Statistical Analysis Plan J2G-OX-JZJE Final Version

A Phase 1, Open-Label, Parallel-Cohort, Single-Dose Study to Evaluate the Effect of Renal Impairment on the Pharmacokinetics of LOXO-292

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16.1.9 Documentation of Statistical Methods

16.1.9.1 Statistical Analysis Plan

Statistical Analysis Plan

A Phase 1, Open-Label, Parallel-Cohort, Single-Dose Study to Evaluate the Effect of Renal Impairment on the Pharmacokinetics of LOXO-292

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Statistical Analysis Plan Signature Page

Compound Name: LOXO-292

Protocol: LOXO-RET-18023

Study Title: A Phase 1, Open-Label, Parallel-Cohort, Single-Dose Study to Evaluate the Effect of Renal Impairment on the Pharmacokinetics of LOXO-292

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1. INTRODUCTION

The following statistical analysis plan (SAP) provides the framework for the summarization of the data from study LOXO-RET-18023. The SAP may change due to unforeseen circumstances. Any changes made from the planned analysis within the protocol or after the locking of the database will be documented in the clinical study report (CSR). The section referred to as Table Shells within this SAP describes the traceability of the tables, figures, and listings (TFLs) back to the data. Note that the header for this page will be the one used for the main body of the CSR.

Any additional exploratory analyses not addressed within this SAP and/or driven by the data, or requested by Loxo Oncology, Inc., will be considered out of scope and will be described in the CSR as needed.

2. OBJECTIVES AND ENDPOINTS

2.1 Objectives

Primary:

To compare the plasma pharmacokinetics (PK) of LOXO-292 following administration in subjects with varying degrees of renal impairment (RI) (i.e., mild, moderate, and severe) compared to healthy matched control subjects.

Secondary:

1. To evaluate the safety and tolerability of LOXO-292 in subjects with RI.
2. To compare the urine PK of LOXO-292 following administration in subjects with varying degrees of RI (i.e., mild, moderate, and severe) compared to healthy matched control subjects.

2.2 Endpoints

Pharmacokinetics:

The following PK parameters will be calculated for LOXO-292 in plasma, as appropriate: AUC0-t, AUC0-inf, AUC%extrap, Cmax, Tmax, Kel, t½, CL/F, and Vz/F.

The following PK parameters will be calculated for unbound LOXO-292: AUC0-t,u, AUC0-inf,u, Cmax,u, CL/F,u, and Vz/F,u.

The following PK parameters will be calculated for LOXO-292 in urine, as appropriate, in all cohorts: Ae, Fe, and CLr.

Safety:

Safety endpoints will include 12-lead electrocardiograms (ECGs), physical examinations, vital signs, clinical laboratory tests, and adverse events (AEs).

3. STUDY DESIGN

This is a non-randomized, open-label, parallel-cohort, multiple-site, single-dose study to compare the PK of LOXO-292 in subjects with mild, moderate, and severe RI compared to healthy matched control subjects matched 1:1 for age, body mass index (BMI), and sex.

Up to 48, adult male and female subjects will be enrolled.

Subjects with RI:

Up to 24 subjects with RI will be enrolled as follows:

Up to eight (8) subjects with mild RI.

Up to eight (8) subjects with moderate RI.

Up to eight (8) subjects with severe RI.

Healthy Matched Control Subjects:

Up to 24 healthy subjects will be enrolled to ensure that each subject in the RI cohorts will be matched with a healthy subject based on sex, age (± 10 years), and BMI (± 20%). An individual healthy subject may be matched to one subject from each of the RI cohorts (mild, moderate, and severe) providing matching criterion are met, and such that each healthy subject may be matched to a maximum of 3 subjects with RI. However, no healthy subject can be matched to more than one subject in any single RI cohort.

Screening of subjects will occur within 28 days prior to LOXO-292 dosing.

On Day 1, subjects will receive a single oral dose of LOXO-292. Plasma and urine samples will be collected predose (if possible) and through 168 hours postdose for healthy subjects and subjects with RI for LOXO-292 PK assessment.

Assignment to a renal function panel will be as follows:

Cohort	Renal Function	eGFR (mL/min/1.73m^2) *
1	Healthy Matched Control	≥ 90 **
2	Mild	60 ≤ eGFR < 90

Cohort	Renal Function	eGFR (mL/min/1.73m^2) *
3	Moderate	30 ≤ eGFR < 60
4	Severe (not on dialysis)	< 30
	* Estimated glomerular filtration rate (eGFR) based on Modification of Diet in Renal Disease (MDRD) equation at Screening. Baseline eGFR will be obtained for all subjects (i.e., subjects with RI and healthy-matched control subjects) by taking the mean of the eGFR obtained from Screening and from historical values within a 3-month period from Screening. If no historical measurement is available, a second Screening eGFR sample will be taken during the Screening period (≥ 14 days apart) and the mean of the two values will be used as the Baseline eGFR for cohort assignment. Individual eGFR values recorded for each measurement contributing to the subject mean baseline value must fall within the specified eGFR ranges for each cohort (i.e., healthy, mild, moderate, and severe) to categorize subjects' renal impairment status. ** For healthy-matched control subjects, a single assessment of actual creatinine clearance computed over a 24 hour urine collection may be used in place of the eGFR (based on the MDRD equation), at the Principal Investigator (PI)'s discretion.	

Safety will be monitored throughout the study by repeated clinical and laboratory evaluations.

Subjects may be replaced at the discretion of the Sponsor.

Subjects will be housed in the clinical research unit (CRU) from Check-in (Day -1), at the time indicated by the CRU, until after completion of the Day 8 (End of Treatment [EOT]) or Early Termination (ET) study procedures. EOT is defined as the day on which the subject is released from the CRU, following all study procedures.

