Statistical Analysis Plan (SAP)

PROTOCOL NUMBER: OG-KORATO-001 V4.1, 27 JUN 2024

A phase 4, multicenter, randomized, open-label, active-controlled study to evaluate the effectiveness and safety of early add-on of ezetimibe with atorvastatin in very high-risk patients.

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VERSION NUMBER AND DATE: V1.3; 31 OCT 2024

STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

Statistical Analysis Plan V1.3, 31 Oct 2024 for Protocol OG-KORATO-001 V4.1, 27 Jun 2024.

The SAP signature page applies to both SAP text and SAP Templates (outputs shells or Table/ Listing/ Figure (TLF) shells).

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MODIFICATION HISTORY

Unique Identifier for this Version	Date of the Document Version	Author	Significant Changes from Previous Authorized Version
1.0	06 Jul 2023	PPD	Not Applicable – First draft
1.1	05 Feb 2024	PPD	**Section 2** • Updated the CRF version to the latest 1.3 **Section 5.2** • Removed the notion of IQVIA Biostatistician due to change in BIOS SoW **Section 7.3** • Corrected the error on target study day and analysis visit windows **Section 11.2 & Table 10** • Added the medical history variable related to dyslipidemia according to the CRF version 1.3 **Section 16.4** • Separated the bilirubin variable into total and direct Bilirubin according to the CRF version 1.3 • Clarified the analysis method for quantitative laboratory test **Section 16.2 & 171. Appendix 1**

			• Updated the criteria or algorithm for TEAE at 6 weeks according to the correction of target study day
1.2	22nd APRIL 2024	PPD	• General comments. Rationale for redefining the analysis is to revise the visit windows and the LOCF from baseline which was deemed inappropriate for obtaining valid study results. Primary analysis based on FAS (not LOCF) and Sensitivity analysis based on LOCF for LDL-C endpoint. • Revised visit windows: Week 6 – (Day 14 to Day 64) Week 12- (Day 65 to Day 105) • Updated the change in the analysis of triglycerides due to the known nonnormal distribution of triglycerides
1.3	31 Oct 2024	PPD	Revised Section 6.2 Per Protocol Set (PPS) • Changed "Possible major protocol violations are listed as follow:" to "Possible reasons excluded from PPS including major protocol violations are listed as follow:" • Removed "No baseline LDL-C assessment" and "Not treated" from Section 6.2, Table 5 and

			Table 7 as these are covered under FAS already and PPS is a subset of FAS. • Changed “Noncompliance” to “IP noncompliance”. • Chamged the population from Ranodmized Patients to Full Analysis Set in Table 7. • Updated the tables containing Percentage Change in Triglycerides from Baseline – changed ANCOVA to Nonparametric with difference in medians and 95% CI for difference. This will make analysis and reporting of Triglycerides to be consistent with the SAP. The tables affected are: 30, 31, 40, 41, 54, 55, 68, 69, 82, 83, 96, 97, 110, 111, 124, 125, 138, & 139.

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1. ABBREVIATIONS

Abbreviation	Definition
ACS	Acute coronary syndrome
AE	Adverse event
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
ANCOVA	Analysis of covariance
AST	Aspartate aminotransferase
BMI	Body mass index
BUN	Blood urea nitrogen
CABG	Coronary artery bypass graft surgery
CI	Confidence interval
CK	Creatine kinase
DBP	Diastolic blood pressure
eCRF	Electronic case report form
FAS	Full analysis set
GGT	Gamma glutamyl transferase
HDL-C	High-density lipoprotein cholesterol
IMP	Investigational medicinal product
IWRS	Interactive web response system
LDH	Lactate dehydrogenase
LDL-C	Low-density lipoprotein cholesterol
LOCF	Last observation carried forward
LS	Least squares
MedDRA	Medical dictionary for regulatory activities
MI	Myocardial infarction
PCI	Percutaneous coronary intervention
PPS	Per-protocol set
PT	Preferred term
Q1	1st quartile
Q3	3rd quartile
SAP	Statistical analysis plan
SAS	Safety analysis set
SBP	Systolic blood pressure
SD	Standard deviation
SE	Standard error
SOC	System organ class
TEAE	Treatment-emergent adverse event
TESAE	Treatment-emergent serious adverse event
TRAE	Treatment-related adverse event

UA	Unstable angina
ULN	Upper limit of normal
WBC	White blood cell

2. INTRODUCTION

This statistical analysis plan (SAP) describes the rules and conventions to be used in the presentation and analysis of a phase 4, multicenter, randomized, open-label, active-controlled study to evaluate the effectiveness and safety of early add-on of ezetimibe with atorvastatin in very high-risk patients. It describes the data to be summarized and analyzed, including specifics of the statistical analyses to be performed.

This SAP is based on protocol OG-KORATO-001 version 4.1, dated 27 Jun 2024 and Case Report Forms (CRFs) version 1.3, dated 21 Aug 2023. This SAP supersedes the relevant statistical analysis sections of the protocol.

3. STUDY OBJECTIVES AND ENDPOINTS

The following table presents the primary and secondary objectives and corresponding endpoints of the study.

Objectives	Endpoints
Primary • To evaluate the effectiveness of early add-on of ezetimibe with atorvastatin in very high-risk patients.	• Percentage change in low-density lipoprotein cholesterol (LDL-C) from baseline to week 6
Secondary • To evaluate the clinical effectiveness of early add-on of ezetimibe with atorvastatin in very high-risk patients. • To evaluate the safety of early add-on of ezetimibe with atorvastatin in very high-risk patients.	• Proportion of patients achieving LDL-C goal of <55 mg/dL after 6 weeks and 12 weeks of treatment • Proportion of patients achieving LDL-C goal of <70 mg/dL after 6 weeks and 12 weeks of treatment • Percentage change in LDL-C from baseline to week 12 • Percentage change in high-density lipoprotein cholesterol (HDL-C), non-HDL-C, triglycerides, and total cholesterol from baseline to week 6 and week 12 • Treatment-emergent adverse events (TEAEs) at 6 weeks and 12 weeks

	• Dropout rate due to TEAEs at 6 weeks and 12 weeks

4. STUDY DESIGN

4.1 General Description

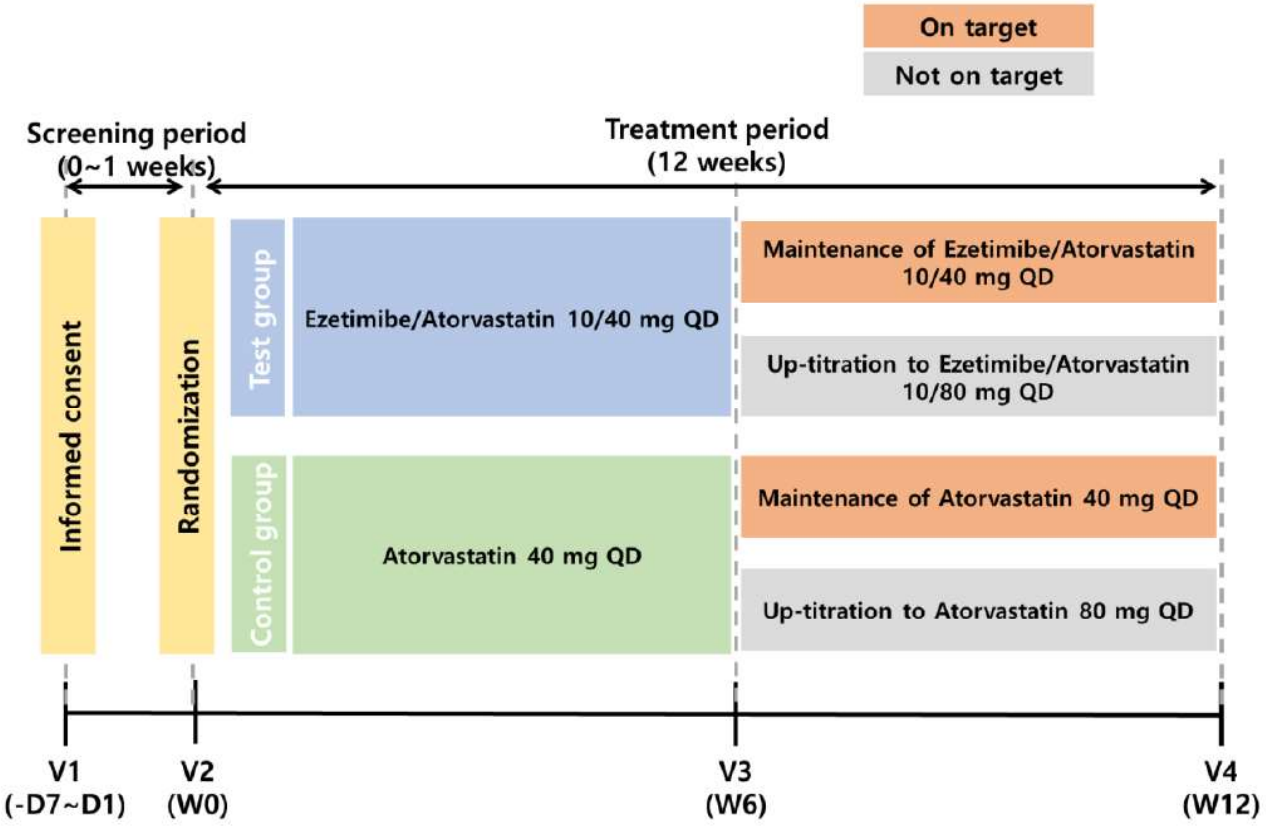
This is a phase 4, multicenter, randomized, open-label, active-controlled study. The study has been designed to evaluate the effectiveness and safety of early add-on of ezetimibe with atorvastatin in very high-risk patients.

