Total tau [pg/mL]

14.2.10.4 Neurodegenerative Biomarker - Neurofilament light chain [pg/mL]

14.2.10.5 Neurodegenerative Biomarker - Phosphorylated neurofilament heavy chain [pg/mL]

14.2.10.6 Neurodegenerative Biomarker - Glial fibrillary acidic protein [pg/mL]

14.2.10.7 Neurodegenerative Biomarker - Ubiquitin C-terminal hydrolase L1 [pg/mL]

*<**Use Layout 1**; except*
Visits will be Visit 5, Visit 7, Visit 8.
footnote: "Not Detectable" and "Not Tested" values will be set as missing.>

14.2.11 Neurodegenerative Biomarkers – By Main Study Treatment Group

14.2.11.1 Neurodegenerative Biomarker - $A\beta_{1-40}$ Peptide [pg/mL]

14.2.11.2 Neurodegenerative Biomarker - $A\beta_{1-42}$ Peptide [pg/mL]

14.2.11.3 Neurodegenerative Biomarker - Total tau [pg/mL]

14.2.11.4 Neurodegenerative Biomarker - Neurofilament light chain [pg/mL]

14.2.11.5 Neurodegenerative Biomarker - Glial fibrillary acidic protein [pg/mL]

14.2.12 Anti-Measles Antibody (Measles IgG), Anti-HBV Surface Antibody (HBsAb)

14.2.12.1 Anti-Measles Antibody

14.2.12.2 Anti-HBV Surface Antibody

Population: Modified Intent-to-Treat Population

Characteristics	Treatment Group
Visit 0 (Screening), Baseline	
N (Missing)	XXX (XXX)
Positive	XXX (XXX)
Equivocal	XXX (XXX)
Negative	XXX (XXX)
Visit 3 (Week 13), Visit 8 (ET)	
N (Missing)	XXX (XXX)
Positive	XXX (XXX)
Equivocal	XXX (XXX)

Characteristics	Treatment Group
Negative	XXX (XXX)
. Baseline to Visit	
N (Missing)	XXX (XXX)
Positive to Negative/ Equivocal	XXX (XXX)
Unchanged	XXX (XXX)
Negative/ Equivocal to Positive	XXX (XXX)

14.2.13 Memory T Cell Response Test For UbithR 1

14.2.13.1 Memory T Cell Responses (observed values) –Interferon gamma [Spot number]

14.2.13.2 Memory T Cell Responses (observed values) –Interleukin 2 [Spot number]

14.2.13.3 Memory T Cell Responses (observed values) –Tumor necrosis factor-alpha [Spot number]

<Observed values will be used>
*<**Use Layout 1**; except*
1. The tabulation will be separated by 5 levels {Negative Control, Positive Control, Antigen- 2.5 ug/ml , Antigen - 5 ug/ml, Antigen - 10 ug/ml}
2. Baseline will be Visit 0 (Screening),
3. Visits will be Visit 3 (Week 13), Visit 8 (ET).
***footnote**:*
1. Normalized result of average will be used
2. Refer to Note of title pages for data handling rule >

14.2.13.4 Memory T Cell Responses (fold change values) – Interferon gamma [Spot number]

14.2.13.5 Memory T Cell Responses (fold change values) – Interleukin 2 [Spot number]

14.2.13.6 Memory T Cell Responses (fold change values) – Tumor necrosis factor-alpha [Spot number]

<1. Fold change values from Negative Control will be used
2. Assume Negative Control 0 as 1>
*<**Use Layout 1**; except*
1. The tabulation will be separated by 3 levels { Antigen- 2.5 ug/ml , Antigen - 5 ug/ml, Antigen - 10 ug/ml }
2. Baseline will be Visit 0 (Screening),
3. Visits will be Visit 3 (Week 13), Visit 8 (ET).
***footnote**:*
1. Fold change value= Visit value / Negative Control value
2..Refer to Note of title pages for fold change values at each visit and fold change values for change from baseline>

