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STATISTICAL ANALYSIS PLAN

TANGO

Prepared and drafted by the biostatistics department of ICTA PM

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Protocol No.	:	CER-001-CLIN-009
Title	:	Phase III, multi-center, randomized, 48 weeks, double-blind, parallel-group, placebo-controlled study to evaluate efficacy and safety of CER-001 on vessel wall area in patients with genetically defined familial primary hypoalphalipoproteinemia and receiving background optimized lipid therapy
Phase	:	III
Study treatment	:	CER-001
Date	:	25OCT2018
Version	:	2.0

This study is conducted in adherence with the Good Clinical Practices (GCPs)

History of versions:

Version No.	Date of version	Comments / Main modifications
1.0	26JUL2018	First approved version
2.0	25OCT2018	Modifications following DR meeting

Contents:

List of abbreviations and specialized terms:

AE	Adverse Event
ANCOVA	ANalysis of COVAriance
ATC	Anatomic Therapeutic Class
BMI	Body Mass Index
CI	Confidence Interval
CRF	Case Report Form
CRO	Contract Research Organization
DSMB	Data and Safety Monitoring Board
FPFV	First Patient First Visit
HLGT	Highest Level Group Terms
HLT	Highest Level Terms
ICH	International Conference on Harmonisation
LOCF	Last Observation Carried Forward
LPFV	Last Patient First Visit
LPLV	Last Patient Last Visit
MedDRA	Medical Dictionary for Regulatory Activities
MI	Multiple Imputation
mITT	modified Intention-To-Treat
MRI	Magnetic Resonance Imaging
MVWA	Mean Vessel Wall Area
MVWV	Mean Vessel Wall Volume
PP	Per Protocol
PT	Preferred Term
Q1	1st quartile
Q3	3rd quartile
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOC	System Organ Class
SOP	Standard Operating Procedure
TBR	Target to Background Ratio
TFL	Tables Figures Listings
WHO-DD	World Health Organisation Drug Dictionary

Introduction

The Statistical Analysis Plan (SAP) was developed from the following documents:

- Protocol (version 3.0 dated 13DEC2016)
- Case Report Form (CRF, version 18.2 on 30MAY2017)
- The International Conference on Harmonization (ICH) topics E3 (July 1996) [1] and E9 (September 1998) [2].

Analyses described throughout this document were planned before database lock. All analysis decisions were made prior to unblinding as well.

This SAP supersedes the protocol. Changes to the protocol (if any) will be reported in section *10 Modifications with respect to the protocol*. Finally, additional analyses not planned in this document should be clearly mentioned in the appropriate section of the clinical study report.

1. Study objectives

1.1 Primary objectives

The primary objectives of the study are:

- To evaluate the effect of 24 week treatment with CER-001 on carotid Mean Vessel Wall Area (MVWA) as compared to placebo using 3T Magnetic Resonance Imaging (3T-MRI);
- To evaluate the safety and tolerability of CER-001 administered for 24 weeks.

1.2 Secondary objectives

The secondary objectives of the study are:

- To evaluate the effect of 8 week and 48 week treatment with CER-001 on carotid artery MVWA as compared to placebo using 3T-MRI;
- To evaluate the effect of 8 week, 24 week and 48 week treatment with CER-001 on femoral artery MVWA as compared to placebo using 3T-MRI;
- To evaluate the effect of 24 week treatment with CER-001 in the target (plaque) to background (blood) ratio (TBR) from an index vessel (either right carotid or left carotid) based on the standardized ^{18}FDG uptake measured with PET/CT.
- To evaluate safety and tolerability of 48 week treatment with CER-001.

1.3 Exploratory objectives

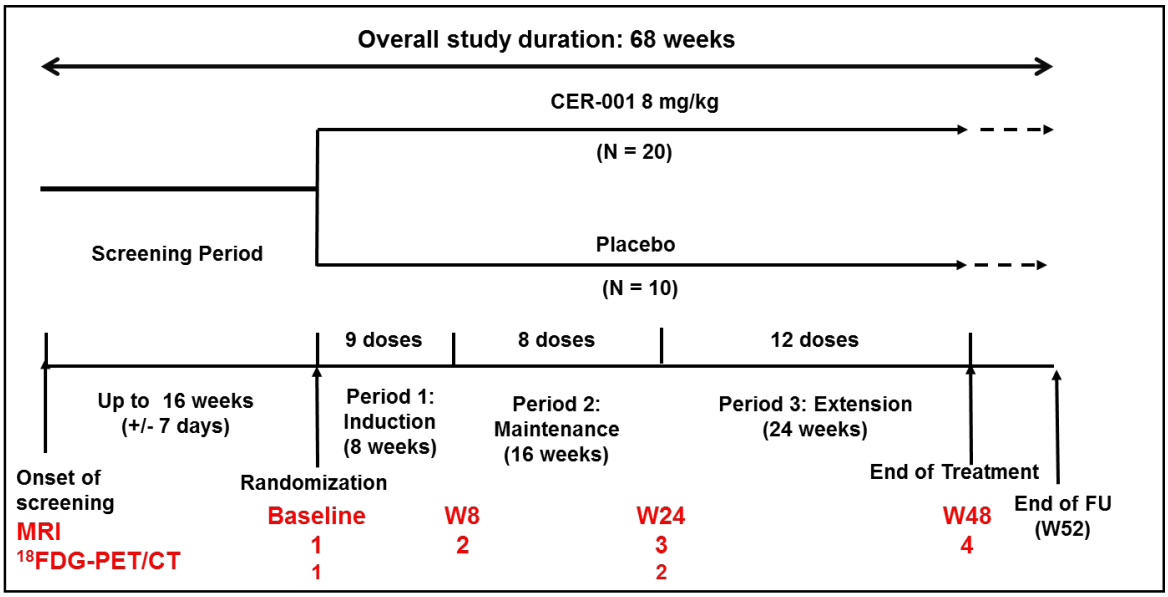
The exploratory objectives of the study are:

- To evaluate the effect of treatment with CER-001 with respect to other efficacy measurements including carotid artery and carotid normalized wall index using 3T-MRI;
- To evaluate the effect of treatment with CER-001 with respect to potential surrogate markers on vessel wall biology including laboratory variables;
- To evaluate the effect of treatment with CER-001 with respect to inflammation;
- To evaluate plasma-mediated cellular Cholesterol efflux capacity;
- To measure ApoA-1 levels (pharmacokinetic parameters);
- To measure Cholesterols, triglycerides, lipids, apolipoprotein and lipoprotein levels (pharmacodynamics parameters).