The CRUs will contact all subjects who received LOXO-292 (including subjects who terminate from the study early) at the End of Study (EOS,) by a follow up phone call (FU). The EOS/FU phone call will be performed 7 days (± 2 days) after the EOT visit or ET visit to determine if any study drug-related adverse event (AE) or serious adverse event (SAE) has occurred since the EOT or ET visit.

4. ANALYSIS POPULATIONS

4.1 Analysis Populations

Safety Population

All subjects who received a dose of the study drug will be included in the safety evaluations.

Pharmacokinetic Population

Samples from all subjects will be assayed even if the subjects do not complete the study. All subjects who comply sufficiently with the protocol and display an evaluable PK profile (e.g., exposure to treatment, availability of measurements and absence of major protocol violations) will be included in the statistical analyses.

Data for each subject will be included in the summary statistics and statistical comparisons of PK parameters with the exceptions described as follows:

- Data from subjects who experience emesis at or before 2 times median Tmax for LOXO-292 during the PK sampling period of the study may be excluded from the summary statistics and from the statistical comparison of PK parameters.
- All protocol deviations that occur during the study will be considered for their severity/impact and will be taken into consideration when subjects are assigned to analysis populations.

Any subject or data excluded from the analysis will be identified, along with their reason for exclusion, in the CSR.

4.2 Preliminary Data and Interim Analysis

No formal interim analysis is planned.

5. TREATMENT DESCRIPTIONS

LOXO-292 will be supplied as 80 mg capsules.

Subjects will receive a single oral dose of 160 mg LOXO-292 (2 x 80 mg capsules) on Day 1 following a fast from food of at least 2 hours (not including water), with approximately 240 mL of water, followed by a fast from food (not including water) for at least 1 hour postdose.

Subjects will be instructed not to crush, split, or chew LOXO-292.

Table 5.1 Cohort Description

Cohort	Short Description (text, tables headers, footers, figures, listings, SAS output)	Description
Mild	Subjects with Mild RI (n = 8)	Administration of a single oral dose of 160 mg LOXO-292 to subjects with mild renal impairment following a 2-hour fast.
Moderate	Subjects with Moderate RI (n = 8)	Administration of a single oral dose of 160 mg LOXO-292 to subjects with moderate renal impairment following a 2-hour fast.
Severe	Subjects with Severe RI (n = 8)	Administration of a single oral dose of 160 mg LOXO-292 to subjects with severe renal impairment following a 2-hour fast.
Healthy	Healthy Matched Control Subjects (n = 8 up to 24)	Administration of a single oral dose of 160 mg LOXO-292 to healthy match control subjects following a 2-hour fast.

6. PHARMACOKINETIC ANALYSIS

6.1 Measurements and Collection Schedule

Plasma

Blood samples for PK assessment of LOXO-292 will be taken at the following time points: CCI [redacted]

CCI [redacted]

Urine

Urine will be collected at predose (spot collection) and during the following postdose intervals: CCI [redacted]

All concentration data will be included in the calculation of the individual PK parameters, the individual concentration-time plots (based on actual sample times), and in the mean concentration-time plots (based on nominal sample times). However, if there are any significant deviations from nominal sample times, some concentration data may be excluded from mean concentration-time plots and/or additional concentration-time plots of the mean data may be provided. The exclusion of data will be made in agreement between the Sponsor and Celerion. All deviations and excluded data will be provided and discussed in the CSR.

6.2 Bioanalytical Method

Plasma and urine concentrations of LOXO-292 will be determined using a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method validated with respect to accuracy, precision, linearity, sensitivity, and specificity at Alturas Analytics, Inc. (Moscow, Idaho, USA). The analytical rang CCI [redacted] Samples that contain concentrations greater than 1000 ng/mL may be diluted up to CCI [redacted], if necessary, to be within the quantification range. The analytical range CCI [redacted] Samples of urine that contain concentrations greater than CCI [redacted] may be diluted, if necessary, to be within the quantification range.

6.3 Investigational Product and PK Analyte Information of LOXO-292

LOXO-292 has a molecular weight of approximately CCI [redacted]. LOXO-292 will be supplied as a simple blend with excipients containing 80 mg of drug substance (freebase) in a hard gelatin capsule.

6.4 Pharmacokinetic Concentrations

Plasma and urine concentrations of LOXO-292 as determined at the collection times and per the bioanalytical method described in Sections 6.1 and 6.2, respectively, will be used for the calculation of the plasma LOXO-292 PK parameters.

6.5 Noncompartmental Pharmacokinetic Analysis and Parameter Calculation for LOXO-292

6.5.1 Plasma Pharmacokinetic Parameters

The appropriate noncompartmental PK parameters will be calculated from the total plasma LOXO-292 concentration-time data using Phoenix® WinNonlin® Version 7.0 or higher. Actual sample collection times, relative to the administration time of LOXO-292, will be used in the calculations of the PK parameters. All total plasma PK parameters included in the protocol are listed in Table 6.1 below, and are defined as appropriate for study design.