In Visit 1, screening is conducted for patients in the very high-risk group. LDL-C needs to be above 70 mg/dL in patients (a) who failed to achieve their target LDL-C goals with mild to moderate intensity statin; (b) who are statin-naive or have not been on a stable statin regimen for at least 4 weeks prior to enrollment. However, by tracking the registration status of patients, (b) patients should be enrolled not to exceed 40% of each group. All laboratory tests are performed in the local laboratory and the Visit 1 results may be substituted if available within 2 weeks prior to the screening visit. The study participation is determined through the inclusion/exclusion criteria based on the test results conducted for Visit 1. In the case of the lipid parameter, Visit 1 results are used as the baseline. Individuals who do not meet the criteria for participation in this study (screen failure) may be rescreened once.

In Visit 2, randomization is performed on patients who meet the inclusion criteria and do not meet any of the exclusion criteria and will be distributed 1:1 between test group (arm Eze/Ato) and control group (arm Ato). The results of laboratory tests at the Visit 2 are used as baseline except lipid parameters. Visit 1 and Visit 2 may be conducted on the same date.

In Visit 2 and Visit 3, the appropriate investigational medical product (IMP) is given to each group. In principle, IMPs are administered orally once a day from the day of distribution.

For patients whose LDL-C value has reached the target (LDL-C < 55 mg/dL) according to the lipid indicator test at Visit 3, they will continue treatment with the same dose for 6 weeks. If the LDL-C level has not reached target, the dose of atorvastatin should be increased to ezetimibe/atorvastatin 10/80 mg or atorvastatin 80 mg according to the group assigned. In principle, a morning visit is recommended so that the laboratory test results can be checked, and the IMP can be prescribed and taken on the same day. However, if the test results are not confirmed on the same day and a patient has enough IMP to take until the next visit, IMP compliance is checked, and the same dose of IMP (ezetimibe/atorvastatin 10/40 mg or atorvastatin 40 mg) is continued. An additional visit is made within 1 week to return the remaining IMP and receive new IMP. If the test results are not confirmed on the same day and a patient does not have remaining IMP, the investigator prescribes the same dose of IMP (ezetimibe/atorvastatin 10/40 mg or atorvastatin 40 mg) that the patient was taking previously, and an additional visit is made within 1 week to receive new IMP. Visit 4 is the end of study visit, and tests for effectiveness and safety are conducted.



4.2 Sample Size

The number of patients in each treatment group is about 57, assuming that the treatment difference in percentage change in LDL-C between Ezetimibe/Atorvastatin and Atorvastatin would be 10% with an SD of 19%. This calculation is based on a two-sided significance level $\alpha = 0.05$, power $1-\beta = 0.80$ with a randomization ratio $\lambda = 1$. Considering the dropout rate of 10%, 63 patients for each group and thus, a total of 126 patients will be randomized in this study.

4.3 Treatment Groups and Duration

Arm Title	Eze/Ato	Ato
Arm Type	Experimental	Active comparator

[Arm Description]	Patients will receive ezetimibe/atorvastatin 10/40 mg QD from Visit 2 (Day 1) to Visit 3 (Week 6). If the LDL-C target is reached (LDL-C < 55 mg/dL) at Visit 3, maintain the dose to Visit 4 (Week 12). If the LDL-C target level is not reached at Visit 3, dose is increased to ezetimibe/atorvastatin 10/80 mg QD from Visit 3 to Visit 4.	Patients will receive atorvastatin 40 mg QD from Visit 2 (Day 1) to Visit 3 (Week 6). If the LDL-C target is reached (LDL-C < 55 mg/dL) at Visit 3, maintain the dose to Visit 4 (Week 12). If the LDL-C target is not reached at Visit 3, dose is increased to atorvastatin 80 mg QD from Visit 3 to Visit 4.
Associated Intervention Labels	Ezetimibe/Atorvastatin	Atorvastatin

4.4 Schedule of Activities

The schedule of activities can be found in section 1.3 of the protocol.

4.5 Changes to Analysis from Protocol

No change to analysis from protocol.

5. PLANNED ANALYSES

5.1 Interim Analysis

No interim analysis is planned for this study.

5.2 Final Analysis

All final, planned analyses identified in this SAP will be performed by Organon after Database Lock.

6. ANALYSIS SETS

6.1 Full Analysis Set [FAS]

The full analysis set (FAS) comprises all randomized patients who received at least one dose of study treatment and had a baseline assessment of LDL-C and at least one valid post baseline measurement of LDL-C.

Patients in the FAS will be included in their randomized treatment group, regardless of their actual treatment. The FAS is the primary analysis set for effectiveness analyses.

6.2 Per Protocol Set [PPS]

The per-protocol set (PPS) is a subset of the FAS who completed the 6-week follow-up observation with no major protocol deviations. Possible reasons excluded from PPS including major protocol violations are listed as follow:

- Violation of inclusion or exclusion criteria
- Randomization error
- No 6-week LDL-C assessment
- IP noncompliance (less than 80% or more than 120% of study intervention)
- Administration of prohibited concomitant medications
- Study discontinuation before 6-week
- Other major protocol deviations

The efficacy analysis based on the PPS will be considered supportive.

6.3 Safety Analysis Set [SAS]

The safety analysis set (SAS) includes all randomized patients who received at least one dose of study treatment. Patients in the SAS will be included in the actual treatment group, regardless of their randomized treatment.

7. GENERAL CONSIDERATIONS

7.1 Reference Start Date

Study Day will be calculated from the reference start date, and will be used to assign corresponding study visits of assessments or events.

Reference start date is defined as the day of the first dose of study medication, (Day 1 is the day of the first dose of study medication). In case the first dose date is missing, the randomization date will be used instead.

- If the date of the event is on or after the reference start date then:
  Study Day = (date of event – reference start date) + 1.
- If the date of the event is prior to the reference start date then:
  Study Day = (date of event – reference start date).

If the situation where the date of assessment or event is partial or missing, the date will appear partial or missing in the listings, and unless otherwise specified in the relevant section, Study Day and any corresponding visit will be assigned based on the imputations specified in Appendix 1; Partial Date Conventions.

7.2 Baseline

Except for the lipid parameters for which Visit 1 measurement will be used as the baseline, baseline is defined as the last non-missing measurement taken prior to reference start date. In the case where the last non-missing measurement and the reference start date coincide, that measurement will be considered pre-baseline, but Adverse Events (AEs), medications, and medical procedures commencing on the reference start date are considered post-baseline.

7.3 Windowing Conventions

Protocol-defined assessments will be assigned to study weeks based on collection date and applying the rules summarized in the following table. If there is more than one scheduled visit in a visit window, the visit closest to the target date will be used. If there is a tie between the numbers of days from the target date, the visit after the target date will be used. Unscheduled visits that fall within the protocol-defined visit windows will be summarized in the by-visit analyses if there is no

scheduled visit available. If there is more than one unscheduled visit within the protocol-defined visit window and no scheduled visit available, the unscheduled visit closest to the scheduled visit date will be used. If there is a tie between the numbers of days from the target date, the visit after the target date will be used.

Visit	Visit 1 (screening)	Visit 2	Visit 3	Visit 4
Assigned Study Week	-1	0	6	12
Target Study Day	-7	1	43	85
Analysis Visit Windows	[-7, 1*]	[1,1]	[**14,64]	[65,105]

* Visit 1 and Visit 2 may be conducted on the same date.

** Target Day 2 to Target Day 13 will be assigned as unscheduled visit 2.x.

7.4 Common Calculations

Change from baseline will be calculated as:

- Value at Week X – Value at Baseline

Percentage change from baseline will be calculated as:

- 100 x (Value at Week X – Value at Baseline) / Value at Baseline

7.5 Software Version

All analyses will be performed using SAS VIYA or above.

8. STATISTICAL CONSIDERATIONS

8.1 General Methodologies

Medical history, prior/concomitant procedures and AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 25.1 or later and summarized by MedDRA system organ class (SOC) and preferred term (PT), displayed by descending frequencies. Each patient will be counted only once within each SOC or PT.

Prior/concomitant medications will be coded using the World Health Organization Drug Dictionary (WHO-DD) version C3 Sep 2022 or later and summarized by therapeutic subgroup and preferred name, displayed by descending frequencies. Each patient will be counted only once within each therapeutic subgroup or preferred name.

Descriptive statistics will include number of patients without missing values, mean, standard deviation (SD), median, 1st quartile, 3rd quartile, minimum, and maximum for continuous variables, and the number of patients without missing values and the number and percentage of patients for each category for categorical variables.

8.2 Statistical Tests and Confidence Intervals

For continuous efficacy variables (except triglycerides), the statistical comparisons between treatment groups are performed using an analysis of covariance (ANCOVA) with treatment group and history of statin administration as factors and the corresponding baseline as a covariate. For categorical efficacy variables, the statistical significance of the differences between treatment groups is tested using Chi-square test or Fisher's exact test. All the statistical tests use a two-sided test at the significance level of 0.05.

Due to the known distribution of triglycerides, normality assumption is usually difficult to satisfy. A nonparametric approach will be used for the analysis of percent change from baseline for triglycerides. The Hodges-Lehmann method will be used to estimate the median difference and its corresponding 95% CI for percent changes between the treatment groups.

Inferential conclusion will be drawn only for primary endpoint based on p-value at 0.05 significance level as described in section 15.1.2 of this analysis plan.

8.3 Adjustments for Covariates and Factors to be Included in Analyses

The following covariates and factors are used in ANCOVA models. For details of their inclusion in the models, see the specific analysis section.