2. Study summary

This is a phase III, multi-centre, randomized, 48 weeks, double-blind, parallel-group, placebo-controlled study to evaluate efficacy and safety of CER-001 on ApoA-1 and vessel wall area in patients with genetically defined familial primary hypoalphalipoproteinemia and receiving background optimized lipid therapy.

The study design is illustrated in the following figure:



3. Sample size

The assumptions upon which the power calculations are based are data from the 7 patients completing the CER-001-CLIN-007 SAMBA study, given the similarity of the genetic mutations. Those patients presented with a median value for MVWA of 25.0 mm^2 and had a follow-up median value at 6 months of 21.8 mm2. The mean percent reduction is reported as 6.7%, standard deviation = 4.5%. These observed values would provide a conservative estimate of the effect of CER-001 in the more severe population for this FPHA study.

Using these results from SAMBA (i.e. an assumed standard deviation of 4.5%) and a 2:1 randomization scheme to maximize exposure to active drug, 16 completing patients in the CER-001 group and 8 in the placebo group (24 total completers for mITT) would yield 90% power to detect a difference from baseline versus placebo of 6.7%, using two-tailed testing with α=0.05. A total of 30 patients are planned to be randomized that would provide a buffer such that a 20% discontinuation rate would still allow the study to retain sufficient power for a supporting per protocol efficacy analysis (MVWA).

4. Randomization

After obtaining written informed consent, completing screening procedures, and ensuring the patient meets all of the inclusion criteria and none of the exclusion, the patient will be randomized. Stratification according to the genetic mutation (ABCA-1/ApoA-1) will be done to ensure appropriate balanced distribution of the mutations across treatment groups. The patient will be randomized to receive 29 infusions of either active drug or placebo using a 2:1 randomization scheme.

5. Unblinding

Unblinding will be performed by the ICTA PM statistician in charge of the study once database is locked, at the end of the study, with sponsor's agreement.

The unblinding process will be conducted according to ICTA SOP46 ("Randomization and unblinding"). ICTA Quality Assurance department will give the CD-Rom containing the randomization number and the corresponding randomization treatment to the statistician. The database will then be imported in the statistical database of the study. A 100% review of the imported data will be performed by the statistician, compared to initial data provided in the CD-Rom.

6. Populations to be analysed

6.1 Analysis populations of patients

The statistical analysis will be based on the three populations defined below. To be part of a population, patients should have signed informed consent and fullfill all inclusion / exclusion criteria. Some criteria have been added after the start of the study. Hence patients included before will be considered as compliant to these criteria via a Not Applicable (NA) status.

Safety population

The safety population will comprise all randomized patients who received at least one dose of study medication.

Safety analysis will be performed on the safety population according to the actual treatment received.

Modified Intent-To-Treat (mITT) population

The mITT population will comprise all randomized patients for whom at least one of the following conditions is satisfied:

- 3T-MRI assessment available at baseline (W0) and at least one post-baseline 3T-MRI assessment available
- 18FDG-PET/CT assessment available at baseline (W0) and at least one post-baseline 18FDG-PET/CT assessment available

Per Protocol (PP) population

The PP population will comprise all patients of the mITT population without any major protocol deviations (*Cf.* section 6.3).

Defining study populations and excluding patients from the analysis will be a joint decision taken by Sponsor and ICTA PM' representatives (Statistician and Project Leader). Patients to be excluded and

reasons for their exclusion will be discussed during data review meetings, before database lock and unblinding.

6.2 Protocol deviations

A list of protocol deviations has been written by ICTA PM and sent to the sponsor for approval. The list contains possible protocol deviations (according to inclusion/exclusion criteria, disallowed treatments, minimum treatment exposure, and calendar of visits...), and significant deviations which require immediate information to the Sponsor. This list may be updated in the course of the data management process, and will be finalized during the data review meetings before database lock and unblinding.

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During the data review, the impact of each deviation (minor/major) on the primary endpoint will be discussed and thus, the list of patients to be excluded from the PP population will be defined.

Number and percentage of patients with at least one deviation, at least one major deviation, at least one deviation by type (Entry criteria / Study procedures / Investigational medicinal product) will be described. Each deviation will also be summarized by the number and percentage of patients who experienced it.

6.3 Disposition of patients

The following data will be described:

- Number of screened patients [a]
- Number of screening failures and reasons for screening failures
- Number of randomized patients grouped by treatment
- Number of patients for whom the blind was broken
- Number of patients with ABCA-1, ApoA-1 or both mutations
- Number of patients who did not receive any medication and reason for non-treatment
- Number of patients who received double-blind medication
- Treatment actually received (CER-001/Placebo)
- Number of patients who completed the study
- Number of premature discontinuations of the study treatment and reason for premature discontinuation (at each visit, and overall)
- Number of premature withdrawals and reason for premature withdrawal (at each visit, and overall)
- Number of patients who completed the induction period grouped by treatment (visit at W8 performed)
- Number of patients who completed the maintenance period grouped by treatment (visit at W24 performed)
- Number of patients who completed the extension period grouped by treatment (visit at W48 performed)
- Patient's follow-up duration
- Inclusion date of the first patient (FPFV: First Patient First Visit), date of first visit of the last patient (LPFV) and last visit date of the last patient (LPLV: Last Patient Last Visit)
- Number of patients in each analysis set and reasons for exclusion from the analysis sets
- Number of visits performed

- Flow chart for analysis populations
- Flow chart for disposition of patients
- Flow chart for visits

[a] A screened patient is a patient who completed a screening visit

7. Statistical methodology

7.1 General principles

7.1.1 Software

All statistical analyses will be performed using Statistical Analysis System (SAS®) release 9.4. All computer programs will be developed and validated according to ICTA PM (CRO) standard operating procedures (SOP).

7.1.2 Descriptive statistics

Quantitative data will be summarized by the following descriptive statistics: number of data available, number of missing data, mean, standard deviation, first quartile (Q1), median, third quartile (Q3), minimum and maximum. If relevant, a 95% t-based mean confidence interval (CI) will also be presented.

Qualitative data will be summarized by the following descriptive statistics: number of data available, number of missing data, frequency and percentage for each modality.

Percentages will be calculated without taking into account missing data.

7.1.3 General statistical tests

No general statistical tests are planned. Statistical tests will be performed when running analysis of covariance (ANCOVA) and are detailed in section 7.5.

7.1.4 Management of missing or incomplete data

Previous and concomitant medications

For the purposes of determining whether a medication was taken during the conduct of the study, any missing or partial start or stop dates for which a definitive determination cannot be made will result in that medication will be assumed to be concomitant, to be conservative.