Table 6.1. Noncompartmental Total Plasma Pharmacokinetic Parameters to be Calculated for LOXO-292

Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
AUC0-t	Area under the concentration-time curve for LOXO-292 concentration from time 0 to the time of the last observed non-zero concentration	Calculated using the Linear Trapezoidal with Linear Interpolation Method
AUC0-inf	Area under the concentration-time curve for LOXO-292 concentration from time 0 extrapolated to infinity	Calculated as AUC0-t + (Clast/Kel) where Clast is the last observed/measured concentration
AUC%extrap	Percent of AUC0-inf extrapolated	Calculated as (1 - AUC0-t/AUC0-inf)*100
Cmax	Maximum observed LOXO-292 concentration	Taken directly from bioanalytical data
Tmax	The time to reach Cmax. If the maximum value occurs at more than one time point, Tmax is defined as the first time point with this value	Taken from clinical database as the difference in the time of administration and the time of the blood draw which is associated with the Cmax.
Kel	Apparent terminal elimination rate constant; represents the fraction of drug eliminated per unit time	Calculated as the negative of the slope of a linear regression of the log(concentration)-time for all concentrations >LLOQ during the terminal elimination phase
t½	Apparent first-order terminal elimination half-life	Calculated as 0.693/Kel

Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
CL/F	Apparent total plasma clearance after oral (extravascular) administration	Calculated as Dose/(AUC0-inf)
Vz/F	Apparent volume of distribution of LOXO-292 during the terminal elimination phase after extravascular administration	Calculated as Dose/(AUC0-inf x Kel)

Pharmacokinetic parameters will not be calculated for subjects with fewer than 3 consecutive postdose time points with quantifiable concentrations. Subjects for whom there are insufficient data to calculate the PK parameters will be included in the concentration tables only and excluded from the statistical analysis.

For the calculation of the PK parameters, plasma concentrations below the limit of quantitation (BLQ) prior to the first quantifiable concentration will be set to 0 and plasma concentrations BLQ after the first quantifiable concentration will be treated as missing.

The Kel will be determined using linear regressions composed of least 3 data points. The Kel will not be assigned if 1) the terminal elimination phase is not apparent, 2) if Tmax is one of the 3 last data points, or 3) if the R^2 value is less than 0.75. In cases where the Kel interval is not assigned, the values of t½, AUC0-inf, AUC%extrap, CL/F, Vz/F are considered not calculable and will not be reported. Wherever the resulting t½ is more than half as long as the sampling interval, the Kel values and associated parameters (t½, AUC0-inf, AUC%extrap, CL/F, and Vz/F) may not be presented as judged appropriate and in accordance with Celerion SOPs.

6.5.2 Unbound Plasma LOXO-292 Pharmacokinetic Parameters

An analysis to determine the unbound plasma LOXO-292 PK parameters will be conducted. The fraction of unbound (fu) LOXO-292 in plasma for each subject will be estimated via an ex vivo protein binding analysis using a predose plasma sample. Unbound plasma concentrations of LOXO-292 will be calculated by multiplying the measured plasma concentrations by the fraction unbound of each subject (Cu = measured concentration x fu) at each sampling time point for that subject. The following unbound PK parameters using the individual Cu values and actual sampling times using Phoenix® WinNonlin® Version 7.0 or higher:

Table 6.2. Noncompartmental Plasma Pharmacokinetic Parameters to be Calculated for Unbound LOXO-292

Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
AUC0-t,u	Area under the concentration-time curve for unbound LOXO-292 concentration from time 0 to the time of the last observed non-zero	Calculated using the Linear Trapezoidal with Linear Interpolation Method
AUC0-inf,u	Area under the concentration-time curve for unbound LOXO-292 concentration from time 0 extrapolated to infinity	Calculated as AUC0-t,u + (Clast,u/Kel,u) where Clast is the last observed/measured unbound concentration
Cmax,u	Maximum observed unbound LOXO-292 concentration	Taken directly from unbound plasma concentration of LOXO-292
Kel,u	Apparent terminal elimination rate constant; represents the fraction of unbound drug eliminated per unit time	Calculated as the negative of the slope of a linear regression of the log(unbound concentration)-time for all unbound concentrations >LLOQ during the terminal elimination phase
CL/F,u	Apparent total plasma clearance of unbound LOXO-292 after extravascular (oral) administration	Calculated as Dose/(AUC0-inf,u)
Vz/F,u	Apparent volume of distribution of unbound LOXO-292 during the terminal elimination phase after extravascular administration	Calculated as Dose/(AUC0-inf,u x Kel,u*)

* The same timepoints selected for the calculation of Kel will be selected for the calculation of Kel,u. Kel,u will be calculated in WinNonLin but will not be presented in tables.

Unbound PK parameters will not be calculated for subjects with fewer than 3 consecutive postdose time points with quantifiable concentrations. Subjects for whom there are insufficient data to calculate the PK parameters will be included in the concentration tables only and excluded from the statistical analysis.

For the calculation of the unbound PK parameters, plasma concentrations BLQ prior to the first quantifiable concentration will be set to 0 and plasma concentrations BLQ after the first quantifiable concentration will be treated as missing.

The Kel,u will be determined using linear regressions composed of least 3 data points. The Kel,u will not be assigned if 1) the terminal elimination phase is not apparent, 2) if Tmax,u is one of the 3 last data points, or 3) if the R^2 value is less than 0.75. In cases where the Kel,u interval is not assigned, the values of t½,u, AUC0-inf,u, CL/F,u, and Vd/F,u are considered not calculable and will not be reported. Wherever the resulting t½,u is more than half as long as the sampling interval, the Kel,u values and associated parameters (t½,u, AUC0-inf,u, CL/F,u, and Vd/F,u) may not be presented as judged appropriate and in accordance with Celerion SOPs.

6.5.3 Urine Pharmacokinetic Parameters

The following PK parameters will be calculated from urine LOXO-292 data using SAS® Version 9.3 or higher. All urine PK parameters included in the protocol are listed in Table 6.3 below, and are defined as appropriate for study design.

Table 6.3. Noncompartmental Urine Pharmacokinetic Parameters to be Calculated for LOXO-292

Label to be Used in Text, Tables and Figures	Definition	Method of Determination
Aet1-t2	Amount of unchanged LOXO-292 excreted during urine collection interval from t1 to t2; the collection [redacted]	Calculated as: Urine LOXO-292 concentration * urine volume Note: If the amount of urine excreted was captured in the CRF as urine weight (g), it will be converted to volume (mL) using the assumed density of 1 g/mL.