14.2.14 Memory T Cell Response Test For UbithR 1 – By Main Study Treatment Group

14.2.14.1 Memory T Cell Responses (observed values) –Interferon gamma [Spot number]

14.2.14.2 Memory T Cell Responses (observed values) –Interleukin 2 [Spot number]

14.2.14.3 Memory T Cell Responses (observed values) –Tumor necrosis factor-alpha [Spot number]

14.2.14.4 Memory T Cell Responses (fold change values) –Interferon gamma [Spot number]

14.2.14.5 Memory T Cell Responses (fold change values) –Interleukin 2 [Spot number]

14.2.14.6 Memory T Cell Responses (fold change values) –Tumor necrosis factor-alpha [Spot number]

14.3 SAFETY DATA

14.3.1 Treatment Emergent Adverse Events – Subject Based Analyses

14.3.1.1 Treatment Emergent AEs – Subjects with AEs – by Intensity/Grade

14.3.1.2 Treatment Emergent AEs – Subjects with AEs At Injection Site – by Intensity/Grade

<Event # and subject # of Brain Microhemorrhages will be presented in this table if any.>

Population: Safety Population

Characteristics	Treatment
-All sites, Site 1, Site 2, Site 3, Site 4	
. By MedDRA SOC, Preferred Term, and Severity Grade	
N	XXX
At least one below [Event#:Subj#]	XXX : XXX (XXX.X%)
~ <MedDRA Body System1>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX : XXX (XXX.X%)
~ Grade 1, Grade 2, Grade 3, Grade 4, Grade 5	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX : XXX (XXX.X%)
~ Grade 1, Grade 2, Grade 3, Grade 4, Grade 5	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX : XXX (XXX.X%)
~ Grade 1, Grade 2, Grade 3, Grade 4, Grade 5	XXX : XXX (XXX.X%)
~ <MedDRA Body System2>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX : XXX (XXX.X%)
~ Grade 1, Grade 2, Grade 3, Grade 4, Grade 5	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX : XXX (XXX.X%)
~ Grade 1, Grade 2, Grade 3, Grade 4, Grade 5	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX : XXX (XXX.X%)
~ Grade 1, Grade 2, Grade 3, Grade 4, Grade 5	XXX : XXX (XXX.X%)

For each MedDRA SOC or Preferred Term, Subject with multiple events are counted as one incidence. Based on the Medical Dictionary for Regulatory Activities (MedDRA version 21.1)

14.3.1.3 Treatment Emergent AEs – Subjects with AEs – by Causality

14.3.1.4 Treatment Emergent AEs – Subjects with AEs At Injection Site – by Causality

<Event # and subject # of Brain Microhemorrhages will be presented in this table if any.>

Population: Safety Population

Characteristics	Treatment
-All sites, Site 1, Site 2, Site 3, Site 4	
. By MedDRA SOC, Preferred Term, and Causality	
N	XXX
At least one below [Event#:Subj#]	XXX : XXX (XXX.X%)
~ <MedDRA Body System1>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)

Characteristics	Treatment
-All sites, Site 1, Site 2, Site 3, Site 4	
~ <MedDRA Body System2>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)

For each MedDRA SOC or Preferred Term, Subject with multiple events are counted as one incidence.
Based on the Medical Dictionary for Regulatory Activities (MedDRA version 21.1)

14.3.1.5 Treatment Emergent AEs – Subjects with Drug Related AEs

14.3.1.6 Treatment Emergent AEs – Subjects with Drug Related AEs At Injection Site

<Event # and subject # of Brain Microhemorrhages will be presented in this table if any.>

Population: Safety Population

Characteristics	Treatment
-All sites, Site 1, Site 2, Site 3, Site 4	
. By MedDRA SOC, Preferred Term	
N	XXX
At least one below [Event#:Subj#]	XXX : XXX (XXX.X%)
~ <MedDRA Body System1>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX : XXX (XXX.X%)
~ <MedDRA Body System2>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX : XXX (XXX.X%)

For each MedDRA SOC or Preferred Term, Subject with multiple events are counted as one incidence.
Based on the Medical Dictionary for Regulatory Activities (MedDRA version 21.1)
Drug Related is defined as Definitely Related, Probable Related, or Possibly Related