Linear Mixed Model

Missing data handling for assessing efficacy endpoints using linear mixed model will be described in section 7.4.1.

Adverse Events (AE)

If part of the date/time of an AE is missing, but the existing parts allow determination of timing of AE onset/end relative to start and stop date of the study drug, then the AE will be classified (treatment-emergent or not treatment-emergent) per review of the existing parts of the date/time field. If timing of the AE onset/end relative to start and stop date of the study medication cannot be made, then the AE will be assumed to be a Treatment-Emergent Adverse Event (TEAE).

Vital signs, physical examination, ECG and laboratory values

For absolute, relative changes and shifts from baseline (W0), in case of missing data for the baseline value, the latter will be replaced by the value obtained at screening visit.

7.1.5 Handling of dropouts

Dropouts will be handled for the primary endpoint as described in section 7.1.4.

The reasons of study termination will be assessed among treatment groups as well as the proportion of dropouts at each visit performed (*Cf.* section 6.4).

7.1.6 Handling of study centre effects

No centre effect will be assessed.

7.1.7 Presentation of results

Statistical Tables, Figures and Listing (TFL) will be produced in English, and templates are shown in appendix 12.2.

For summary statistics, mean, standard deviation and median will be presented with 1 more decimal place than the raw data; min and max with the same number of decimal places as the raw data. P-values will be presented with three decimal places.

7.1.8 Examination of subgroups

Individual genetic mutation will compose the three following subgroups:

- ABCA-1
- ApoA-1
- ABCA-1 & ApoA-1

These subgroups will be used as independent variable for each primary and secondary ANCOVA. Description of each exploratory outcome will also be performed on these subgroups.

7.1.9 Validation levels

Internal review by the statistician in charge of the project will be performed, including SAS® codes and programming, SAS® logs and outputs and edition of the TFL. Then, an external review of the TFL will be performed by the ICTA PM project manager and by the sponsor.

A double-programming of the primary endpoint analysis will be performed.

7.2 Demographic and other baseline characteristics

Demographic and other baseline characteristics will be described according to randomization group for all randomized patients. Description will also be performed for each subgroup of interest (based on genetic mutation). Baseline is defined as the last observation for any given parameter observed prior to the first infusion of study drug.

The following characteristics will be summarized using standard descriptive statistics (Cf. 7.1.2):

7.2.1 Demography

- Age at inclusion (years)

Patient's age will be a derived variable, defined in years according to the formula:
Age = (date of signature of written informed consent– date of birth) / 365.25.

- Sex (Male/Female)
    - If Female, Childbearing potential assessed (Yes / Not done / NA)
        - If Not done, reason

  - If Yes, Childbearing potential (Childbearing potential with contraceptive protection / Uncertain childbearing potential or post-menopausal status / Surgically sterilized / Post-menopausal)
    - If Childbearing potential with contraceptive protection, method(s) of contraception
  - If Yes, FSH value (IU/L)
  - If Yes, Pregnancy test result (Negative/Positive/NA)
- Race (Caucasian / Asian / Black or African American / American Indian or Alaska native / Native Hawaiian / Other pacific island / Other / NA)
  - If Other, specification
- Ethnicity (Hispanic/Non-Hispanic/NA)

7.2.2 Medical history and concomitant diseases

Medical history and concomitant diseases will be assigned to the Lowest Level Term (LLT), and a Preferred Term (PT) will be classified by a High Level Term (HLT), a High Level Group Term (HLGT) and a System Organ Class (SOC) according to the Medical Dictionary for Regulatory Activities (MedDRA) thesaurus, version 19.1.

Concomitant diseases will be defined as all diseases/conditions which are ongoing at screening visit. All others will be considered as medical history.

Concomitant diseases and medical history will be summarized according to the Table 2 template (*Cf.* Section 12.2) as follows:

- Number and percentage of patients presenting at least one event (medical history / concomitant disease)
- Number and percentage of patients presenting at least one event (medical history / concomitant disease) tabulated by SOC and PT

7.2.3 Risk factors

- Smoking status (Smoker / Former smoker / Non-smoker)
  - If Smoker, Current daily consumption (cigarettes/day)
  - If Former smoker, time since smoking cessation (< 1 year / Between 1-5 years / > 5 years)

7.2.4 Patient profile

- Cardiovascular disease background (Symptomatic/Asymptomatic)
  If Symptomatic:
  - History of cardio or cerebrovascular events (Yes/No)
  - Diagnosed coronary artery disease (Yes/No)
  - Diagnosed carotid or peripheral stenosis (Yes/No)
  - Previous myocardial revascularisation - percutaneous coronary intervention, or coronary artery bypass graft (Yes/No)

  If Asymptomatic, imaging methods used for diagnosis:
  - Doppler ultrasound (Yes/No)
  - B-mode ultrasonography (Yes/No)
  - Intravascular ultrasonography (Yes/No)
  - Computed Tomography (Yes/No)
  - Magnetic Resonance Imaging (Yes/No)

7.3 Treatment exposure and compliance

7.3.1 Treatment exposure

Duration of treatment exposure (weeks) will be described on the safety population according to the actual treatment received. It will be calculated as follows:

Duration of treatment exposure (weeks) = (Date of last infusion – Date of first infusion + 1) / 7

7.3.2 Treatment compliance

Treatment compliance will be assessed on the mITT population according to randomized treatment group. Compliance (%) with the study treatment will be summarized on each study period (Induction / Maintenance / Extension) and at W24, W48 as follows:

- *Compliance during induction phase (%) = Number of infusions totally administered between W0 and W8 / 9 * 100*
- *Compliance during maintenance phase (%) = Number of infusions totally administered between W10 and W24 / 8* 100*
- *Compliance during extension phase(%) = Number of infusions totally administered between W26 and W48 / 12 * 100*
- *Compliance at W24 (%) = Number of infusions totally administered between W0 and W24 / 17 * 100*
- *Compliance at W48 (%) = Number of infusions totally administered between W0 and W48 / 29* 100*

Average dose, total dose of CER-001 as well as administered dose *vs* expected dose will be summarized at W8, W24, W48, and are defined as follows:

- *Total dose at Wi (mg) =* $\sum_{v=1}^{ni} CER001\ dose\ prescription\ for\ infusion\ v\ \left(\frac{mg}{kg}\right) * Weight\ at\ infusion\ v\ (kg) * Actual\ volume\ administered\ at\ infusion\ v\ (mL)\ /\ 250$*, when* n_i *= number of infusions received between W0 and Wi*
- *Average dose at Wi (mg) = Total dose at Wi (mg) / number of infusions received between W0 and Wi*
- *Administered dose vs expected dose at Wi (%) = Total dose at Wi (mg) / (8 ** $\sum_{v=1}^{mi} Weight\ at\ infusion\ v$*) * 100, when* m_i *= number of infusions planned between W0 and Wi*

In addition, a by-patient listing will be produced for each patient who verified for at least one visit:

- Dose prescription different from 8 mg/kg
- Time elapsed between study medication infusion preparation and study medication administration > 72h (48h for Canadian sites)
- Start infusion time – stop infusion time > 65 min or < 55 min
- Total volume administered = No

For these patients, the listing will include, for all available visits:

- Patient ID, visit, treatment arm
- Dose prescription (mg/kg)
- Date and time of study medication infusion preparation
- Date of infusion, start and stop infusion time
- If not administered, reason
- If infusion duration different from 60 min, reason

- Total volume administered (Yes/No)
- If No, volume administered (mL)

7.4 Efficacy data

7.4.1 Primary endpoint

The primary efficacy endpoint is defined as the difference in the change from baseline in carotid artery MVWA at 24 weeks in patients treated with CER-001 compared to patients treated with placebo.

Analysis of the primary endpoint will consist of a main analysis, a supportive analysis and several sensitivity analyses.

7.4.1.1 Main analysis

A linear mixed model with repeated measures (MMRM) will be fitted to observed data for the mITT population without any imputation. An unstructured covariance matrix will be used to model random effects. The model will include the following variables:

- Change from baseline in carotid artery MVWA (mm^2, dependent variable)
- Randomized treatment group (CER-001 *vs* Placebo, independent variable)
- Genetic mutation (ABCA-1/ApoA-1/ABCA-1 and ApoA-1), independent variable)
- Carotid artery MVWA at W0 (mm^2, covariate)
- Visit (W8/W24/W48, independent variable)
- Treatment-by-Visit interaction (independent variable)
- Carotid artery MVWA at W0 by Visit interaction (independent variable)
- Treatment-by-carotid artery MVWA at W0 (independent variable)
- Subject (random factor)

Sample SAS Code

```
proc mixed data=DATASET method=reml covtest asycov alpha=0.05;
    class USUBJID TRTGRP (ref="Placebo") VISIT (ref=LAST) GENETIC_MUT (ref="REF");
    model CHANGE = BASELINE GENETIC_MUT BASELINE*VISIT TRTGRP VISIT
                        VISIT*TRTGRP BASELINE*TRTGRP / s ddfm=kr;
    repeated visit / subject=USUBJID type=UN r rcorr;
    lsmeans VISIT*TRTGRP / diff cl om e;
    estimate "Treatment Effect" TRTGRP 1 -1 VISIT*TRTGRP 0 1 0 0 -1 0 / cl;
run;
```

Adjusted means in change from baseline for each treatment group (with 95%CI) as well as treatment effect (with 95%CI) at W24 will be provided. Treatment effect will be calculated as the difference in adjusted mean values for the two treatment groups at W24.

Adjusted means in change from baseline and treatment effect will also be estimated at W24 within each genetic mutation subgroup.

A scatter plot will also be drawn representing the evolution of the carotid artery MVWA (mm^2) according to the carotid artery MVWA at week 0 (mm^2) grouped by treatment group.

Adjusted means (with 95%CI) of each randomized treatment group will also be plotted.

Results will be displayed according to table 5 of section 12.1.

7.4.1.2 Supportive analysis

As a supportive analysis, the linear mixed model described in the previous section (7.4.1.1) will also be fitted to observed and imputed data for the mITT population. Thus, a multiple imputation procedure will be set up and is described below.

First, in case of non-monotone missing data pattern, a MI procedure will be applied using a MCMC algorithm to create 20 imputed datasets with a monotone missing data pattern. The number of burn-in iterations before each imputation will be set to 200. Sample SAS code is displayed below.

Sample SAS Code

```
proc mi data=DATWIDE   nimpute=20 seed=111 out=MONODAT;
     var TRTGRP GENETIC_MUT BASELINE CHANGE8 CHANGE24 CHANGE48;
     mcmc chain=MULTIPLE impute=MONOTONE nbiter=200;
run;
```

Second, the 20 datasets with a monotone missing data pattern will be fully imputed based on a monotone method. Corresponding sample SAS code is provided below.

Sample SAS Code

```
proc mi data= MONODAT nimpute=1 seed=222 out=MONODAT;
     by _IMPUTATION_;
     class TRTGRP GENETIC_MUT;
     var TRTGRP GENETIC_MUT BASELINE CHANGE8 CHANGE24 CHANGE48;
     monotone regression (CHANGE8 CHANGE24 CHANGE48);
run;
```

Finally, the linear mixed model described in section 7.4.1.1 will be applied for each complete data sets producing 20 analysis results. The final treatment effect estimate will be obtained combining these 20 estimates as follows:

Sample SAS Code

```
proc mianalyze data=MRESULTS_;
    modeleffects ESTIMATE;
    stderr STDERR;
    ods output parameterestimates=RESULTS_;
run;
```

7.4.1.3 Sensitivity analyses

7.4.1.3.1 Missing Not At Random data mechanism

These sensitivity analyses require partitioning the analysis mITT population into groups, based on treatment group and available information about the reasons for missing values, before multiple imputation.

Control-based I: all dropouts grouped with placebo

In the first control-based sensitivity analysis, all monotone missing values will be imputed such as all dropouts and the placebo group form a subset with similar trajectories. A dataset, MONOREF_all, containing all the placebo group subjects and the treatment group subjects with missing data, will be imputed as shown in sample SAS code below. The complement of MONOREF_all will be the complete observation treated group data, so this could be concatenated with the 20 imputed datasets in DATIMP1.