Label to be Used in Text, Tables and Figures	Definition	Method of Determination
Ae0-t	Total amount of LOXO-292 excreted unchanged in the urine over the entire urine collection period (0-t hours)	Calculated as: The sum of the individual Aet1-t2 (urine LOXO-292 concentration * urine volume) over the entire urine collection interval Note: If the amount of urine excreted was captured in the CRF as urine weight (g), it will be converted to volume (mL) using the assumed density of 1 g/mL.
CLr	Renal clearance	Calculated as: Ae(t1-t2)/AUC(t1-t2) Where t1-t2 is the longest interval of time during which Ae and AUC are both obtained.
Fe	The percent of dose excreted unchanged into urine from time 0 to the time at the end of the urine collection interval	Calculated as: 100*[Ae0-t]/Dose Where Ae0-t is the cumulative amount of LOXO-292 excreted unchanged in the urine over the entire urine collection period (0-t hours) and dose is the dose of the free base LOXO-292

For the calculation of the urine PK parameters, urine data BLQ concentrations will be treated as 0. See Section 6.6 for further information on missing urine data.

6.6 Data Summarization and Presentation

All LOXO-292 PK concentrations and PK parameters descriptive statistics will be generated using SAS® Version 9.3 or higher.

The total and unbound plasma concentrations of LOXO-292 will be listed and summarized by cohort and time point for all subjects in the PK Population. For the protein binding assay, the buffer chamber (BC) and plasma chamber (PC)

concentrations, % recovery, and fraction unbound will be listed and summarized by cohort for all subjects in the PK Population. The urine concentrations of LOXO-292 will be listed and summarized by cohort and collection-intervals for all subjects in the PK Population.

Plasma and urine concentrations of LOXO-292 will be presented with the same level of precision as received from the bioanalytical laboratory. Unbound plasma concentrations of LOXO-292 will be presented with the same level of precision as received from the bioanalytical laboratory. Data from the protein binding assay will be presented with the same level of precision as received from the bioanalytical laboratory.

Summary statistics, including sample size (n), arithmetic mean (Mean), standard deviation (SD), coefficient of variation (CV%), standard error of the mean (SEM), minimum, median, and maximum will be calculated for all nominal concentration time points and collection intervals. Excluded subjects will be included in the concentration listings, but will be excluded from the summary statistics and noted as such in the tables. All BLQ values will be presented as "BLQ" in the concentration listings and footnoted accordingly.

Mean and individual total and unbound plasma concentration-time profiles will be presented on linear and semi-log scales. Linear mean plots will be presented with and without SD. Urine data will be graphically summarized with mean and individual cumulative amounts of LOXO-292 excreted (Ae0-t) and cumulative % dose excreted unchanged versus end of collection interval, on linear plots (with and without SD for mean).

Total and unbound plasma LOXO-292 PK parameters will be listed and summarized by cohort for all subjects in the PK Population. PK parameters will be reported to 3 significant figures for individual parameters, with the exception of Tmax and t½, which will be presented with 2 decimal places. Summary statistics (n, Mean, SD, CV%, SEM, minimum, median, maximum, geometric mean [Geom Mean], geometric CV% [Geom CV%], and 95% CI Geom Mean [presented for AUC0-t, AUC0-inf and Cmax only]) will be calculated for total and unbound plasma LOXO-292 PK parameters. Excluded subjects will be listed in the PK parameter tables, but will be excluded from the summary statistics and noted as such in the tables.

For urine data, in cases where a subject was unable to void during a given interval, the urine volume for that interval will be set to zero, labeled as "UTV" (i.e., "unable to void"), and footnoted accordingly. All urinary parameters requiring volume in their calculation, for that interval only, will be set to zero. The cumulative amount excreted for that interval will be calculated as the previous cumulative amount plus 0. If a sample was collected, but volume was not recorded or only a partial volume was recorded, the urine volume for this that interval will be set to missing and footnoted accordingly. All urinary parameters requiring volume in their calculation, for that interval only, will be set to missing. The cumulative amount excreted for that interval

and all intervals thereafter, including the total cumulative amount excreted, are not calculable and will be set to missing. With the exception of those parameters set to missing, no parameters will be excluded from summary statistics. Furthermore, only results up to the missing interval will be included in summary statistics and in presentation of cumulative urinary excretion plots. Urine concentration results from and beyond the missing interval will be listed in the table and summarized accordingly.

The level of precision for each concentration and PK parameter statistic will be presented as follows:

- minimum/maximum in same precision as in bioanalytical data and parameter output,
- mean/median/Geom Mean in one more level of precision than minimum/maximum,
- SD/SEM in one more level of precision than mean/median/Geom Mean,
- n will be presented as an integer, and
- CV%/ Geom CV% will be presented to the nearest tenth.
- 95% CI Geom Mean will be presented with 2 decimals.

6.7 Statistical Analysis of PK Parameters

6.7.1 Primary Analysis

A comparison of natural-log (ln)-transformed PK parameters (total: AUC0-t, AUC0-inf, and Cmax, and unbound: AUC0-t,u, AUC0-inf,u, and Cmax,u) will be made to evaluate the effect of renal function group on the PK of a single dose of LOXO-292. Since the comparison groups of subjects are independent in terms of degrees of RI and dependent based on the matching criteria, paired t-tests will be performed, using PROC TTEST of SAS®, to assess the differences in PK parameter between each hepatic impairment group versus the corresponding healthy matched control group with respect to 1 to 1 matching. Geometric mean ratios (GMRs) and ninety percent (90%) confidence intervals (CIs) for the ratios will be derived by exponentiation of the mean difference and the CIs obtained for the difference in mean between each renal function cohort and the matching healthy control group.