- Baseline value of interest
- Treatment group: Eze/Ato, Ato
- History of statin administration: Yes (≥ 4 weeks), No (< 4 weeks, naïve)

- Yes if 'Is the patient under statin treatment?' is 'Yes for 4 weeks or more from today' from 'Medical history related to dyslipidemia risk factors' page of eCRF
- No if 'Is the patient under statin treatment?' is 'Yes, but for less than 4 weeks from today' or 'No' from 'Medical history related to dyslipidemia risk factors' page of eCRF

8.4 Missing Data

For primary analysis, no imputation will be used.

For the sensitivity analysis of LDL-C missing postbaseline LDL-C data for Week 6 will be imputed by last observation carried forward (LOCF) method based on the last valid postbaseline measurement prior to the visit.

Baseline values will not be used for imputation purpose..

Missing safety data will not be imputed.

Unless otherwise specified in the relevant section, partial date handling is described in Appendix 1.

8.5 Examination of Subgroups

Subgroup analyses will be conducted as stated in the exploratory analysis section 15.3.

The following subgroups will be assessed and described within the exploratory analysis sections:

- Sex: Female, Male
- Age (years): <65, ≥65
- History of statin administration: Yes, No (refer to section 8.3 for categorization)
- Status of a dose up-titration at Week 6: Yes, No
  - Yes (if study treatment dose is increased at Visit 3)
  - No (if study treatment dose is unchanged at Visit 3)

8.6 Randomization Schedule

In Visit 2, randomization is performed on patients who meet the inclusion criteria and do not meet any of the exclusion criteria and will be distributed 1:1 between test group (arm Eze/Ato) and control group (arm Ato).

All patients will be centrally assigned to randomized study intervention using an interactive web response system (IWRS).

Stratified block randomization

The randomization code will be set so that the test group and control group can be assigned in a 1:1 ratio by the stratified block randomization method for each institution and using statin administration history as a stratification factor.

9. OUTPUT PRESENTATIONS

Appendix 2 shows conventions for presentation of data in outputs.

10. DISPOSITION AND WITHDRAWALS

Participant disposition table will be based on the patients who were randomized.

The following summaries will be included in the disposition table: the number of patients who were randomized and the numbers and percentages of patients who were treated (= received at least one study medication), not treated, completed the study, and discontinued from the study overall with the reason of discontinuation by treatment group and total. Possible reasons for discontinuation include: violation of inclusion/exclusion criteria, lost to follow-up, aspartate aminotransferase (AST) or alanine aminotransferase (ALT) level > 3× upper limit of normal (ULN) for 2 consecutive times, creatine kinase (CK) > 10×ULN for 2 consecutive times, pregnancy, termination of the study by the investigator or Sponsor, difficult to continue the study according to the judgment of the investigator, adverse event, informed consent withdrawal and other.
A listing of patients who were discontinued from the study early will be provided. The listing will identify the visits completed and when the study was discontinued including the corresponding reasons, participant number, institution name, treatment group, sex, age, date of informed consent, and date of last visit as necessary.

The number and percentage of patients who failed screening (i.e. were not randomized) will be presented by reason among all enrolled patients. Possible reasons for screen failures include: violation of inclusion/exclusion criteria, informed consent withdrawal and other. A listing of all screen failures along with the corresponding reason will also be presented including participant number, institution name, sex, age, and date of informed consent.

The number and percentage of patients who were excluded from each of the SAS, FAS, and PPS will be presented by treatment group and total. Possible reasons for exclusion from each of analysis sets are found in section 6.

A listing of patients along with the analysis set that they were excluded from and the corresponding reasons will also be presented including participant number, institution name, treatment group, sex, age, date of informed consent, and status of study completion/discontinuation.

The number and percentage of patients with major protocol deviations will be presented overall and by deviation category and by treatment group and total.

A listing of patients with major protocol deviations will also be presented including the corresponding deviation category, participant number, institution name, treatment group, sex, age, date of informed consent, and status of study completion/discontinuation.

11. BASELINE CHARACTERISTICS

11.1 Demographic and Other Baseline Characteristics

Demographic data and other baseline characteristics will be presented for the FAS.

No statistical testing will be carried out for demographic or other baseline characteristics.

The following demographic and other baseline characteristics will be reported for this study:

- Age (years)
- Age categories: <65, ≥65
- Sex: Male, Female
- Height (cm)
- Weight (kg)
- Body mass index (BMI) (kg/m^2)
  - BMI (kg/m^2) = weight (kg)/ height $(m)^2$

- Smoking history: Currently smoking, Past smoker, Never smoked
- Alcohol history: Now drinking, Past drinking, Never
- Alcohol consumption (only in case of 'Now drinking'): Less than 2 drinks a week, 2 to 3 drinks a week, 4 or more drinks a week

Continuous variables will be summarized using number of patients without missing values, mean, standard deviation, median, 1st quartile, 3rd quartile, minimum, and maximum by treatment group and total. Categorical variables will be summarized using the total number of patients without missing values and the number and percentage of patients for each category by treatment group and total.

11.2 Medical and Treatment History Related to Dyslipidemia

Medical and treatment history related to dyslipidemia will be presented for the FAS.

The following information on medical and treatment history related to dyslipidemia will be reported:

- Dyslipidemia duration (years): (randomization date – dyslipidemia diagnosis date + 1) / 365.25
  - Unknown date and/or month of the dyslipidemia diagnosis date will be replaced by 1
  - Missing or unknown year of the dyslipidemia diagnosis date will not be replaced and dyslipidemia duration will be considered missing
- Medical history related to dyslipidemia including acute coronary syndrome (ACS) (myocardial infarction (MI) or unstable angina (UA)), stable angina, coronary revascularization (percutaneous coronary intervention (PCI), coronary artery bypass graft surgery (CABG) and other arterial revascularization procedures), stroke, transient ischemic attack, peripheral arterial disease, and other clinical or unequivocal ASCVD on imaging: Yes (prior or current), No
- Family history status: Yes, No
  - Yes: if any of 'father', 'mother', 'brothers/sisters', 'Others' is selected
  - No: if none is selected
- Family history: father, mother, brothers/siters, other
  - As a multiple choice item, categories are not mutually exclusive
- History of statin administration: Yes (≥ 4 weeks), No (<4 weeks, Naïve)
- Baseline LDL-C (mg/dL)
- Baseline LDL-C categories: <130, ≥130 to <160, ≥160
- Baseline HDL-C (mg/dL)

- Baseline non-HDL-C (mg/dL): defined as (total cholesterol – HDL-C)
- Baseline triglycerides (mg/dL)
- Baseline total cholesterol (mg/dL)

Continuous variables will be summarized using number of patients without missing values, mean, standard deviation, median, 1st quartile, 3rd quartile, minimum, and maximum by treatment group and total. Categorical variables will be summarized using the total number of patients without missing value and the number and percentage of patients for each category by treatment group and total.

12. GENERAL MEDICAL HISTORY

Medical History information will be presented for the FAS.

All data on medical history will be categorized as medical history or concomitant illness using the following definitions, which will be summarized respectively.

- Medical history: any condition with the ongoing status that is 'No'
- Concomitant Illness: any condition with the ongoing status that is 'Yes'

For each medical history and concomitant illness, the number and percentage of patients will be summarized overall and by MedDRA SOC and PT for treatment group and total.

13. MEDICATIONS

Medications will be presented for the FAS.

All data on medications will be categorized as prior or concomitant using the following definitions, which will be summarized respectively. See Appendix 1 for handling of partial dates.

- Prior medications: any medication with a stop date that is prior to the first administration of the study drug.
- Concomitant medications: any medication with a stop date that is on or after the first administration of the study drug or any medication with the ongoing status that is 'Yes'.

For each prior and concomitant medications, the number and percentage of patients will be summarized overall and by WHO-DD therapeutic subgroup and preferred name for treatment group and total.

14. MEDICAL PROCEDURES

Medical procedures will be presented for the FAS.

All data on procedures will be categorized as prior or concomitant using the following definitions, which will be summarized respectively. See Appendix 1 for handling of partial dates.

- Prior procedures: any procedure with a stop date that is prior to the first administration of the study drug.
- Concomitant procedures: any procedure with a stop date that is on or after the first administration of the study drug or any procedure with the ongoing status that is 'Yes'.

For each prior and concomitant procedures, the number and percentage of patients will be summarized overall and by MedDRA SOC and PT for treatment group and total.

15. EFFECTIVENESS OUTCOMES

15.1 Primary Effectiveness

15.1.1 Primary Effectiveness Variable & Derivation

The primary objective of this study is to evaluate the effectiveness of early add-on of ezetimibe with atorvastatin in very high-risk patients.

The primary endpoint is percentage change in LDL-C from baseline (Visit 1) to week 6 (Visit 3).

15.1.2 Primary Analysis of Primary Effectiveness Variable

The primary endpoint analysis will be performed on the FAS.

The statistical hypothesis of this study is as follows.

$$H_0: \mu_t - \mu_c = 0 \text{ vs. } H_1: \mu_t - \mu_c \neq 0$$

μ_t = Percentage change in LDL-C from baseline to 6 weeks in ezetimibe/atorvastatin 10/40 mg
μ_c = Percentage change in LDL-C from baseline to 6 weeks in atorvastatin 40 mg

The primary endpoint will be analyzed by fitting an ANCOVA model with treatment group (Eze/Ato, Ato) and history of statin administration (Yes, No) as fixed effects and baseline LDL-C as a covariate. In addition to descriptive statistics for LDL-C at each visit and its percentage change from baseline by treatment group, least squares (LS) means for each treatment group with corresponding standard errors (SEs) and treatment differences of LS means with corresponding two-sided 95% confidence interval (CI) and p-value which will be derived from the fitted model will be presented. If the upper limit of the 95% two-sided CI for the corresponding treatment difference (Eze/Ato - Ato) is less than 0, Eze/Ato is considered superior to Ato.