Sample SAS Code

```
proc mi data= MONOREF_all nimpute=1 seed=333 out=DATIMP1;
    by _IMPUTATION_;
    class GENETIC_MUT;
    var GENETIC_MUT BASE CHANGE8 CHANGE24 CHANGE48;
    monotone regression (CHANGE8 CHANGE24 CHANGE48);
run;
```

Control-based II (informative-dropout): poor-outcome dropouts grouped with placebo

In the informative-dropout sensitivity analysis, some subjects are characterized as likely to have poor unobserved outcomes, for example if study withdrawal is due to clinical worsening. In this case, the datasets in MONODAT (monotone dataset) will be first split by treatment groups, either randomized to the experimental (TRTGRP) or reference/placebo (REF) condition, and then the poor-outcome dropouts will be shifted to the REF group, resulting in the datasets MONOTRT_minus and MONOREF_plus. The multiple imputation will be conducted separately for each subset as shown in the following sample code. The output datasets, DATIMP2T and DATIMP2R, will simply be concatenated before the analysis step.

```
proc MI data= MONOTRT_minus nimpute=1 seed=444 out=DATIMP2T;
    by _IMPUTATION_;
    class GENETIC_MUT;
    var GENETIC_MUT BASE CHANGE8 CHANGE24 CHANGE48;
    monotone regression (CHANGE8 CHANGE24 CHANGE48);
run;

proc MI data= MONOREF_plus nimpute=1 seed=555 out=DATIMP2R;
    by _IMPUTATION_;
    class GENETIC_MUT;
    var GENETIC_MUT BASE CHANGE8 CHANGE24 CHANGE48;
    monotone regression (CHANGE8 CHANGE24 CHANGE48);
run;
```

Control-based III: poor-outcome dropouts act like reference

In the third control-based sensitivity analysis, the MNAR statement will be used to allow poor-outcome subjects to follow the expected trajectory of a subject in the reference group (see sample code below). Since the treated subjects from MONOTRT_minus are treated similarly as in the informative-dropout scenario, the results here in DATIMP3R could be contatenated with DATAIMP2T for analysis.

```
proc MI data= MONOREF_plus nimpute=1 seed=666 out=DATIMP3R;
    by _IMPUTATION_;
    class GENETIC_MUT;
    var GENETIC_MUT BASE CHANGE8 CHANGE24 CHANGE48;
    monotone regression;
    mnar model (CHANGE8 CHANGE24 CHANGE48) / modelobs=(TRTGRP=”REF”);
run;
```

For each scenario, every 20 analysis estimates will be combined in one final estimate.

7.4.1.3.2 Analysis on the PP population

Primary efficacy analysis described for ITT population will also be performed on PP population in the same way (see sections 7.4.1.1 & 7.4.1.2).

7.4.2 Secondary endpoints

All secondary endpoints will be analysed on the mITT population.

7.4.2.1 Change from baseline in carotid artery MVWA

Estimators of the secondary endpoints listed below will be obtained using the mixed model already fitted in section 7.4.1.1:

- Difference in change (Experimental treatment *vs* placebo) from baseline (W0) in carotid artery MVWA at 8 weeks
- Difference in change (Experimental treatment *vs* placebo) from baseline (W0) in carotid artery MVWA at 48 weeks

7.4.2.2 Change from baseline in femoral artery MVWA

A linear mixed model with repeated measures (MMRM) will be fitted to observed data for the mITT population without any imputation. An unstructured covariance matrix will be used to model random effects. The model will include the following variables:

- Change from baseline in femoral artery MVWA (mm^2, dependent variable)
- Randomized treatment group (CER-001 *vs* Placebo, independent variable)
- Genetic mutation (ABCA-1/ApoA-1/ABCA-1 and ApoA-1), independent variable)
- Femoral artery MVWA at W0 (mm^2, covariate)
- Visit (W8/W24/W48, independent variable)
- Treatment-by-Visit interaction (independent variable)
- Femoral artery MVWA at W0 by Visit interaction (independent variable)
- Treatment-by-femoral artery MVWA at W0 (independent variable)
- Subject (random factor)

Analysis will be based on that described for the main analysis of the primary endpoint (section 7.4.1.1). No multiple imputation will be performed.

The following differences between placebo and the experimental treatment will be estimated:

- Change from baseline (W0) in femoral artery MVWA at 8 weeks
- Change from baseline (W0) in femoral artery MVWA at 24 weeks
- Change from baseline (W0) in femoral artery MVWA at 48 weeks.

These estimators will also be calculated within each genetic mutation.

7.4.2.3 Change from baseline in target (plaque) to background (blood) ratio

An analysis of covariance (ANCOVA) will be fitted to observed data for the mITT population without any imputation. The model will include the following variables:

- Change from baseline (W0) in TBR based on standardized 18FDG uptake measured with 18FDG-PET/CT MVWA at 24 weeks (dependent variable)
- Randomized treatment group (CER-001 *vs* Placebo, independent variable)
- Genetic mutation (ABCA-1/ApoA-1/ABCA-1 and ApoA-1), independent variable)
- TBR at W0 (covariate)
- Interaction Treatment by TBR at W0 (independent variable)

Adjusted means for the change in TBR and the associated 95%CI will be provided for each randomized treatment group. Adjusted mean difference and the associated 95%CI will also be displayed.

Sample SAS Code

```
proc glm data=DATWIDE alpha=0.05;
    class TRTGRP GENETIC_MUT;
    model CHANGE24 = BASELINE GENETIC_MUT BASELINE*TRTGRP TRTGRP / s;
    lsmeans TRTGRP / cl pdiff=control("REF");
run;
```

The previous statistics will also be estimated within each genetic mutation.

A scatter plot will be drawn representing the evolution of the TBR at week 24 according to the baseline TBR grouped by treatment group. Adjusted means (with 95%CI) for the change from baseline in each randomized treatment group will also be plotted.

7.4.3 Exploratory endpoints

The following exploratory endpoints will be summarized on the mITT population overall according to randomized study treatment and for each genetic subgroup within the randomized group using descriptive statistics:

- Percent change from baseline in femoral artery MVWA at 8, 24, 48, 72 weeks
- Percent change from baseline in maximum vessel wall thickness (MaxVWT) at 8, 24, 48, 72 weeks
- Percent change from baseline in mean vessel wall thickness at 8, 24, 48, 72 weeks
- Absolute and percent change in carotid mean vessel wall volume (MVWV) at 8, 24, 48, 72 weeks
- Percent change from baseline in the mean of the carotid normalized wall index at 8, 2448, 72 weeks
- Absolute and percent change from baseline in femoral artery MVWV at 8, 24, 48, 72 weeks

Percent change from baseline at Wi is defined as follows:

*(Value at Wi – Value at baseline (W0)) / Value at baseline (W0)*100*

Vessel wall biology (C-reactive protein (mg/L), PON-1 (IU/L), MMP-9, TNFα, IL-6, soluble VCAM-1, sMCP1, oxysterols, ABCA-1 mRNA and protein levels) will be summarized at screening, W0 (baseline), W4, W8, W24, W48. Absolute and relative changes from W0 (baseline) at W8, W24 and W48 will also be summarized. For changes calculation, if value at W0 is missing then value observed at screening will be used.