The paired t-test analysis for each PK parameter will be performed using the following SAS® code for each renal function cohort and its corresponding healthy matched control group:

CCI [redacted]

CCI

RUN;

Programmer note: The paired t-test will be performed for each renal function group and the subset of corresponding healthy matched control subjects separately. LPKri refers to the set of ln-transformed PK parameters for the subjects in the renal impaired function group of interest (i.e., Mild, Moderate, or Severe) and LPKhealthy refers to the ln-transformed PK parameters for the set of corresponding matching healthy control subjects.

6.7.2 Analysis of Covariance

An analysis of covariance (ANCOVA) will also be performed on the ln-transformed PK parameters (total: AUC0-t, AUC0-inf, and Cmax, and unbound: AUC0-t,u, AUC0-inf,u, and Cmax,u) of LOXO-292 to evaluate the effect of various degrees of RI on the PK of LOXO-292. The ANCOVA model will contain a categorical factor of population for subjects with various degrees of RI (mild, moderate, severe, and healthy matched control subjects), a categorical covariate (sex), and continuous covariates (age and BMI).

Ratios of least-squares means (LSMs) and 90% CIs of ratios will be calculated using the exponentiation of the difference between two cohort LSMs and the corresponding CIs from the ANCOVA analyses on the ln-transformed AUC0-t, AUC0-inf, and Cmax and the corresponding unbound parameters, AUC0-t,u, AUC0-inf,u, and Cmax,u. These ratios will be expressed as a percentage relative to the healthy matched control cohort. Geometric LSM, GMRs, and 90% CIs will be presented.

The ANCOVA analysis will be performed using the following SAS® code:

CCI

Programmer Note: The coefficients in the estimate statements presented above assume that the following decodes will be used for cohort in the database: Mild RI = A, Moderate RI = B, Severe RI = C, Healthy Matched Control = D. Please confirm these coefficients with the Biostatistician prior to data analysis.

6.7.3 Additional Analysis

The relationship between LOXO-292 PK parameters (i.e., Cmax and AUC, total and unbound) and measures of renal function (such as eGFR and CLcr) will be examined in an exploratory manner via a graphically linear regression approach. The PK parameters will be the dependent variable and show on y-axis and measurements for renal impairment will be independent variables and show on the x-axis. The regression equation with slope and intercept, the r-square, and the p-value for slope will be presented in the graphs as footnotes.

If data permits and judged necessary, an exploratory analysis will be performed to assess the relationship between LOXO-292 PK and renal impairment and the effect of covariates (age, BMI, and gender) using an appropriate approach.

7. SAFETY

No inferential statistics are to be performed for the safety analysis.

All clinical safety and tolerability data will be listed by cohort, subject and assessment time points, chronologically. This will include unscheduled assessments (including rechecks) and ET records.

Continuous variables will be summarized using n, mean, SD, minimum, median, and maximum. Frequency counts will be reported for categorical data when appropriate. The level of precision will be presented as follows: “n” as an integer, minimum/maximum in same precision as in the database, mean/median in one more precision level than minimum/maximum, and SD in one more precision level than mean/median. Where individual data points are missing because of dropouts or other reasons, the data will be summarized based on reduced denominators.

When change from baseline is calculated, baseline is the last scheduled or unscheduled assessment before dosing on Day 1, whichever is later. Unscheduled assessments and ET measurements taken after dosing will not be used in the summarization.

Note: The term ‘unscheduled’ assessment used in this SAP may also refer to recheck assessments.

7.1 Subject Discontinuation

Subjects will be summarized by the number of subjects enrolled, completed, and discontinued from the study with discontinuation reasons by cohort and overall. Discontinuation data will be listed by-subject.

7.2 Demographics

Descriptive statistics will be calculated for continuous variables (age, weight, height, and body mass index) by cohort and over all the study. Weight, height and body mass index are summarized at screening. Age will be derived from the date of birth to the date of dosing. Frequency counts will be provided for categorical variables (race, ethnicity, and sex) by cohort and over all the study. A by-subject listing will also be provided.

7.3 Adverse Events

All AEs occurring during this clinical trial will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®), Version 21.1.

Each AE will be graded, by the clinical site, on the National Institution of Health's Common Terminology Criteria for Adverse Events (CTCAE, version 5.0) 5-point severity scale (Grade 1, 2, 3, 4 and 5). Not all grades are appropriate for all AEs. Therefore, some AEs are listed within the CTCAE with fewer than 5 options for grade selection.

The following clinical descriptions of severity for each AE are based on the following general guideline [CTCAE Nov2017]:

Table 7.3: Adverse Event Severity Level and Description

Grade	Description
Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living (ADL)*.
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**.
Grade 4	Life-threatening consequences; urgent intervention indicated.

Grade	Description
Grade 5	Death related to AE.
* Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc. ** Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications and not bedridden.□	

Similarly, the causal relationship of the study drug to the AE will be described as Related or Not related to study drug (LOXO-292). All AEs captured in the database will be listed in by-subject data listings including verbatim term, coded term, cohort, severity grade, relationship to study drug, and action; however, only treatment-emergent AEs (TEAEs) will be summarized.

A TEAE is defined as an undesirable event not present prior to medical treatment, or an already present event that worsens either in intensity or frequency following the treatment. Each TEAE will be attributed to the treatment based on Investigator (or designee) judgment as well as on its onset date and time. If an AE has a change in severity grade, the original AE will be given a resolution date and time of the time of severity grade increase or decrease and a new AE record will be initiated with the new severity grade, and the new AE record will use the resolved date/time of the previous record as the onset date/time. If the severity grade of an AE remains the same, the AE will be kept open through to resolution.