14.3.1.7 Treatment Emergent AEs – Subjects with Grade ≥3 AEs

14.3.1.8 Treatment Emergent AEs – Subjects with Grade ≥3 AEs At Injection Site

<Event # and subject # of Brain Microhemorrhages will be presented in this table if any.>

Population: Safety Population

Characteristics	Treatment
-All sites, Site 1, Site 2, Site 3, Site 4	
. By Severity Grade, MedDRA SOC and Preferred Term	
N	XXX
At least one below [Event#:Subj#]	XXX : XXX (XXX.X%)
~ Grade ≥3, Grade 4, Grade 5	XXX : XXX (XXX.X%)
~ <MedDRA Body System1>	XXX : XXX (XXX.X%)

Characteristics	Treatment
-All sites, Site 1, Site 2, Site 3, Site 4	
~ <MedDRA Preferred Term 1>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ <MedDRA Body System2>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)

Based on the Medical Dictionary for Regulatory Activities (MedDRA version 21.1)

14.3.1.9 Treatment Emergent AEs – Action Taken with Study Medication

Population: Safety Population

Characteristics	Treatment
-All sites, Site 1, Site 2, Site 3, Site 4 . By Injection Site (At Injection Site + Not At Injection Site, At Injection Site, Not At Injection Site), Action Taken, MedDRA SOC and Preferred Term	
N	XXX
At least one below [Event#:Subj#]	XXX : XXX (XXX.X%)
~ Drug interrupted / withdrawn, Drug interrupted, Drug withdrawn	XXX : XXX (XXX.X%)
~ <MedDRA Body System1>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX : XXX (XXX.X%)
~ <MedDRA Body System2>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX : XXX (XXX.X%)

Based on the Medical Dictionary for Regulatory Activities (MedDRA version 21.1)

14.3.1.10 Treatment Emergent AEs – Subjects with SAEs

14.3.1.11 Treatment Emergent AEs – Subjects with SUSARs

SUSAR: Suspected Unexpected Serious Adverse Reaction (Unexpected Treatment Related SAE)

Population: Safety Population

Characteristics	Treatment
-All sites, Site 1, Site 2, Site 3, Site 4 for 14.3.1.10 -All sites for 14.3.1.11 By SAE Criteria, MedDRA SOC and Preferred Term, Causality, and Severity Grade	
N	XXX
At least one below [Event#:Subj#]	XXX : XXX (XXX.X%)
<SAE Criterion: Either SAE Criterion, Requires or Prolongs Hospitalization, death, … >	XXX : XXX (XXX.X%)
<MedDRA Body System1>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ Grade 1, Grade 2, Grade 3, Grade 4, Grade 5	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ Grade 1, Grade 2, Grade 3, Grade 4, Grade 5	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ Grade 1, Grade 2, Grade 3, Grade 4, Grade 5	XXX : XXX (XXX.X%)
<MedDRA Body System2>	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ Grade 1, Grade 2, Grade 3, Grade 4, Grade 5	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ Grade 1, Grade 2, Grade 3, Grade 4, Grade 5	XXX : XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX : XXX (XXX.X%)
~ Definitely Related, Probably Related, Possibly Related, Unlikely, Unrelated	XXX : XXX (XXX.X%)
~ Grade 1, Grade 2, Grade 3, Grade 4, Grade 5	XXX : XXX (XXX.X%)

Based on the Medical Dictionary for Regulatory Activities (MedDRA version 21.1)

14.3.2 Neurological Examinations and Local Tolerability at Injection Site

14.3.2.1 Neurological Examinations

Population: Safety Population

Characteristics	Treatment Group
Neurological Examination \\	
Visit 1 (Day 1)	
Visit 2 (Week 5)	
Visit 3 (Week 13)	
Visit 5 (Week 49)	
Visit 7 (Week 97)	
N (Missing)	XXX (XXX)
Normal	XXX (XX.X%)
NCS	XXX (XX.X%)
CS (Medical History)	XXX (XX.X%)
CS (Adverse Event)	XXX (XX.X%)