Cholesterol efflux capacity will be summarized at screening, W0, W8, W24 and W48. Absolute and relative changes from W0 (baseline) at W8, W24 and W48 will also be summarized. For changes calculation, if value at W0 is missing then value observed at screening will be used.

Lipid profile will be summarized at screening, W0, W8, W24 and W48. Absolute and relative changes from screening at W8, W24 and W48 will also be summarized (LABTYPE = Lipids):

- Total Cholesterol (mmol/L)
- Free Cholesterol (mmol/L)

- Esterified Cholesterol (mmol/L)
- LDL Cholesterol (mmol/L)
- HDL Cholesterol (mmol/L)
- Triglycerides (mmol/L)
- Apolipoprotein A-1 (g/L)
- Apolipoprotein A-2 (g/L)
- Apolipoprotein B (g/L)
- Apolipoprotein C-3 (g/L)
- Apolipoprotein E (g/L)

For changes calculation, if value at W0 is missing then value observed at screening will be used.

HDL-C Particle Size (2D-gel/NMR) will be summarized at screening, W0, W8, W24 and W48. NMR laboratory tests are the following (LABTYPE = Liposcience):

HDL particles (µmol/L), Large HDL particles (µmol/L), Medium HDL particles (µmol/L), Small HDL particles (µmol/L), HDL size (nm), IDL particles (nmol/L), LDL particles (nmol/L), Large LDL particles (nmol/L), Small LDL particles (nmol/L), LDL size (nm), HDL cholesterol (mg/dL), Triglyceride (total) (mg/dL), VLDL & Chylomicron Triglyceride (total) (mg/dL), Large VLDL & Chylomicron Particles (nmol/L), VLDL & Chylomicron Particles (total) (nmol/L), Medium VLDL Particles (nmol/L), Small VLDL Particles (nmol/L), VLDL Size (nm).

7.5 Safety data

All safety analyses will be performed on the safety population according to the actual treatment received.

7.5.1 Adverse events (AE)

AE term (Investigator term) will be assigned to the lowest level term (LLT), and a preferred term (PT) will be classified by a high level term (HLT), a high level group term (HLGT) and a system organ class (SOC) according to the Medical Dictionary for Regulatory Activities (MedDRA) thesaurus, version 19.1 or higher.

An adverse event will be considered as treatment-emergent (TEAE) if AE onset date is between first infusion of CER-001 and last infusion of CER-001 + 28 days, or if AE occurred before the first infusion of CER-001 but gets worse on study treatment. In case of incomplete date(s), see section 7.1.4.

An overview of the number of patients with at least one AE and the corresponding number of AEs will be presented including:

- Any AE
- Any TEAE
- Any serious TEAE
- Any severe TEAE
- Any TEAE leading to dose reduction of the study medication
- Any TEAE leading to temporary discontinuation of the study medication
- Any TEAE leading to permanent discontinuation of the study medication
- *Any TEAE related to the study medication (Related = definite, probable or possible)*
- Fatal AE
- Fatal TEAE
- Any coronary event (*Coronary event = event for which HLGT = Coronary artery disorders)*

All PT with HLGT = Coronary artery disorders will be described in the same way in a separate table.

Note: recurring AEs (*i.e.* AEs classified with the same Preferred Term (PT)) for a given patient will be only counted once and only their most severe intensity or most severe relationship to the study medication will be described.

TEAEs will also be tabulated by System Organ Class (SOC) and PT. They will be presented according to seriousness (Serious / Not serious), severity (Mild/Moderate/Severe) and relationship with the study medication (Related / Not related). They will finally be tabulated by SOC and PT according to relationship with the study medication within severity.

The different analyses described above will be summarized overall, on the induction period and on the post-induction period (AEs that occurred during maintenance or extension phase). Assignment of AEs to periods will be performed as follows:

Period	**Assignment**
Induction	Start date of TEAE < date of infusion at W10 (if day of AE is missing then impute to first of the month)
Post-induction	Start date of TEAE ≥ date of infusion at W10 (if day of AE is missing then impute to first of the month)

TEAE leading to death, other SAE (AE leading to death excluded) and other significant AE (any events leading to dose reduction, leading to temporary/permanent discontinuation of the study medication) will also be described on an individual basis. These listings will include the following information:

- Randomization group
- Patient identifier
- Age, race, ethnicity, sex, weight at inclusion
- Investigator's reported term, preferred term
- Duration of the adverse event
- Severity
- Seriousness
- Action taken
- Outcome
- Relationship with the study medication
- Timing of onset of the adverse event in relation to last dose of study medication
- Study treatment at time of event or most recent study treatment taken
- Study drug dose in absolute amount
- Total number of infusions received

7.5.2 Vital signs, physical examination, ECG

Clinical examination and vital signs will be summarized at each time point (screening, W0 (baseline), W4, W8, W16, W24, W32, W40, W48, 4 weeks after last dose). In addition, absolute changes from W0 (baseline) will be calculated at each post-baseline time point. Absolute change at Wi is defined as follows: Value at Wi - Value at W0.

- Respiratory rate (breaths/min)
- Systolic blood pressure (mmHg)
- Diastolic blood pressure (mmHg)
- Heart rate (beats/min)
- Body temperature (°C)
- Body weight (kg)
- Body mass index (kg/m²)

ECG diagnosis (Normal / Abnormal, not clinically significant (NCS) / Abnormal and clinically significant (CS)) will be summarized at screening and presented through shift tables from W0 (baseline) for the following time points: W4, W8, W16, W24, W32, W40, W48, 4 weeks after last dose).

In case of abnormal result regarding ECG (clinically significant or not) for a given patient, a listing will be produced including patient's identification, visit, date of assessment, ECG diagnosis, specification for the result and remarks, whatever the visit.

Assessment of physical examination (Normal / Abnormal non-clinically significant / Abnormal clinically significant) will be described at screening and presented through shift tables from W0 (baseline) for the following time points: W4, W8, W16, W24, W32, W40, W48, 4 weeks after last dose).

In case of missing value at W0 for a variable, imputation will be performed using the value obtained at screening. This imputation will be performed for shift tables only and absolute changes.