If the onset date and/or time of an AE is/are missing, the AE will be treated as a TEAE, unless the onset date of the AE is known to have occurred prior to dosing. TEAEs will be tabulated by system organ class and preferred term. Summary tables will include the number of subjects reporting the AE and as a percent of the number of subjects dosed by cohort and overall. In addition, the number of AEs will be summarized. For an AE with multiple changes in severity, a new record with severity less or equal to its maximum severity will not be included in the adverse event summary tables. Tables will also be presented by severity grade and relationship to study drug. If a subject experienced the same TEAE at more than once with different level of severity grade, only the most severe one will be counted. Similarly, if a subject experienced the same TEAE more than once with different level of drug relationship, only the one most closely related to the study drug will be counted.

Should any serious adverse events (SAEs) occur during the study, the SAEs will be displayed in a table and a narrative included in the Clinical Study Report.

7.4 Clinical Laboratory Tests (Serum Chemistry, Hematology, Coagulation, and Urinalysis)

All clinical laboratory test results will be presented in by-subject data listings, however, only serum chemistry, hematology, coagulation and urinalysis values will be summarized. Given that this study was conducted at multiple sites, by-subject data listings will be provided in conventional units and international system of units (SI units). Summary tables will be provided in SI units.

Hematology, coagulation, serum chemistry and urinalysis tests will be conducted at the following time points:

Table 7.4 Lab Test Time Points

Day
Screening*
Day -1*
Day 2
Day 5
Day 8**
* performed following a fast of at least 12 hours ** performed at EOT or prior to ET

Out-of-normal range flags will be presented in the clinical laboratory listings as recorded in the database. The reference ranges used during the study will be provided in conventional and SI units by study site in Appendix 16.1.10.1. Out-of-range values and unscheduled results will be listed. Results that are indicated as CS by the PI (either in the PI flag or in PI comments) will be listed in the table.

For all laboratory values that are numeric, descriptive statistics (n, mean, SD, minimum, median, and maximum) will be presented for each laboratory test by cohort and time point. Change from baseline will also be summarized. Postdose unscheduled assessments and ET results will not be summarized.

For each laboratory test, a shift table will be developed comparing the frequency of the results at baseline (above normal, normal, or below normal) to postdose results. For urinalysis tests, the categories are normal and outside normal.

Baseline is the last non-missing predose measurement prior to dosing (Day -1), including unscheduled assessments.

7.5 Vital Signs (Blood Pressure, Pulse Rate, Respiration Rate, and Temperature)

Vital signs will be performed at the following time points:

Table 7.5 Vital Signs Time Points

Day	Time Point	Parameter
Screening		HR, BP, RR, T
Day -1	Check-in	HR, BP, RR, T
Day 1	Predose	HR, BP, RR, T
Day 1	Hour 2 , Hour 4	HR, BP, RR
Day 2		HR, BP, RR
Day 3		HR, BP, RR
Day 4		HR, BP, RR
Day 5		HR, BP, RR
Day 6		HR, BP, RR
Day 7		HR, BP, RR
Day 8	EOT or ET*	HR, BP, RR, T
*performed at EOT or prior to ET		

Descriptive statistics will be reported for vital sign measurements (blood pressure [BP], pulse [HR], and respiration rate [RR]) and change from baseline by cohort and time point. Baseline is the last non-missing predose measurement prior to dosing (Day 1 Predose), including unscheduled assessments. Postdose unscheduled values and ET results will not be used for calculation of descriptive statistics. All vital signs results will be listed by subject.

7.6 ECG (Heart Rate, PR, QRS, QT, and QTcF [QT with Fridericia correction])

Single 12-lead ECGs will be performed at the following time points:

Table 7.6: ECG Time Points

Day
Screening
Day -1
Day 8*
* performed at EOT or prior to ET

Descriptive statistics will be reported for ECG parameters and change from baseline by cohort and time point. Baseline is the last non-missing predose measurement prior to dosing (Day -1), including unscheduled assessments. Postdose unscheduled values and ET results will not be used for calculation of descriptive statistics. All ECG interval parameters will be listed by subject and time point of collection with QTcF > 450 msec and change from baseline > 30 msec flagged.

7.7 Concomitant Medications

All concomitant medications recorded during the study will be coded with the WHO Dictionary, Version 01Sep2018 B3 and listed.

7.8 Physical Examination

A full physical examination will be performed at Screening and on Day 8 or upon ET. Abbreviated physical examinations will be performed at Check-in (Day -1) and 1 hour postdose. Symptom-driven physical examinations may be performed at other times, at the PI's or designee's discretion. Abnormal findings will be reported as medical history or adverse events by the clinical site. Physical examination results will be listed by subject and time point.

8. SUMMARY OF CHANGES FROM PROTOCOL-PLANNED ANALYSIS

Paired t-tests to evaluate the effect of renal function group were added in the analysis plan.

The rest of the analyses described in this SAP are aligned with those analyses described in the protocol.

9. SUMMARY TABLES AND FIGURES

Summary tables and figures are numbered following the International Conference on Harmonization (ICH) structure but may be renumbered as appropriate during the compilation of the tables and figures for the CSR. Note that all summary tables and figures will be generated using SAS® Version 9.3 or higher.

9.1 In-text Summary Tables and Figures

The following is a list of table and figure titles that will be included in the text of the CSR. Tables and figures will be numbered appropriately during compilation of the CSR.