15.1.3 Sensitivity Analysis of Primary Effectiveness Variable

The same model as in the primary analysis will be fitted for PPS. In addition to descriptive statistics for LDL-C at each visit and its percentage change from baseline by treatment group, LS means for each treatment group with corresponding SEs and treatment differences of LS means with corresponding two-sided 95% CIs and p-value will be presented.
Sensitivity analysis using the LOCF imputation method will be performed for the primary endpoint, percent change from baseline in LDL-C. The same model as in the primary analysis will be fitted for the sensitivity analysis (LOCF).

15.2 Secondary Effectiveness

15.2.1 Secondary Effectiveness Variables & Derivations

To evaluate the clinical effectiveness of early add-on of ezetimibe with atorvastatin in very high-risk patients, following endpoints will be examined.

- Proportion of patients achieving LDL-C goal of <55 mg/dL at 6 weeks and 12 weeks of treatment.
- Proportion of patients achieving LDL-C goal of <70 mg/dL at 6 weeks and 12 weeks of treatment.

- Percentage change in LDL-C from baseline to week 12
- Percentage change in HDL-C, non-HDL-C, triglycerides, and total cholesterol from baseline to week 6 and week 12

Percentage change in LDL-C, HDL-C, non-HDL-C, triglycerides, and total cholesterol will be derived as described in section 7.4.

LDL-C, HDL-C, non-HDL-C, triglycerides, and total cholesterol values at baseline , Week 6 and Week 12 will be used.

15.2.2 Missing Data Methods for Secondary Effectiveness Variable(s)

No missing data imputation will be used for the analysis of the secondary effectiveness variables.

15.2.3 Analysis of Secondary Effectiveness Variables

All secondary endpoint analyses will be performed on the FAS.

The number and percentage of patients achieving LDL-C goal of < 55 mg/dL and LDL-C goal of < 70 mg/dL at 6 weeks and 12 weeks will be presented by treatment group and tested using Chi-square test or Fisher's exact test as appropriate. The difference in the percentage will be presented with its corresponding 95% CI and p-value.

The continuous secondary endpoints (except triglycerides) will be analyzed by fitting ANCOVA models with treatment group (Eze/Ato, Ato) and history of statin administration (Yes, No) as fixed effects and baseline value of interest as a covariate. In addition to descriptive statistics for variables of interest at each visit and its percentage change at a period from baseline by treatment group, LS means for each treatment group with corresponding SEs and treatment differences of LS means with corresponding two-sided 95% CIs and p-value will be presented. The ANCOVA model will be fitted separately at 6 weeks and 12 weeks.

A nonparametric approach will be used for the analysis of triglycerides (percent change from baseline). The Hodges-Lehmann method will be used to estimate the median difference and its corresponding 95% CI for percent changes between the treatment groups.

15.2.4 Sensitivity Analysis of Secondary Effectiveness Variables

The same models as in the secondary analysis will be fitted for PPS, and corresponding descriptive statistics will be also presented.

15.3 Exploratory Effectiveness

If possible, subgroup analysis will be performed on the primary endpoint and all secondary endpoints at 6 and/or 12 weeks to assess the homogeneity of the treatment effect across various subgroups including history of statin administration, age, sex, and status of a dose up-titration. The subgroups are defined in section 8.5.

The same models as in the primary and secondary analysis will be fitted for each subgroup in FAS and PPS, and corresponding descriptive statistics will be also presented.

16. SAFETY OUTCOMES

All safety analyses will be performed on the SAS.

16.1 Study Medication Exposure and Compliance

The following information on exposure and compliance to study medications will be reported:

- Treatment exposure (days): date of last dose of study medication – date of first dose of study medication + 1
- Total number of tablets taken: sum of all 'actual amount administered' during the study period
- Compliance (%): (total number of tablets taken / treatment exposure) x 100
- Status of a dose-up-titration at Week 6: Yes, No

Continuous variables will be summarized using number of patients without missing values, mean, standard deviation, median, 1st quartile, 3rd quartile, minimum, and maximum by treatment group and total. Categorical variables will be summarized using the total number of patients without missing values and the number and percentage of patients for each category by treatment group and total.

16.2 Adverse Events

The definition of AEs in the study protocol is restricted to the treatment-emergent adverse events (TEAEs) occurring after the first treatment exposure, while for this study AEs were collected from screening.

A TEAE is defined as AEs that first occurred or worsened in severity on or after the first administration of the study treatment during the treatment period.

TEAEs at 6 weeks will include TEAEs with the start date prior to 6 week (< Day 43) after the first administration of the study treatment. Imputation rules of partial/missing start/stop date on the AEs will be applied according to Appendix 1. Except for imputation of partial dates, no imputation will be done for missing values for all safety analyses.

A treatment-emergent serious adverse event (TESAE) and a treatment-related adverse event (TRAE) is identified by the response of 'Yes' on the Seriousness and Causality, respectively, on the AE page of eCRF. A TEAE leading to the premature discontinuation of the study is one with the response of 'Drug Withdrawn' on 'Action Taken with Study Drug' on the AE page of eCRF.

The number and percentage of patients experiencing at least one of TEAEs, TESAEs, TRAEs, and TEAEs leading to the premature discontinuation of the study at 6 weeks and 12 weeks will be presented by treatment group and tested using Chi-square test or Fisher's exact test as appropriate. The difference in the percentages will be presented with its corresponding 95% CI and p-value.

In addition, the numbers and percentages of patients experiencing at least one of TEAEs will be summarized by SOC and PT according to the MedDRA dictionary for each treatment group.

Individual TESAEs and TEAEs leading to the premature discontinuation of the study will be also listed with details including patient number, institution name, treatment group, sex, age, reported term, SOC, PT, start and stop date, severity, seriousness with criteria, causality, action taken and outcome.

16.3 Vital Signs

The following vital sign parameters will be reported:

- Weight (kg)

- Systolic blood pressure (SBP) (mmHg)
- Diastolic blood pressure (DBP) (mmHg)
- Heart rate (Beat/min)

Each parameter at each visit and its change from baseline will be summarized using number of patients without missing values, mean, standard deviation, median, 1st quartile, 3rd quartile, minimum, and maximum by treatment group.

16.4 Laboratory tests

The following hematology, clinical chemistry and urinalysis parameters will be reported:

- Hematology: Platelet count, Red blood cell count, Total white blood cell (WBC), Hemoglobin, Hematocrit, Neutrophils, Lymphocytes, Monocytes, Eosinophils, Basophils
- Clinical chemistry: Blood urea nitrogen (BUN), Creatinine, Glucose, HbA1c, Gamma glutamyl transferase (GGT), Potassium, Sodium, Calcium, Albumin, Lactate Dehydrogenase (LDH), Uric acid, AST, ALT, Alkaline phosphatase (ALP), CK, Chloride, Total bilirubin, Direct bilirubin, Total protein, Phosphate, C-reactive protein
- Urianalysis: pH, Specific Gravity, Leucocytes, Protein, Bilirubin, Urobilinogen, Ketones, Red blood cells, Nitrite, Glucose

For quantitative laboratory tests, each parameter at each visit and its change from baseline will be summarized using number of patients without missing values, mean, standard deviation, median, 1st quartile, 3rd quartile, minimum, and maximum by treatment group.

A listing of patients with clinically significant changes in each parameter from baseline will be presented including patient number, institution name, treatment group, sex, age, visit, assessment date, parameter, observed value, baseline value, and normal range.

16.5 12-lead ECG

A listing of patients with clinically significant changes in 12-lead ECG from baseline will be presented including patient number, institution name, treatment group, sex, age, visit, date of 12-lead ECG, PR intervals, QRS intervals, QT intervals, QTc intervals, baseline value and normal range.

17. REFERENCES

Not applicable.

17.1 APPENDIX 1. Partial Date Conventions

Imputed dates will NOT be presented in the listings.

ALGORITHM FOR TREATMENT EMERGENCE OF ADVERSE EVENTS:

START DATE	STOP DATE	ACTION
Known	Known	• The start date of AE < the first date of study treatment, Non-TEAEs • the start date of AE ≥ the first date of study treatment, TEAEs (For TEAE at 6 weeks, the start date of AE ≥ the first date of study treatment and the start date of AE < the first date of study treatment + 6 weeks)
	Partial	
	Missing	
Partial	Known	In case of missing or unknown month and day of the start date of AE, • The year of the start date of AE < the year of the first date of study treatment, Non-TEAEs; • The year of the start date of AE = the year of the first date of study treatment and the stop date of AE < the first date of study treatment, Non-TEAEs; • The year of the start date of AE = the year of the first date of study treatment and the stop date of AE ≥ the first date of study treatment, TEAEs; • The year of the start date of AE > the year of the first date of study treatment, TEAEs; (For TEAEs at week 6, the year of the start date of AE > the year of the first date of study

START DATE	STOP DATE	ACTION
		treatment and the month and day of the first date of study treatment ≥ 21st Nov) In case of missing or unknown day of the start date of AE, • The year and month of the start date of AE < the year and month of the first date of study treatment, Non-TEAEs; • The year and month of the start date of AE = the year and month of the first date of study treatment and the stop date of AE < the first date of study treatment, Non-TEAEs; • The year and month of the start date of AE = the year and month of the first date of study treatment and the stop date of AE ≥ the first date of study treatment, TEAEs; • The year and month of the start date of AE > the year and month of the first date of study treatment, TEAEs (For TEAEs at week 6, the year and month of start date ≤ the year and month of the first date of study treatment + 6 weeks)
	Partial	Missing or unknown month and day of the stop date of AE will be replaced by 31st Dec. Missing or unknown day of the stop date of AE will be replaced by the last day of the month.