14.3.2.2 Local Tolerability at Injection Site

Population: Safety Population

Characteristics	Treatment Group
Local Tolerability at Injection Site \\	
Visit 1 (Day 1)	
Visit 2 (Week 5)	
Visit 3 (Week 13)	
Visit 5 (Week 49)	
Visit 7 (Week 97)	
N (Missing)	XXX (XXX)
Tolerable	XXX (XX.X%)
Not tolerable	XXX (XX.X%)
Not done	XXX (XX.X%)

14.3.3 Laboratory Assessment – Hematology

14.3.3.1 Hematology - <Hematology Item 1 and Unit>

14.3.3.2 Hematology - <Hematology Item 2 and Unit>

14.3.3.3 Hematology - <Hematology Item 3 and Unit>

14.3.3.4 …

14.3.4 Laboratory Assessment – Biochemistry

14.3.4.1 Biochemistry - <Biochemistry Item 1 and Unit>

14.3.4.2 Biochemistry - <Biochemistry Item 2 and Unit>

14.3.4.3 Biochemistry - <Biochemistry Item 3 and Unit>

14.3.4.4 …

14.3.5 Laboratory Assessment – Inflammatory

14.3.5.1 Inflammatory - < Inflammatory Item 1 and Unit>

14.3.5.2 Inflammatory - < Inflammatory Item 2 and Unit>

14.3.5.3 Inflammatory - < Inflammatory Item 3 and Unit>

14.3.5.4 …

<For continuous Laboratory Assessment – Hematology, Biochemistry and Inflammatory>

Population: Safety Population

Characteristics	Treatment Group
Visit 0 (Screening)	
Visit 1 (Day 1), Baseline	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
N (Missing)	XXX (XXX)
Normal	XXX (XX.X%)
NCS	XXX (XX.X%)
CS (Medical History)	XXX (XX.X%)
CS (Adverse Event)	XXX (XX.X%)
Visit 2 (Week 5)	
Visit 3 (Week 13)	
Visit 5 (Week 49)	
Visit 7 (Week 97)	
Visit 8 (ET)	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
N (Missing)	XXX (XXX)
Normal	XXX (XX.X%)
NCS	XXX (XX.X%)
CS (Medical History)	XXX (XX.X%)
CS (Adverse Event)	XXX (XX.X%)

Characteristics	Treatment Group
Visit – Baseline, for all above visits except Visit 0 (Screening), Visit 1 (Day 1) and Baseline	
N (Missing)	XXX (XXX)
Relieved	XXX (XX.X%)
Unchanged	XXX (XX.X%)
Worsened	XXX (XX.X%)

Improved: CS (Medical History or Adverse Event) at baseline to Normal / NCS at visit.
Unchanged: including Normal at baseline to NCS at visit, NCS at baseline to Normal at visit.
Worsened: Normal / NCS / CS (Medical History) at baseline to CS (Adverse Event) at visit

14.3.6 Physical Examination

14.3.6.1 Physical Examination – All Abnormalities

Population: Safety Population

Characteristics	Treatment Group
Visit 0 (Screening), Visit 1 (Day 1), Visit 2 (Week 5), Visit 3 (Week 13), Visit 4 (Week 25), Visit 5 (Week 49), Visit 6 (Week 73), Visit 7 (Week 97), Visit 8 (ET)	
N (Missing)	XXX (XXX)
At least one below	XXX (XXX.X%)
~ <Body System 1>	XXX (XXX.X%)
~CS (Medical History)	XXX (XXX.X%)
~CS (Adverse Event)	XXX (XXX.X%)
~ <Body System 2>	XXX (XXX.X%)
~CS (Medical History)	XXX (XXX.X%)
~CS (Adverse Event)	XXX (XXX.X%)
~ <Body System 3>	XXX (XXX.X%)
~CS (Medical History)	XXX (XXX.X%)
~CS (Adverse Event)	XXX (XXX.X%)
…	…