Shift tables will be:

- No change (from normal to normal / from abnormal NCS to abnormal NCS / from abnormal CS to abnormal CS)
- Improvement (from abnormal NCS to normal / from abnormal CS to abnormal NCS / from abnormal CS to normal)
- Deterioration (from normal to abnormal CS / from normal to abnormal NCS / from abnormal NCS to abnormal CS)

7.5.3 Laboratory parameters

All laboratory parameters will be summarized using descriptive statistics. Then, shift tables and absolute changes for each laboratory parameter will be displayed summarizing individual patient changes from baseline to each post-baseline time point. In case of missing value at W0 (baseline) for a variable, imputation will be performed using the value obtained at screening. This imputation method will only be applied for generation of shift tables. Unreportable values will be replaced by 0.

Haematology results will be assessed at screening, W0 (baseline), W4, W8, W16, W24, W32, W40, W48):

- Red blood cell count (10^9/L)
- Haemoglobin (g/L)
- Haematocrit (%)
- White blood cell count (10^9/L)
- Platelet count (10^9/L)

- Neutrophils (10^9/L)
- Lymphocytes (10^9/L)
- Monocytes (10^9/L)
- Eosinophils (10^9/L)
- Basophils (10^9/L)

Biochemistry results will be assessed at screening, W0 (baseline), W4, W8, W16, W24, W32, W40, W48:

- Glucose (mmol/L)
- Blood urea nitrogen (mmol/L)
- Creatinine (µmol/L)
- Creatinine clearance (mL/min)
- Uric acid (µmol/L)
- Albumin (g/L)
- Total protein (g/L)
- Total bilirubin (µmol/L)
- Indirect bilirubin (µmol/L)
- Creatine Kinase (IU/L)
- Alkaline phosphatase (IU/L)
- AST (SGOT) (IU/L)
- ALT (SGPT) (IU/L)
- Lactate dehydrogenase (IU/L)
- Calcium (mmol/L)
- Potassium (mmol/L)
- Sodium (mmol/L)
- Phosphorous (mmol/L)
- Chloride (mmol/L)
- Total CO2 (mmol/L)

Urinalysis will be assessed at screening, W0 (baseline), W4, W8, W16, W24, W32, W40, W48:

- White Blood Cell (WBC) (per HPF)
- Red Blood Cell (RBC) (per HPF)
- Total protein (positive/negative)
- Glucose (positive/negative)
- Total bilirubin (positive/negative)
- Ketones (positive/negative)
- pH
- Microalbuminuria (mg/L)
- Casts (per LPF)
- Specific gravity

Fasting blood glucose will be summarized at screening, W0, W4, W8, W16, W24, W32, W40 and W48.

In case of abnormal and clinically significant result for a parameter, a by-patient listing of all laboratory values for the parameter during the study will be produced.

Shift tables will be:

- No change (from positive to positive / from negative to negative)
- Improvement (from negative to positive)

- Deterioration (from positive to negative)

7.6 Previous and concomitant medications

All medications for which end date is prior to the first study drug infusion will be considered as previous medication. Otherwise they will be concomitant.

Previous and concomitant medications will be described by randomization groups by their therapeutic class (ATC) level 2 and ATC level 4 (WHO Drug Dictionary, version of March 2016 or later) according to the Table 3 template (*Cf.* Section 12.2):

- Number and percentage of patients presenting at least one previous/concomitant medication will be described in each treatment group.
- Previous/concomitant medication will also be presented per ATC and PT in a frequency table, for each treatment group.

7.7 Listings of individual data

All collected data and derived variables used for the statistical analysis will also be presented in individual patient listings, in accordance with ICH appendix 16.2. Each patient will be identified in these listings by his/her unique patient number.

8. Interim analyses

No interim analysis is planned.

9. Data and Safety Monitoring Board

The Data and Safety Monitoring Board (DSMB) will formally review unblinded study safety data to ensure there is no avoidable increased risk for harm to patients. Analyses for the DSMB meetings will be performed by an independent statistician (different from the one who will perform the final analysis). A specific SAP displays the safety data generated needed for the DSMB review.

10. Modifications with respect to the protocol

Analysis of efficacy endpoints

Statistical analysis of the primary and secondary outcomes (changes from baseline) were modified with respect to the protocol. In order to gain in terms of power, model will be fitted using all observations available for each patient during the study. Hence, linear mixed model with repeated measures will be used instead of analysis of covariance, Changes from baseline for a specified outcome could therefore be estimated at different time points based on the same model.

11. Approval of the Statistical Analysis Plan

ICTA PM	SPONSOR
Project Manager: **Banu DEMIRCI-GUILLERMET** Date: Signature:	Sr VP Clinical Development & Operations: **Constance KEYSERLING** Date: Signature:
Biostatistician: **Stéphanie PEROT** Date: Signature:	
Head of Medical and Scientific Development: **Jérémy SJRZYPSKI** Date: Signature:	

12. Appendices

12.1 Tables and graphs templates

Table 1 Disposition of patients

		CER-001	Placebo	Total
Patients screened				xx
Screening failures				xx
Reason for screening failures	xxxxx			xx
	xxxxx			xx
Patients randomized		xx	xx	xx
Patients with ABCA-1 mutation		xx	xx	xx
Patients with homozygous ABCA-1 mutation		xx	xx	xx
Patients with ApoA-1 mutation		xx	xx	xx
Patients with homozygous ApoA-1 mutation		xx	xx	xx
Patients with both ABCA-1 and ApoA-1 mutation		xx	xx	xx
Patients who did not receive any medication		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reasons	xxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	xxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Patients who received double-blind medication		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Treatment actually received	CER-001	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Placebo	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Study completed		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Study prematurely withdrawn		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason for premature withdrawal	xxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	xxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Study treatment prematurely discontinued		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason for premature discontinuation	xxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	xxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Induction period completed		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Maintenance period completed		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Extension period completed		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

		CER-001	Placebo	Total
Patient's follow-up duration	N	xx	xx	xx
	Missing values	xx	xx	xx
	Mean ± SD	xx ± xx	xx ± xx	xx ± xx
	Median	xx	xx	xx
	Q1 ; Q3	xx ; xx	xx ; xx	xx ; xx
	Min ; Max	xx ; xx	xx ; xx	xx ; xx
First Patient First Visit (FPFV)				DD/MM/YYYY
Last Patient First Visit (LPFV)				DD/MM/YYYY
Last Patient Last Visit (LPLV)				DD/MM/YYYY