START DATE	STOP DATE	ACTION
		In case of missing or unknown month and day of the start date of AE, • The year of the start date of AE < the year of the first date of study treatment, Non-TEAEs; • The year of the start date of AE = the year of the first date of study treatment and the stop date < the first date of study treatment, Non-TEAEs; • The year of the start date of AE = the year of the first date of study treatment and the stop date ≥ the first date of study treatment, TEAEs; • The year of the start date of AE > the year of the first date of study treatment, TEAEs (For TEAEs at 6 weeks, the year of the start date of AE > the year of the first date of study treatment and the month and day of the first date of study treatment ≥ 21st Nov) In case of missing or unknown day of the start date of AE, • The year and month of the start date of AE < the year and month of the first date of study treatment, Non-TEAEs; • The year and month of the start date of AE = the year and month of the first date of study treatment and the stop date < the first date of study treatment, Non-TEAEs;

START DATE	STOP DATE	ACTION
		• The year and month of the start date of AE = the year and month of the first date of study treatment and the stop date ≥ the first date of study treatment, TEAEs • The year and month of the start date of AE > the year and month of the first date of study treatment, TEAEs (For TEAEs at 6 weeks, the year and month of start date ≤ the year and month of the first date of study treatment + 6 weeks)
	Missing	In case of missing or unknown month and day of the start date of AE, • The year of the start date of AE < the year of the first date of study treatment, Non-TEAEs; • the year of the start date of AE ≥ the year of the first date of study treatment, TEAEs (For TEAEs at 6 weeks, the year of the start date of AE = the year of the first date of study or the year of the start date of AE > the year of the first date of study treatment and the month and day of the first date of study treatment ≥ 21st Nov) In case of missing or unknown day of the start date of AE, • The year and month of the start date of AE < the year and month of the first date of study treatment, Non-TEAEs;

START DATE	STOP DATE	ACTION
		• The year and month of the start date of AE ≥ the year and month of the first date of study treatment, TEAEs (For TEAEs at 6 weeks, the year and month of start date ≤ the year and month of the first date of study treatment + 6 weeks)
Missing	Known	• The stop date of AE < the first date of study treatment, Non-TEAEs; • The stop date of AE ≥ the first date of study treatment, TEAEs and TEAEs at 6 weeks
	Partial	Missing or unknown month and day of the stop date of AE will be replaced by 31st Dec. Missing or unknown day of the stop date of AE will be replaced by the last day of the month. • The stop date of AE < the first date of study treatment, Non-TEAEs; • The stop date of AE ≥ the first date of study treatment, TEAEs and TEAEs at 6 weeks
	Missing	TEAEs as well as TEAEs at 6 weeks

ALGORITHM FOR PRIOR/ CONCOMITANT MEDICATIONS/ PROCEDURES:

START DATE	STOP DATE	ACTION
Will not imputed	Known	If the stop date of medications/procedures < the first date of study treatment, assign as prior; If the stop date of medications/procedures ≥ the first date of study treatment or if ongoing is checked, assign as concomitant
	Partial	Impute the stop date of medications/procedures as the latest possible date (i.e. last day of month if day unknown or 31st December if day and month are unknown), then: If the stop date of medications/procedures < the first date of study treatment, assign as prior; If the stop date of medications/procedures ≥ the first date of study treatment or ongoing is checked, assign as concomitant
	Missing	Assign as concomitant

17.2 APPENDIX 2. TLF Shells

Table 1. Patient Disposition (Randomized Patients)

	Eze/Ato n(%)	Ato n(%)	Total n(%)
Randomized	00	00	00
Treated	00 (00.00)	00 (00.00)	00 (00.00)
Not treated	00 (00.00)	00 (00.00)	00 (00.00)
Completed	00 (00.00)	00 (00.00)	00 (00.00)
Early discontinued	00 (00.00)	00 (00.00)	00 (00.00)
Violation of inclusion/exclusion criteria	00 (00.00)	00 (00.00)	00 (00.00)
Lost to follow-up	00 (00.00)	00 (00.00)	00 (00.00)
AST or ALT level > 3×ULN for 2 consecutive times	00 (00.00)	00 (00.00)	00 (00.00)
CK > 10×ULN for 2 consecutive times	00 (00.00)	00 (00.00)	00 (00.00)
Pregnancy	00 (00.00)	00 (00.00)	00 (00.00)
Termination of the study by the investigator or Sponsor	00 (00.00)	00 (00.00)	00 (00.00)
Difficult to continue the study according to the judgment of the investigator	00 (00.00)	00 (00.00)	00 (00.00)
Adverse event	00 (00.00)	00 (00.00)	00 (00.00)
Informed consent withdrawal	00 (00.00)	00 (00.00)	00 (00.00)
Other	00 (00.00)	00 (00.00)	00 (00.00)

AST: aspartate aminotransferase; ALT: alanine aminotransferase; CK: creatine kinase; ULN: upper limit of normal.
n = the number of patients in each category.
Percentage (%) = 100 * (n / the number of randomized patients).

Table 2. Individual Listing of the Patients Discontinued from the Study (Randomized Patients)

Patient number	Institution name	Treatment group	Sex	Age	Date of informed consent	Date of last visit	Reason for discontinuation
000	000	000	000	000	000	000	000

Table 3. Information on Screening Failures (Enrolled Patients)

	Total n(%)
All screened	00
Screen failure	00 (00.00)
Violation of inclusion/exclusion criteria	00 (00.00)
Informed consent withdrawal	00 (00.00)
Other	00 (00.00)

n = the number of patients in each category.
Percentage (%) = 100 * (n / the number of enrolled patients).

Table 4. Individual Listing of the Participants Who Failed Screening from the Study (Enrolled Patients)

Participant number	Institution name	Sex	Age	Date of informed consent	Reason for screen failure
000	000	000	000	000	000

Table 5. Disposition by Analysis Sets (Randomized Patients)

	Eze/Ato (N=00) n(%)	Ato (N=00) n(%)	Total (N=00) n(%)
Safety Analysis Set			
Yes	00 (00.00)	00 (00.00)	00 (00.00)
No	00 (00.00)	00 (00.00)	00 (00.00)
Not treated	00 (00.00)	00 (00.00)	00 (00.00)
Full Analysis Set			
Yes	00 (00.00)	00 (00.00)	00 (00.00)
No	00 (00.00)	00 (00.00)	00 (00.00)
Not treated	00 (00.00)	00 (00.00)	00 (00.00)
No baseline LDL-C assessment	00 (00.00)	00 (00.00)	00 (00.00)
No on-treatment LDL-C assessment	00 (00.00)	00 (00.00)	00 (00.00)
Per Protocol Analysis Set			
Yes	00 (00.00)	00 (00.00)	00 (00.00)
No	00 (00.00)	00 (00.00)	00 (00.00)
Violation of inclusion/exclusion criteria	00 (00.00)	00 (00.00)	00 (00.00)
Randomization error	00 (00.00)	00 (00.00)	00 (00.00)
No 6-week LDL-C assessment	00 (00.00)	00 (00.00)	00 (00.00)
IP noncompliance	00 (00.00)	00 (00.00)	00 (00.00)
Administration of prohibited concomitant medications	00 (00.00)	00 (00.00)	00 (00.00)
Study discontinuation before 6-week	00 (00.00)	00 (00.00)	00 (00.00)
Other	00 (00.00)	00 (00.00)	00 (00.00)

Deviations categories are not mutually exclusive. LDL-C: low-density lipoprotein cholesterol.
N = the number of randomized patients; n = the number of patients in each category.
Percentage (%) = 100 * (n / N).

Table 6. Individual Listing of the Patients Excluded from Each of the Analysis Set (Randomized Patients)

Patient number	Institution name	Treatment group	Sex	Age	Date of informed consent	Status of study completion	Analysis set excluded	Reasons for exclusion
000	000	000	000	000	000	000	000	000

Table 7. Major Protocol Deviations by Deviation Category (FAS)

	Eze/Ato (N=00) n(%)	Ato (N=00) n(%)	Total (N=00) n(%)
Any Major Protocol Deviation	00 (00.00)	00 (00.00)	00 (00.00)
Violation of inclusion/exclusion criteria	00 (00.00)	00 (00.00)	00 (00.00)
Randomization error	00 (00.00)	00 (00.00)	00 (00.00)
No 6-week LDL-C assessment	00 (00.00)	00 (00.00)	00 (00.00)
IP noncompliance	00 (00.00)	00 (00.00)	00 (00.00)
Administration of prohibited concomitant medications	00 (00.00)	00 (00.00)	00 (00.00)
Other	00 (00.00)	00 (00.00)	00 (00.00)

LDL-C: low-density lipoprotein cholesterol.
N = the number of randomized patients; n = the number of patients in each category.
Percentage (%) = 100 * (n / N).