Section 10:

Table 10-1 Summary of Disposition (Safety Population)

Section 11:

Table 11-1 Demographic Summary (Safety Population)

Total Plasma LOXO-292

Table 11-2 Summary of Total Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 160 mg LOXO-292 to

Unbound Plasma LOXO-292

Urine LOXO-292

Table 11-16 Summary of Urine LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Pharmacokinetic Population)

Figure 11-9 Arithmetic Mean Cumulative % Dose of LOXO-292 Excreted Unchanged in Urine Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Pharmacokinetic Population)

Section 12:

Table 12-1 Treatment-Emergent Adverse Event Frequency by Cohort – Number of Subjects Reporting the Event (% of Subjects Dosed) (Safety Population)

9.2 Section 14 Summary Tables and Figures

The following is a list of table and figure titles that will be included in Section 14 of the report. Table and figure titles may be renumbered as appropriate during the compilation of the report.

14.1 Demographic Data Summary Tables

14.1.1 Demographic Tables

Table 14.1.1.1 Summary of Disposition (Safety Population)

Table 14.1.1.2 Demographic Summary (Safety Population)

14.2 Pharmacokinetic Data Summary Tables and Figures

14.2.1 Total Plasma LOXO-292 Tables

Table 14.2.1.1 Total Plasma LOXO-292 Concentrations (ng/mL) Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild Renal Impairment (Pharmacokinetic Population)

Table 14.2.1.2 Total Plasma LOXO-292 Concentrations (ng/mL) Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Moderate Renal Impairment (Pharmacokinetic Population)

Figure 14.2.2.4 Individual Total Plasma LOXO-292 AUC0-t Values, Geometric Means With Corresponding 95% CIs, and GMR With Corresponding 90% CIs Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Pharmacokinetic Population)

Figure 14.2.2.5 Individual Total Plasma LOXO-292 AUC0-inf Values, Geometric Means With Corresponding 95% CIs, and GMR With Corresponding 90% CIs Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Pharmacokinetic Population)

Figure 14.2.2.6 Individual Total Plasma LOXO-292 Cmax Values, Geometric Means With Corresponding 95% CIs, and GMR With Corresponding 90% CIs Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Pharmacokinetic Population)

Note:

- Figures 14.2.2.4-6 are plots of AUCs and Cmax versus the cohorts.
- The x-axis will be the renal function and the y-axis will be the individual plasma PK parameters.

Figure 14.2.2.7 Scatter/Regression Plot of Individual Plasma LOXO-292 AUC0-t Versus eGFR

Figure 14.2.2.8 Scatter/Regression Plot of Individual Plasma LOXO-292 AUC0-inf Versus eGFR

Figure 14.2.2.9 Scatter/Regression Plot of Individual Plasma LOXO-292 Cmax Versus eGFR

Note:

- Figures 14.2.2.7-9 are scatter plots with regression lines.
- The x-axis will be the individual eGFR values and the y-axis will be the individual plasma PK parameters

Figure 14.2.2.10 Scatter/Regression Plot of Individual Plasma LOXO-292 AUC0-t Versus CLcr

Figure 14.2.2.11 Scatter/Regression Plot of Individual Plasma LOXO-292 AUC0-inf Versus CLcr

Figure 14.2.2.12 Scatter/Regression Plot of Individual Plasma LOXO-292 Cmax Versus CLcr

Note:

- Figures 14.2.2.10-12 are scatter plots with regression lines.
- The x-axis will be the individual CLcr values (found in the RFA dataset) and the y-axis will be the individual CLcr values

14.2.3 Unbound Plasma LOXO-292 Tables

Table 14.2.3.1 Concentrations of LOXO-292 (LOXO-292) (ng/mL), and Concentrations in the Buffer Chamber (LOXO-292 BC), Concentrations in the Plasma Chamber (LOXO-292 PC), % Recovery, and Fraction Unbound Obtained Following the Plasma Protein Binding Assay in Subjects with Mild Renal Impairment (Pharmacokinetic Population)

Table 14.2.3.2 Concentrations of LOXO-292 (LOXO-292) (ng/mL), and Concentrations in the Buffer Chamber (LOXO-292 BC), Concentrations in the Plasma Chamber (LOXO-292 PC), % Recovery, and Fraction Unbound Obtained Following the Plasma Protein Binding Assay in Subjects with Moderate Renal Impairment (Pharmacokinetic Population)

Table 14.2.3.3 Concentrations of LOXO-292 (LOXO-292) (ng/mL), and Concentrations in the Buffer Chamber (LOXO-292 BC), Concentrations in the Plasma Chamber (LOXO-292 PC), % Recovery, and Fraction Unbound Obtained Following the Plasma Protein Binding Assay in Subjects with Severe Renal Impairment (Pharmacokinetic Population)

Table 14.2.3.4 Concentrations of LOXO-292 (LOXO-292) (ng/mL), and Concentrations in the Buffer Chamber (LOXO-292 BC), Concentrations in the Plasma Chamber (LOXO-292 PC), % Recovery, and Fraction Unbound Obtained Following the Plasma Protein Binding Assay in Healthy Matched Control Subjects (Pharmacokinetic Population)

Table 14.2.3.5 Unbound Plasma LOXO-292 Concentrations (ng/mL) Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild Renal Impairment (Pharmacokinetic Population)

Figure 14.2.4.2 Mean Unbound Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Linear Scale) (Pharmacokinetic Population)

Figure 14.2.4.3 Mean Unbound Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Semi-Log Scale) (Pharmacokinetic Population)

Figure 14.2.4.4 Individual Unbound Plasma LOXO-292 AUC0-t,u Values, Geometric Means With Corresponding 95% CIs, and GMR With Corresponding 90% CIs Following Administration of a Single Dose of 160 mg LOXO 292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Pharmacokinetic Population)

Figure 14.2.4.5 Individual Unbound Plasma LOXO-292 AUC0-inf,u Values, Geometric Means With Corresponding 95% CIs, and GMR With Corresponding 90% CIs Following Administration of a Single Dose of 160 mg LOXO 292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Pharmacokinetic Population)

Figure 14.2.4.6 Individual Unbound Plasma LOXO-292 Cmax,u Values, Geometric Means With Corresponding 95% CIs, and GMR With Corresponding 90% CIs Following Administration of a Single Dose of 160 mg LOXO 292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Pharmacokinetic Population)

Note:

- Figures 14.2.4.4-6 are plot of AUCs and Cmax versus the cohorts.
- The x-axis will be the renal function and the y-axis will be the individual unbound plasma PK parameters.