Table 2 Descriptive statistics of quantitative and qualitative variables

		CER-001 N=xx	Placebo N=xx	Total N=xx
Quantitative variable	N	xx	xx	xx
	Missing values	xx	xx	xx
	Mean ± SD	xx ± xx	xx ± xx	xx ± xx
	Median	xx	xx	xx
	Q1 ; Q3	xx ; xx	xx ; xx	xx ; xx
	Min ; Max	xx ; xx	xx ; xx	xx ; xx
Qualitative variable	N	xx	xx	xx
	Missing values	xx	xx	xx
	Modality 1	xx (xx. x %)	xx (xx. x %)	xx (xx. x %)
	Modality 2	xx (xx. x %)	xx (xx. x %)	xx (xx. x %)
	…	…	…	…

Table 3 Medical History by System Organ Class and Preferred Term

System Organ Class Preferred term	CER-001 N=xx	Placebo N=xx	Total N=xx
At least one medical History	**xx (xx.x%)**	**xx (xx.x%)**	**xx (xx.x%)**
System organ class 1	**xx (xx.x%)**	**xx (xx.x%)**	**xx (xx.x%)**
Preferred term 1	x (x.x%)	x (x.x%)	x (x.x%)
…	x (x.x%)	x (x.x%)	x (x.x%)
Preferred term X	x (x.x%)	x (x.x%)	x (x.x%)
System organ class 2	**xx (xx.x%)**	**xx (xx.x%)**	**xx (xx.x%)**
…	x (x.x%)	x (x.x%)	x (x.x%)

Table 4 Concomitant treatments by Therapeutic Class and Preferred Term

Therapeutic class Preferred term	CER-001 N=xx	Placebo N=xx	Total N=xx
At least one concomitant medication	**xx (xx.x%)**	**xx (xx.x%)**	**xx (xx.x%)**
Therapeutic class 1	**xx (xx.x%)**	**xx (xx.x%)**	**xx (xx.x%)**
Preferred term 1	x (x.x%)	x (x.x%)	x (x.x%)
…	x (x.x%)	x (x.x%)	x (x.x%)
Preferred term X	x (x.x%)	x (x.x%)	x (x.x%)
Therapeutic class 2	**xx (xx.x%)**	**xx (xx.x%)**	**xx (xx.x%)**
…	x (x.x%)	x (x.x%)	x (x.x%)

Table 5 Adverse events by System Organ Class and Preferred Term

System Organ Class Preferred term	CER-001 N=xx	Placebo N=xx	Total N=xx
At least one AE	**xx (xx.x%)**	**xx (xx.x%)**	**xx (xx.x%)**
System organ class 1	**xx (xx.x%)**	**xx (xx.x%)**	**xx (xx.x%)**
Preferred term 1	x (x.x%)	x (x.x%)	x (x.x%)
…	x (x.x%)	x (x.x%)	x (x.x%)
Preferred term X	x (x.x%)	x (x.x%)	x (x.x%)
System organ class 2	**xx (xx.x%)**	**xx (xx.x%)**	**xx (xx.x%)**
…	x (x.x%)	x (x.x%)	x (x.x%)

Table 6 Primary and secondary endpoints: linear mixed model with repeated measures for change in outcome xx from baseline to W8, W24 and W48

Independent variable Covariate	Parameter estimate	P-value
Intercept	xx.x	x.xxx
Genetic mutation		
ABCA-1	xx.x	x.xxx
ApoA-1	xx.x	x.xxx
ABCA-1 and ApoA-1	xx.x	x.xxx
Baseline outcome xx	xx.x	x.xxx
Interaction Baseline outcome * Visit		
W8	xx.x	x.xxx
W24	xx.x	x.xxx
W48	0.0	--
Interaction Baseline outcome * Treatment		
CER-001	xx.x	x.xxx
Placebo	0.0	--
Visit		
W8	xx.x	x.xxx
W24	xx.x	x.xxx
W48	0.0	--
Randomized treatment		
CER-001	xx.x	x.xxx
Placebo	0.0	--
Interaction Visit by Treatment		
W8 * CER-001	xx.x	x.xxx
W24 * CER-001	xx.x	x.xxx
W48 * CER-001	0.0	--
W8 * Placebo	0.0	--
W24 * Placebo	0.0	--
W48 * Placebo	0.0	--

Table 7 Primary and secondary endpoints: linear mixed model with repeated measures for change in outcome xx from baseline to W8, W24 and W48 – Changes adjusted for the model and treatment effect

	CER-001 LS-mean [95% CI] (p-value)	**Placebo** LS-mean [95% CI] (p-value)	**Treatment effect** Difference in LS-means [95% CI] (p-value)
Overall change in outcome x from baseline to:			
W8	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)
W24	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)
W48	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)
(ABCA-1 genetic mutation subgroup) Change in outcome x from baseline to			
W8	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)
W24	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)
W48	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)
(ApoA-1 genetic mutation subgroup) Change in outcome x from baseline to			
W8	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)
W24	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)
W48	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)
(ABCA-1 & ApoA-1 genetic mutations subgroup) Change in outcome x from baseline to			
W8	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)
W24	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)
W48	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)	xx.x [xx.x ; xx.x] (x.xxx)

Table 8 Secondary endpoint: analysis of covariance for change from baseline in TBR:

Independent variable Covariate	Parameter estimate	P-value
Model		x.xxx
Intercept	xx.x	x.xxx
CER-001	xx.x	x.xxx
Placebo	0.00	--
ABCA-1 genetic mutation	xx.x	x.xxx
ApoA-1 genetic mutation	xx.x	x.xxx
ABCA-1 and ApoA-1 genetic mutations	0.00	--
Baseline outcome	xx.x	x.xxx

Table 9 Secondary endpoint: analysis of covariance for change from baseline in TBR - Changes adjusted for the model and treatment effect

See Table 7

Table 10 Shifts from baseline:

		CER-001 N=xx	Placebo N=xx	Total N=xx
Variable available at visit	N	xx	xx	xx
	No	x (x.x%)	x (x.x%)	x (x.x%)
	Yes	x (x.x%)	x (x.x%)	x (x.x%)
If yes, exam result at visit	*N*	xx	xx	xx
	Normal	x (x.x%)	x (x.x%)	x (x.x%)
	Abnormal and not clinically significant	x (x.x%)	x (x.x%)	x (x.x%)
	Abnormal and clinically significant	x (x.x%)	x (x.x%)	x (x.x%)
If yes, shift table at visit (from W0)	*N*	xx	xx	xx
	No change	x (x.x%)	x (x.x%)	x (x.x%)
	Improvement	x (x.x%)	x (x.x%)	x (x.x%)
	Deterioration	x (x.x%)	x (x.x%)	x (x.x%)

12.2 List of Tables, Graphs and Listings

Dry-runs for statistical outputs will be provided and approved by the Sponsor before database lock.