Table 8. Individual Listing of the Patients with Major Protocol Deviations (Randomized Patients)

Patient number	Institution name	Treatment group	Sex	Age	Date of informed consent	Status of study completion	Protocol deviation category
000	000	000	000	000	000	000	000

Table 9. Demographic and Other Baseline Characteristics (FAS)

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)	Total (N=00)
Age (years)	Nx	00	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]	[00.00 - 00.00]
Age categories	Nx	00	00	00
<65	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
≥65	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Sex	Nx	00	00	00
Male	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Female	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Height (cm)	Nx	00	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]	[00.00 - 00.00]

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)	Total (N=00)
Weight (kg)	Nx	00	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]	[00.00 - 00.00]
BMI (kg/m^2)	Nx	00	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]	[00.00 - 00.00]
Smoking history	Nx	00	00	00
Currently smoking	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Past smoker	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Never smoked	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Alcohol history	Nx	00	00	00
Now drinking	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Past drinking	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Never drinking	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Alcohol Consumption [a]	Nx	00	00	00
<2 drinks per week	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
2-3 drinks per week	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
≥4 drinks per week	n(%)	00 (00.00)	00 (00.00)	00 (00.00)

FAS: full analysis set; BMI: body mass index; SD: standard deviation; Q1: 1st quartile; Q3: 3rd quartile; Min: minimum; Max: maximum.
N = the number of patients in FAS; Nx = the number of patients without missing values for each variable; n = the number of patients in each category.
Percentage (%) = 100 * (n / Nx).
[a] Denominator for percentages is number of patients whose alcohol history is 'Now drinking.
Note: BMI (kg/m^2) = weight (kg)/ height (m)^2

Table 10. Medical and Treatment History Related to Dyslipidemia (FAS)

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)	Total (N=00)
Dyslipidemia duration (years)	Nx	00	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00	00.00, 00.00

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)	Total (N=00)
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]	[00.00 - 00.00]
ACS	Nx	00	00	00
Yes	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
No	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Stable angina	Nx	00	00	00
Yes	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
No	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Coronary revascularization	Nx	00	00	00
Yes	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
No	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Stroke	Nx	00	00	00
Yes	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
No	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Transient ischemic attack	Nx	00	00	00
Yes	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
No	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Peripheral arterial disease	Nx	00	00	00
Yes	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
No	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Other clinical or unequivocal ASCVD on imaging	Nx	00	00	00
Yes	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
No	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Family history status	Nx	00	00	00
Yes	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
No	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Family history [a]	Nx	00	00	00
Father	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Mother	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Brothers/sisters	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Other	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
History of stain administration	Nx	00	00	00
Yes (≥4 weeks)	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
No (<4 weeks or naïve)	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
<4 weeks	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Naïve	n(%)	00 (00.00)	00 (00.00)	00 (00.00)

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)	Total (N=00)
Baseline LDL-C (mg/dL)	Nx	00	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]	[00.00 - 00.00]
Baseline LDL-C categories	Nx	00	00	00
<130	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
≥130 to <160	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
≥160	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
Baseline HDL-C (mg/dL)	Nx	00	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]	[00.00 - 00.00]
Baseline non-HDL-C	Nx	00	00	00
(mg/dL)	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]	[00.00 - 00.00]
Baseline triglycerides	Nx	00	00	00
(mg/dL)	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]	[00.00 - 00.00]
Baseline total cholesterol	Nx	00	00	00
(mg/dL)	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]	[00.00 - 00.00]

FAS: full analysis set; ACS: acute coronary syndrome; LDL-C: low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; SD: standard deviation; Q1: 1st quartile; Q3: 3rd quartile; Min: minimum; Max: maximum.
N = the number of patients in FAS; Nx = the number of patients without missing values for each variable; n = the number of patients in each category.
Percentage (%) = 100 * (n / Nx).
[a] as a multiple choice item, categories are not mutually exclusive.

Table 11. Summary of Medical History by SOC & PT (FAS)

Document: Document path and title

Template No.: CCI [redacted] Reference: CCI [redacted]

Effective Date: 15Oct2021

System Organ Class Preferred Term	Eze/Ato (N=00) n(%)	Ato (N=00) n(%)	Total (N=00) n(%)
Any Medical History	**00 (00.00)**	**00 (00.00)**	**00 (00.00)**
System Organ Class 1	**00 (00.00)**	**00 (00.00)**	**00 (00.00)**
Preferred Term 1	00 (00.00)	00 (00.00)	00 (00.00)
Preferred Term 2	00 (00.00)	00 (00.00)	00 (00.00)
System Organ Class 2	**00 (00.00)**	**00 (00.00)**	**00 (00.00)**
Preferred Term 1	00 (00.00)	00 (00.00)	00 (00.00)
Preferred Term 2	00 (00.00)	00 (00.00)	00 (00.00)

FAS: full analysis set.
N = the number of patients in FAS; n = the number of patients in each category.
Percentage (%) = 100 * (n / N).
Note: MedDRA (Version XX.X) SOC (System Organ Class) & PT (Preferred Term).

Table 12. Summary of Concomitant Illness by SOC & PT (FAS)

Repeated style; see Table 11.

Table 13. Summary of Prior Medications by Therapeutic Subgroup & Preferred Name (FAS)

Therapeutic Subgroup Preferred Name	Eze/Ato (N=00) n (%)	Ato (N=00) n (%)	Total (N=00) n (%)
Any Prior Medication	**00 (00.00)**	**00 (00.00)**	**00 (00.00)**
Therapeutic Subgroup 1	**00 (00.00)**	**00 (00.00)**	**00 (00.00)**
Preferred Name 1	00 (00.00)	00 (00.00)	00 (00.00)
Preferred Name 2	00 (00.00)	00 (00.00)	00 (00.00)
Therapeutic Subgroup 2	**00 (00.00)**	**00 (00.00)**	**00 (00.00)**
Preferred Name 1	00 (00.00)	00 (00.00)	00 (00.00)
Preferred Name 2	00 (00.00)	00 (00.00)	00 (00.00)

FAS: full analysis set.
N = the number of patients in FAS; n = the number of patients in each category.
Percentage (%) = 100 * (n / N).
Note: WHO-DD (Global 202X) Therapeutic Subgroup & Preferred Name.

Table 14. Summary of Concomitant Medications by Therapeutic Subgroup & Preferred Name (FAS)

Repeated style; see Table 13.

Table 15. Summary of Prior Medical Procedures by SOC & PT (FAS)

Repeated style; see Table 11.

Table 16. Summary of Concomitant Medical Procedures by SOC & PT (FAS)

Repeated style; see Table 11.

Table 17. Percentage Change in LDL-C from Baseline to Week 6 (FAS)

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)
Baseline	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Week 6	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Percentage change from baseline to Week 6			
a. Descriptive	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
b. ANCOVA [a]	LS Mean (SE)	00.00 (00.00)	00.00 (00.00)
	95% CI for LS Mean	(00.00, 00.00)	(00.00, 00.00)
	LS Mean Difference	00.00	
	95% CI for Difference	(00.00, 00.00)	
	p-value	0.000	

FAS: full analysis set; LDL-C: low-density lipoprotein cholesterol; SD: standard deviation; Q1: 1st quartile; Q3: 3rd quartile; Min: minimum; Max: maximum; ANCOVA: analysis of covariance; LS: least squares; SE: standard error; CI: confidence interval.

N = the number of patients in FAS; Nx = the number of patients without missing values.

[a] ANCOVA model with treatment group (Eze/Ato, Ato), history of statin administration (Yes, No), and baseline LDL-C.

Table 18. Percentage Change in LDL-C from Baseline to Week 6 (PPS)

Repeated style; see Table 17.

Table 19. Percentage Change in LDL-C from Baseline to Week 6 (Sensitivity - LOCF)

Repeated style; see Table 17.

Table 20. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (FAS)

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)
Week 6	Nx	00	00
	n(%)	00 (00.00)	00 (00.00)
	Percentage Difference	00.00	
	95% CI for Difference	(00.00, 00.00)	
	p-value [a]	0.000	
Week 12	Nx	00	00
	n(%)	00 (00.00)	00 (00.00)
	Percentage Difference	00.00	00.00
	95% CI for Difference	(00.00, 00.00)	
	p-value [a]	0.000	

FAS: full analysis set; LDL-C: low-density lipoprotein cholesterol; CI: confidence interval.
N = the number of patients in FAS; Nx = the number of patients without missing values; n = the number of patients achieving LDL-C goal of <55 mg/dL at each timepoint.
Percentage (%) = 100 * (n / Nx).
[a] Chi-square or Fisher's exact test

Table 21. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (PPS)

Repeated style; see Table 20.

Table 22. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (FAS)

Repeated style; see Table 20.

Table 23. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (PPS)

Repeated style; see Table 20.

Table 24. Percentage Change in LDL-C from Baseline to Week 12 (FAS)

Repeated style; see Table 17.

Table 25. Percentage Change in LDL-C from Baseline to Week 12 (PPS)

Repeated style; see Table 17.

Table 26. Percentage Change in HDL-C from Baseline to Week 6 and 12 (FAS)

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)
Baseline	Nx	00	00

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Week 6	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Week 12	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Percentage change from baseline to Week 6			
a. Descriptive	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
b. ANCOVA [a]	LS Mean (SE)	00.00 (00.00)	00.00 (00.00)
	95% CI for LS Mean	(00.00, 00.00)	(00.00, 00.00)
	LS Mean Difference	00.00	
	95% CI for Difference	(00.00, 00.00)	
	p-value	0.000	
Percentage change from baseline to Week 12			
a. Descriptive	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
b. ANCOVA [a]	LS Mean (SE)	00.00 (00.00)	00.00 (00.00)
	95% CI for LS Mean	(00.00, 00.00)	(00.00, 00.00)
	LS Mean Difference	00.00	
	95% CI for Difference	(00.00, 00.00)	
	p-value	0.000	

FAS: full analysis set; HDL-C: high-density lipoprotein cholesterol; SD: standard deviation; Q1: 1st quartile; Q3: 3rd quartile; Min: minimum; Max: maximum; ANCOVA: analysis of covariance; LS: least squares; SE: standard error; CI: confidence interval.

N = the number of patients in FAS; Nx = the number of patients without missing values.

[a] ANCOVA model with treatment group (Eze/Ato, Ato), history of statin administration (Yes, No), and baseline HDL-C.

Table 27. Percentage Change in HDL-C from Baseline to Week 6 and 12 (PPS)

Repeated style; see Table 26.

Table 28. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (FAS)
Repeated style; see Table 26.

Table 29. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (PPS)
Repeated style; see Table 26.