14.3.7 Vital Signs and Body Weight

14.3.7.1 Vital Signs - Temperature [degree C]

14.3.7.2 Vital Signs - Respiratory Rate [breaths/min]

14.3.7.3 Vital Signs - Systolic Blood Pressure [mmHg]

14.3.7.4 Vital Signs - Diastolic Blood Pressure [mmHg]

14.3.7.5 Vital Signs - Heart Rate [beats/min]

14.3.7.6 Vital Signs - Weight [Kg]

Population: Safety Population

Characteristics	Treatment Group
Visit 0 (Screening)	
Visit 1 Day 1 (Pre-Dosing)	
Baseline	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
. Visit	
Visit 1 (Day 1, Post-Dosing)	
Visit 2 (Week 5, Pre-Dosing)	
Visit 2 (Week 5, Post-Dosing)	
Visit 3 (Week 13, Pre-Dosing)	
Visit 3 (Week 13, Post-Dosing)	
Visit 4 (Week 25)	
Visit 5 (Week 49, Pre-Dosing)	
Visit 5 (Week 49, Post-Dosing)	
Visit 6 (Week 73)	
Visit 7 (Week 97, Pre-Dosing)	
Visit 7 (Week 97, Post-Dosing)	
Visit 8 (ET)	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
Visit - Baseline, for all above visits except Visit 0 (Screening), Visit 1 Day 1 (Pre-Dosing) and Baseline	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX

Baseline is Visit 1 (Pre-Dosing) or alternatively as Visit 0 if Visit 1 (Pre-Dosing) data is not available.

14.3.8 Electrocardiography (ECG, EKG)

14.3.8.1 Electrocardiogram - Overall Interpretation

Population: Safety Population

Characteristics	Treatment Group
Visit 0 (Screening), Baseline	
N (Missing)	XXX (XXX)
Normal	XXX (XX.X%)
NCS	XXX (XX.X%)
CS (Medical History)	XXX (XX.X%)
CS (Adverse Event)	XXX (XX.X%)
Visit 5 (Week 49)	
Visit 8 (ET)	
N (Missing)	XXX (XXX)
Normal	XXX (XX.X%)
NCS	XXX (XX.X%)
CS (Medical History)	XXX (XX.X%)
CS (Adverse Event)	XXX (XX.X%)
Visit - Baseline	
N (Missing)	XXX (XXX)
Improved Unchanged	XXX (XX.X%)
Worsened	XXX (XX.X%)
	XXX (XX.X%)

Improved: CS (Medical History or Adverse Event) at baseline to Normal / NCS at visit.
Unchanged: including Normal at baseline to NCS at visit, NCS at baseline to Normal at visit.
Worsened: Normal / NCS / CS (Medical History) at baseline to CS (Adverse Event) at visit

14.3.9 Safety Magnetic Resonance Imaging (sMRI)

14.3.9.1 sMRI - Overall Interpretation

<Use the layout of ECG, where visit are Visit 3 (Week 13), Visit 7 (Week 97)**>**

14.3.9.2 sMRI - Amyloid-related Imaging Abnormalities (ARIA) Types

Population: Safety Population

Characteristics	Treatment Group
Visit 0 (Screening), Baseline	
Visit 3 (Week 13)	
Visit 7 (Week 97)	
Visit 8 (ET)	
N (Missing)	XXX (XXX)
At least one below	XXX (XXX.X%)
~ARIA-E (Vasogenic Edema and/or Sulcal Effusion)	XXX (XXX.X%)
~ARIA-E Parenchyma	XXX (XXX.X%)
~New	XXX (XXX.X%)
~Unchanged	XXX (XXX.X%)
~Improved	XXX (XXX.X%)
~Worsened	XXX (XXX.X%)
~ARIA-E Leptomeninges	XXX (XXX.X%)
~New	XXX (XXX.X%)
~Unchanged	XXX (XXX.X%)
~Improved	XXX (XXX.X%)
~Worsened	XXX (XXX.X%)
~ARIA-H (Hemosiderin Deposits)	XXX (XXX.X%)
~ARIA-H Macrohemorrhages	XXX (XXX.X%)
~New	XXX (XXX.X%)
~Unchanged	XXX (XXX.X%)
~Improved	XXX (XXX.X%)
~Worsened	XXX (XXX.X%)
~ARIA-H Microhemorrhages	XXX (XXX.X%)
~New	XXX (XXX.X%)
~Unchanged	XXX (XXX.X%)
~Improved	XXX (XXX.X%)
~Worsened	XXX (XXX.X%)
~ARIA-H Superficial Siderosis	XXX (XXX.X%)
~New	XXX (XXX.X%)
~Unchanged	XXX (XXX.X%)
~Improved	XXX (XXX.X%)
~Worsened	XXX (XXX.X%)
~ADE (Acute Disseminated Encephalomyelitis Evidence)	XXX (XXX.X%)
~ARWMC (Age-Related White Matter Changes Evidence)	XXX (XXX.X%)
~Non-ARIA (Other Significant Non-ARIA Abnormal Finding)	XXX (XXX.X%)
New Findings	
N (Missing)	XXX (XXX)
At least one below	XXX (XXX.X%)
~ARIA-E (Vasogenic Edema and/or Sulcal Effusion)	XXX (XXX.X%)