Table 30. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (FAS)

Item		Statistics	Eze/Ato (N=00)	Ato (N=00)
Baseline		Nx	00	00
		Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
		Median	00.00	00.00
		Q1, Q3	00.00, 00.00	00.00, 00.00
		[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Week 6		Nx	00	00
		Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
		Median	00.00	00.00
		Q1, Q3	00.00, 00.00	00.00, 00.00
		[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Week 12		Nx	00	00
		Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
		Median	00.00	00.00
		Q1, Q3	00.00, 00.00	00.00, 00.00
		[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Percentage change from baseline to Week 6				
c. Descriptive		Nx	00	00
		Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
		Median	00.00	00.00
		Q1, Q3	00.00, 00.00	00.00, 00.00
		[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
d. +Nonparametric [a]		Difference in Medians	00.00	
		95% CI for Difference	(00.00, 00.00)	
Percentage change from baseline to Week 12				
c. Descriptive		Nx	00	00
		Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
		Median	00.00	00.00
		Q1, Q3	00.00, 00.00	00.00, 00.00
		[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
d. Nonparametric [a]		Difference in Medians	00.00	
		95% CI for Difference	(00.00, 00.00)	

FAS: full analysis set; HDL-C: high-density lipoprotein cholesterol; SD: standard deviation; Q1: 1st quartile; Q3: 3rd quartile; Min: minimum; Max: maximum; SE: standard error; CI: confidence interval.
N = the number of patients in FAS; Nx = the number of patients without missing values.
[a] Estimate of difference in median location using the Hodges Lehmann method and corresponding 95% CIs.

Table 31. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (PPS)
Repeated style; see Table 30.

Table 32. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (FAS)
Repeated style; see Table 26.

Table 33. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (PPS)
Repeated style; see Table 26.

Table 34. Percentage Change in LDL-C from Baseline to Week 6 and 12 (Male in FAS)
Repeated style; see Table 26.

Table 35. Percentage Change in LDL-C from Baseline to Week 6 and 12 (Male in PPS)
Repeated style; see Table 26.

Table 36. Percentage Change in HDL-C from Baseline to Week 6 and 12 (Male in FAS)
Repeated style; see Table 26.

Table 37. Percentage Change in HDL-C from Baseline to Week 6 and 12 (Male in PPS)
Repeated style; see Table 26.

Table 38. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (Male in FAS)
Repeated style; see Table 26.

Table 39. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (Male in PPS)
Repeated style; see Table 26.

Table 40. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (Male in FAS)
Repeated style; see Table 30.

Table 41. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (Male in PPS)
Repeated style; see Table 30.

Table 42. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (Male in FAS)

Repeated style; see Table 26.

Table 43. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (Male in PPS)

Repeated style; see Table 26.

Table 44. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (Male in FAS)

Repeated style; see Table 20.

Table 45. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (Male in PPS)

Repeated style; see Table 20.

Table 46. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (Male in FAS)

Repeated style; see Table 20.

Table 47. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (Male in PPS)

Repeated style; see Table 20.

Table 48. Percentage Change in LDL-C from Baseline to Week 6 and 12 (Female in FAS)

Repeated style; see Table 26.

Table 49. Percentage Change in LDL-C from Baseline to Week 6 and 12 (Female in PPS)

Repeated style; see Table 26.

Table 50. Percentage Change in HDL-C from Baseline to Week 6 and 12 (Female in FAS)

Repeated style; see Table 26.

Table 51. Percentage Change in HDL-C from Baseline to Week 6 and 12 (Female in PPS)

Repeated style; see Table 26.

Table 52. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (Female in FAS)

Repeated style; see Table 26.

Table 53. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (Female in PPS)

Repeated style; see Table 26.

Table 54. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (Female in FAS)

Repeated style; see Table 30.

Table 55. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (Female in PPS)

Repeated style; see Table 30.

Table 56. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (Female in FAS)

Repeated style; see Table 26.

Table 57. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (Female in PPS)

Repeated style; see Table 26.

Table 58. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (Female in FAS)

Repeated style; see Table 20.

Table 59. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (Female in PPS)

Repeated style; see Table 20.

Table 60. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (Female in FAS)

Repeated style; see Table 20.

Table 61. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (Female in PPS)

Repeated style; see Table 20.

Table 62. Percentage Change in LDL-C from Baseline to Week 6 and 12 (Age <65 in FAS)

Repeated style; see Table 26.

Table 63. Percentage Change in LDL-C from Baseline to Week 6 and 12 (Age <65 in PPS)

Repeated style; see Table 26.

Table 64. Percentage Change in HDL-C from Baseline to Week 6 and 12 (Age <65 in FAS)

Repeated style; see Table 26.

Table 65. Percentage Change in HDL-C from Baseline to Week 6 and 12 (Age <65 in PPS)

Repeated style; see Table 26.

Table 66. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (Age <65 in FAS)

Repeated style; see Table 26.

Table 67. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (Age <65 in PPS)

Repeated style; see Table 26.

Table 68. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (Age <65 in FAS)

Repeated style; see Table 30.

Table 69. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (Age <65 in PPS)

Repeated style; see Table 30.

Table 70. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (Age <65 in FAS)

Repeated style; see Table 26.

Table 71. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (Age <65 in PPS)

Repeated style; see Table 26.

Table 72. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (Age <65 in FAS)

Repeated style; see Table 20.

Table 73. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (Age <65 in PPS)

Repeated style; see Table 20.

Table 74. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (Age <65 in FAS)

Repeated style; see Table 20.

Table 75. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (Age <65 in PPS)

Repeated style; see Table 20.

Table 76. Percentage Change in LDL-C from Baseline to Week 6 and 12 (age ≥ 65 in FAS)

Repeated style; see Table 26.

Table 77. Percentage Change in LDL-C from Baseline to Week 6 and 12 (age ≥ 65 in PPS)

Repeated style; see Table 26.

Table 78. Percentage Change in HDL-C from Baseline to Week 6 and 12 (age ≥ 65 in FAS)

Repeated style; see Table 26.

Table 79. Percentage Change in HDL-C from Baseline to Week 6 and 12 (age ≥ 65 in PPS)

Repeated style; see Table 26.

Table 80. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (age ≥ 65 in FAS)

Repeated style; see Table 26.

Table 81. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (age ≥ 65 in PPS)

Repeated style; see Table 26.

Table 82. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (age ≥ 65 in FAS)

Repeated style; see Table 30.

Table 83. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (age ≥ 65 in PPS)

Repeated style; see Table 30.

Table 84. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (age ≥ 65 in FAS)

Repeated style; see Table 26.

Table 85. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (age ≥ 65 in PPS)

Repeated style; see Table 26.

Table 86. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (Age ≥65 in FAS)

Repeated style; see Table 20.

Table 87. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (Age ≥65 in PPS)

Repeated style; see Table 20.

Table 88. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (Age ≥65 in FAS)

Repeated style; see Table 20.

Table 89. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (Age ≥65 in PPS)

Repeated style; see Table 20.

Table 90. Percentage Change in LDL-C from Baseline to Week 6 and 12 (with Statin Administration History in FAS)

Repeated style; see Table 26.

Table 91. Percentage Change in LDL-C from Baseline to Week 6 and 12 (with Statin Administration History in PPS)

Repeated style; see Table 26.

Table 92. Percentage Change in HDL-C from Baseline to Week 6 and 12 (with Statin Administration History in FAS)

Repeated style; see Table 26.

Table 93. Percentage Change in HDL-C from Baseline to Week 6 and 12 (with Statin Administration History in PPS)

Repeated style; see Table 26.

Table 94. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (with Statin Administration History in FAS)

Repeated style; see Table 26.

Table 95. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (with Statin Administration History in PPS)

Repeated style; see Table 26.

Table 96. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (with Statin Administration History in FAS)

Repeated style; see Table 30.

Table 97. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (with Statin Administration History in PPS)

Repeated style; see Table 30.

Table 98. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (with Statin Administration History in FAS)

Repeated style; see Table 26.

Table 99. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (with Statin Administration History in PPS)

Repeated style; see Table 26.

Table 100. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (with Statin Administration History in FAS)

Repeated style; see Table 20.

Table 101. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (with Statin Administration History in PPS)

Repeated style; see Table 20.

Table 102. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (with Statin Administration History in FAS)

Repeated style; see Table 20.

Table 103. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (with Statin Administration History in PPS)

Repeated style; see Table 20.

Table 104. Percentage Change in LDL-C from Baseline to Week 6 and 12 (without Statin Administration History in FAS)

Repeated style; see Table 26.

Table 105. Percentage Change in LDL-C from Baseline to Week 6 and 12 (without Statin Administration History in PPS)

Repeated style; see Table 26.

Table 106. Percentage Change in HDL-C from Baseline to Week 6 and 12 (without Statin Administration History in FAS)

Repeated style; see Table 26.

Table 107. Percentage Change in HDL-C from Baseline to Week 6 and 12 (without Statin Administration History in PPS)

Repeated style; see Table 26.

Table 108. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (without Statin Administration History in FAS)

Repeated style; see Table 26.

Table 109. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (without Statin Administration History in PPS)

Repeated style; see Table 26.

Table 110. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (without Statin Administration History in FAS)

Repeated style; see Table 30.

Table 111. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (without Statin Administration History in PPS)

Repeated style; see Table 26.

Table 112. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (without Statin Administration History in FAS)

Repeated style; see Table 26.

Table 113. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (without Statin Administration History in PPS)

Repeated style; see Table 26.

Table 114. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (without Statin Administration History in FAS)

Repeated style; see Table 20.

Table 115. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 6 and 12 (without Statin Administration History in PPS)

Repeated style; see Table 20.

Table 116. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (without Statin Administration History in FAS)

Repeated style; see Table 20.

Table 117. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and 12 (without Statin Administration History in PPS)

Repeated style; see Table 20.

Table 118. Percentage Change in LDL-C from Baseline to Week 6 and 12 (with Dose Up-Titration at Week 6 in FAS)

Repeated style; see Table 26.

Table 119. Percentage Change in LDL-C from Baseline to Week 6 and 12 (with Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 26.