Characteristics	Treatment Group
~ARIA-E Parenchyma	XXX (XXX.X%)
~ARIA-E Leptomeninges	XXX (XXX.X%)
~ARIA-H (Hemosiderin Deposits)	XXX (XXX.X%)
~ARIA-H Macrohemorrhages	XXX (XXX.X%)
~ARIA-H Microhemorrhages	XXX (XXX.X%)
~ARIA-H Superficial Siderosis	XXX (XXX.X%)
~ADE (Acute Disseminated Encephalomyelitis Evidence)	XXX (XXX.X%)
~ARWMC (Age-Related White Matter Changes Evidence)	XXX (XXX.X%)
~Non-ARIA (Other Significant Non-ARIA Abnormal Finding)	XXX (XXX.X%)

New Findings: None at Visit 0 (Screening) to Observed at visit
Macrohemorrhages was classified under non-ARIA abnormal finding in V203-AD study and classified under ARIA-H in V203-AD-EXT study. There was no finding of macrohemorrhages in V203-AD-study

SAP Amendment History:

Version	Date	Description of Change
1.0	16-DEC-2019	N/A
2.0	10-FEB-2020	• Add Log10_Mean variable and footnote in Table 14.2.1.4-14.2.1.6 and Table 14.2.2.4-14.2.2.6. Per sponsor's request e-mail on 20Dec2019, Log10_Mean variable is added in all raw scale titer corresponding tables. Add log10(mean) in raw scale tables.msg **14.2.1.4 Anti-Aβ1-28 Antibody [raw scale] - by Visit** **14.2.1.5 Anti-Aβ1-42 Monomer Antibody [raw scale] - by Visit** **14.2.1.6 Anti-Aβ1-42 Oligomer Antibody [raw scale] - by Visit** **14.2.2.4 Anti-Aβ1-28 Antibody [raw scale] - by Visit** **14.2.2.5 Anti-Aβ1-42 Monomer Antibody [raw scale] - by Visit** **14.2.2.6 Anti-Aβ1-42 Oligomer Antibody [raw scale] - by Visit** *footnote: Log10_Mean = log10 (Mean)* • Revise the wording of Table 14.1.7, 14.3.8.1 and 14.3.9.1. **14.1.7 Study Drug Administration, Overall Treatment Tolerability and Compliance** **14.3.8.1 Electrocardiogram - Overall Interpretation** **14.3.9.1 sMRI - Overall Interpretation** • Reorder Listing 16.2.11.5-16.2.11.8. **16.2.11.5 Safety Magnetic Resonance Imaging (sMRI) - Overall interpretation** **16.2.11.6 Safety Magnetic Resonance Imaging (sMRI)** **16.2.11.7 Not Done Reason and Comments of Other Safety Measurements** **16.2.11.8 Safety Oversight follow-up via telephone call**

Reference:

1. Administration and Scoring Manual Alzheimer's Disease Assessment Scale – Cognitive (ADAS-cog)
ADAS Manual 10_10_13 Major Edit