Table 120. Percentage Change in HDL-C from Baseline to Week 6 and 12 (with Dose Up-Titration at Week 6 in FAS)

Repeated style; see Table 26.

Table 121. Percentage Change in HDL-C from Baseline to Week 6 and 12 (with Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 26.

Table 122. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (with Dose Up-Titration at Week 6 in FAS)

Repeated style; see Table 26.

Table 123. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (with Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 26.

Table 124. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (with Dose Up-Titration at Week 6 in FAS)

Repeated style; see Table 30.

Table 125. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (with Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 30.

Table 126. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (with Dose Up-Titration at Week 6 in FAS)

Repeated style; see Table 26.

Table 127. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (with Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 26.

Table 128. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 12 (with Dose Up-Titration at Week 6 in FAS)

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)
Week 12	Nx	00	00
	n(%)	00 (00.00)	00 (00.00)
	Percentage Difference	00.00	00.00
	95% CI for Difference	(00.00, 00.00)	
	p-value [a]	0.000	

FAS: full analysis set; LDL-C: low-density lipoprotein cholesterol; CI: confidence interval.
N = the number of patients in FAS; Nx: the number of patients without missing values; n = the number of patients achieving LDL-C goal of <55 mg/dL at Week 12.
Percentage (%) = 100 * (n / N).
[a] Chi-square or Fisher's exact test

Table 129. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 12 (with Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 128.

Table 130. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and Week 12 (with Dose Up-Titration at Week 6 in FAS)

Repeated style; see Table 20.

Table 131. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 6 and Week 12 (with Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 20.

Table 132. Percentage Change in LDL-C from Baseline to Week 6 and 12 (without Dose Up-Titration at Week 6 in FAS)

Repeated style; see Table 26.

Table 133. Percentage Change in LDL-C from Baseline to Week 6 and 12 (without Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 26.

Table 134. Percentage Change in HDL-C from Baseline to Week 6 and 12 (without Dose Up-Titration at Week 6 in FAS)

Repeated style; see Table 26.

Table 135. Percentage Change in HDL-C from Baseline to Week 6 and 12 (without Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 26.

Table 136. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (without Dose Up-Titration at Week 6 in FAS)

Repeated style; see Table 26.

Table 137. Percentage Change in non-HDL-C from Baseline to Week 6 and 12 (without Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 26.

Table 138. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (without Dose Up-Titration at Week 6 in FAS)

Repeated style; see Table 30.

Table 139. Percentage Change in Triglycerides from Baseline to Week 6 and 12 (without Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 30.

Table 140. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (without Dose Up-Titration at Week 6 in FAS)

Repeated style; see Table 26.

Table 141. Percentage Change in Total Cholesterol from Baseline to Week 6 and 12 (without Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 26.

Table 142. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 12 (without Dose Up-Titration at Week 6 in FAS)

Repeated style; see Table 128.

Table 143. Proportion of patients achieving LDL-C goal of <55 mg/dL at Week 12 (without Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 128.

Table 144. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 12 (without Dose Up-Titration at Week 6 in FAS)

Repeated style; see Table 128.

Table 145. Proportion of patients achieving LDL-C goal of <70 mg/dL at Week 12 (without Dose Up-Titration at Week 6 in PPS)

Repeated style; see Table 128.

Table 146. Extent of Exposure to Study Medication (SAS)

Item	Categorization/ Statistics	Eze/Ato (N=00)	Ato (N=00)	Total (N=00)
Treatment exposure (days)	Nx	00	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]	[00.00 - 00.00]
Total number of tablets taken	Nx	00	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]	[00.00 - 00.00]
Compliance (%)	Nx	00	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]	[00.00 - 00.00]
Dose Up-titration at Week 6	Nx	00	00	00
Yes	n(%)	00 (00.00)	00 (00.00)	00 (00.00)
No	n(%)	00 (00.00)	00 (00.00)	00 (00.00)

SAS: safety analysis set; SD: standard deviation; Q1: 1st quartile; Q3: 3rd quartile; Min: minimum; Max: maximum.
N = the number of patients in SAS; Nx = the number of patients without missing values for each variable; n = the number of patients in each category.
Percentage (%) = 100 * (n / Nx).

Note 1: treatment exposure (days) is calculated using (date of last dose of study medication – date of first dose of study medication + 1).
Note 2: total number of tablets taken is calculated as sum of all actual amount administered during the study period.
Note 3: compliance is calculated using (total number of tablets taken/treatment exposure) x 100.

Table 147. Summary of Adverse Events at Week 6 (SAS)

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)
Any TEAE	n(%)	00 (00.00)	00 (00.00)
	Percentage Difference	00.00	
	95% CI for Difference	(00.00, 00.00)	
	p-value [a]	0.000	
Any TESAE	n(%)	00 (00.00)	00 (00.00)
	Percentage Difference	00.00	
	95% CI for Difference	(00.00, 00.00)	
	p-value [a]	0.000	
Any TRAE	n(%)	00 (00.00)	00 (00.00)
	Percentage Difference	00.00	
	95% CI for Difference	(00.00, 00.00)	
	p-value [a]	0.000	
Any TEAE leading to the premature discontinuation	n(%)	00 (00.00)	00 (00.00)
	Percentage Difference	00.00	
	95% CI for Difference	(00.00, 00.00)	
	p-value [a]	0.000	

SAS: safety analysis set; TEAE: treatment-emergent adverse event; TESAE: treatment-emergent serious adverse event; TRAE: treatment-related adverse event; CI: confidence interval.
N = the number of patients in SAS; n = the number of patients in each category.
Percentage (%) = 100 * (n / N).
[a] Chi-square or Fisher's exact test.

Table 148. Summary of Adverse Events at Week 12 (SAS)

Repeated style; see Table 147.

Table 149. Summary of TEAEs by SOC & PT (SAS)

System Organ Class Preferred Term	Eze/Ato (N=00) n(%)	Ato (N=00) n(%)
Any TEAE	**00 (00.00)**	**00 (00.00)**
System Organ Class 1	**00 (00.00)**	**00 (00.00)**
Preferred Term 1	00 (00.00)	00 (00.00)
Preferred Term 2	00 (00.00)	00 (00.00)
System Organ Class 2	**00 (00.00)**	**00 (00.00)**

System Organ Class Preferred Term	Eze/Ato (N=00) n(%)	Ato (N=00) n(%)
Preferred Term 1	00 (00.00)	00 (00.00)
Preferred Term 2	00 (00.00)	00 (00.00)

SAS: safety analysis set; TEAE: treatment-emergent adverse event.
N = the number of patients in SAS; n = the number of patients in each category.
Percentage (%) = 100 * (n / N).
Note: MedDRA (Version XX.X) SOC (System Organ Class) & PT (Preferred Term).

Table 150. Individual Listings of TESAEs (SAS)

Patient No.	Institution Name	Treatment group	Sex	Age	Reported Term / SOC/ PT	Start/ End Date	Severity	Seriousness with criteria	Casualty	Action Taken	Outcome
00	00	00	00	00	00/ 00/ 00	00 - 00	00	00	00	00	00

TESAEs: treatment-emergent serious adverse events.
Note: MedDRA (Version XX.X) SOC (System Organ Class) & PT (Preferred Term).

Table 151. Individual Listings of TEAEs Leading to The Premature Discontinuation (SAS)

Repeated style; see Table 150.

Table 152. Summary of Vital Signs at Week 6 and 12 (SAS)

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)
Weight (kg)			
Baseline	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Week 6	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Week 12	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Change from Baseline to Week 6	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Change from baseline to Week 12	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
SBP (mmHg)			
Baseline	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Week 6	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Week 12	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Change from Baseline to Week 6	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Change from baseline to Week 12	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
DBP (mmHg)			
Baseline	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Week 6	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Week 12	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Change from Baseline to Week 6	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Change from baseline to Week 12	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Heart Rate (beat/min)			
Baseline	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Week 6	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]

Item	Statistics	Eze/Ato (N=00)	Ato (N=00)
Week 12	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Change from Baseline to Week 6	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]
Change from baseline to Week 12	Nx	00	00
	Mean ± SD	00.00 ± 00.00	00.00 ± 00.00
	Median	00.00	00.00
	Q1, Q3	00.00, 00.00	00.00, 00.00
	[Min – Max]	[00.00 - 00.00]	[00.00 - 00.00]

SAS: safety analysis set; SBP: systolic blood pressure; DBP: diastolic blood pressure; SD: standard deviation; Q1: 1st quartile; Q3: 3rd quartile; Min: minimum; Max: maximum.
N = the number of patients in SAS; Nx = the number of patients without missing values.

Table 153. Summary of Hematology at Week 6 and 12 (SAS)

Repeated style; see Table 152.

Table 154. Individual Listings of Clinically Significant Changes in Hematology from Baseline (SAS)

Patient No.	Institution Name	Treatment group	Sex	Age	Visit	Assessment date	Parameter	Observed value	Baseline value	Normal range
00	00	00	00	00	00	00	00	00	00	00

Table 155. Summary of Clinical Chemistry at Week 6 and 12 (SAS)

Repeated style; see Table 152.

Table 156. Individual Listings of Clinically Significant Changes in Clinical Chemistry from Baseline (SAS)

Repeated style; see Table 154.

Table 157. Summary of Urinalysis at Week 6 and 12 (SAS)

Repeated style; see Table 152.

Table 158. Individual Listings of Clinically Significant Changes in Urinalysis from Baseline (SAS)

Repeated style; see Table 154.

Table 159. Individual Listings of Clinically Significant Changes in 12-lead ECG (SAS)

Patient No.	Institution Name	Treatment group	Sex	Age	Visit	Assessment date	PR/QRS/QT/QTc Interval	Baseline PR/QRS/QT/QTc Interval	Normal range
00	00	00	00	00	00	00	00	00	00

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