Figure 14.2.4.7 Scatter/Regression Plot of Individual Unbound Plasma LOXO-292 AUC0-t,u Versus eGFR

Figure 14.2.4.8 Scatter/Regression Plot of Individual Unbound Plasma LOXO-292 AUC0-inf,u Versus eGFR

Figure 14.2.4.9 Scatter/Regression Plot of Individual Unbound Plasma LOXO-292 Cmax,u Versus eGFR

Note:

- Figures 14.2.4.7-9 are scatter plots with regression lines.
- The x-axis will be the individual eGFR values (found in the RFA dataset) and the y-axis will be the individual unbound plasma PK parameters

Figure 14.2.4.10 Scatter/Regression Plot of Individual Unbound Plasma LOXO-292 AUC0-t,u Versus CLcr

Figure 14.2.4.11 Scatter/Regression Plot of Individual Unbound Plasma LOXO-292 AUC0-inf,u Versus CLcr

Figure 14.2.4.12 Scatter/Regression Plot of Individual Unbound Plasma LOXO-292 Cmax,u Versus CLcr

Note:

- Figures 14.2.4.10-12 are scatter plots with regression lines.
- The x-axis will be the individual CLcr values (found in the RFA dataset) and the y-axis will be the individual unbound plasma PK parameters

14.2.5 Urine LOXO-292 Tables

Table 14.2.5.1 Urinary Excretion of LOXO-292 Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild Renal Impairment (Pharmacokinetic Population)

Table 14.2.5.2 Urinary Excretion of LOXO-292 Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Moderate Renal Impairment (Pharmacokinetic Population)

Table 14.2.5.3 Urinary Excretion of LOXO-292 Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Severe Renal Impairment (Pharmacokinetic Population)

Table 14.2.5.4 Urinary Excretion of LOXO-292 Following Administration of a Single Dose of 160 mg LOXO-292 to Healthy Matched Control Subjects (Pharmacokinetic Population)

Table 14.2.5.5 Pharmacokinetic Parameters for Urinary Excretion of LOXO-292 Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild Renal Impairment (Pharmacokinetic Population)

14.2.6 Urine LOXO-292 Figures

14.3 Safety Data Summary Tables

14.3.1 Displays of Adverse Events

Table 14.3.1.1 Treatment-emergent Adverse Event Frequency by Cohort – Number of Subjects Reporting Events (% of Subject Dosed) (Safety Population)

Table 14.3.1.2 Treatment-emergent Adverse Event Frequency by Cohort – Number of Adverse Events (% of Total Adverse Events) (Safety Population)

Table 14.3.1.3 Treatment-Emergent Adverse Event Frequency by Cohort, Severity Grade, and Relationship to Study Drug - Number of Subjects Reporting Events (Safety Population)

Table 14.3.1.4 Treatment-Emergent Adverse Event Frequency by Cohort, Severity Grade, and Relationship to Study Drug - Number of Adverse Events (Safety Population)

14.3.2 Listings of Deaths, other Serious and Significant Adverse Events

Table 14.3.2.1 Serious Adverse Events (Safety Population)

Note: If no serious adverse event occurred, a statement 'There was no serious adverse event recorded during the study.' will be added.

14.3.3. Narratives of Deaths, other Serious and Certain other Significant Adverse Events

14.3.4. Abnormal Laboratory Value Listing (by Subject)

Table 14.3.4.1 Out-of-Range Values and Unscheduled Results - Serum Chemistry (Safety Population)

Table 14.3.4.2 Out-of-Range Values and Unscheduled Results – Hematology and Coagulation

Table 14.3.4.3 Out-of-Range Values and Unscheduled Results – Urinalysis

Table 14.3.4.4 Clinically Significant Laboratory and Corresponding Results (Safety Population)

14.3.5. Displays of Other Laboratory, Vital Signs, Electrocardiogram, Physical Examination, and Other Safety Data

Table 14.3.5.1 Clinical Laboratory Summary – Serum Chemistry (Safety Population)

Table 14.3.5.2 Clinical Laboratory Change from Baseline – Serum Chemistry (Safety Population)

Table 14.3.5.3 Clinical Laboratory Shift from Baseline – Serum Chemistry (Safety Population)

Table 14.3.5.4 Clinical Laboratory Summary – Hematology and Coagulation (Safety Population)
Table 14.3.5.5 Clinical Laboratory Change from Baseline – Hematology and Coagulation (Safety Population)
Table 14.3.5.6 Clinical Laboratory Shift from Baseline – Hematology and Coagulation (Safety Population)
Table 14.3.5.7 Clinical Laboratory Summary – Urinalysis (Safety Population)
Table 14.3.5.8 Clinical Laboratory Change from Baseline – Urinalysis (Safety Population)
Table 14.3.5.9 Clinical Laboratory Shift from Baseline – Urinalysis (Safety Population)
Table 14.3.5.10 Vital Sign Summary (Safety Population)
Table 14.3.5.11 Vital Sign Change from Baseline (Safety Population)
Table 14.3.5.12 12-Lead Electrocardiogram Summary (Safety Population)
Table 14.3.5.13 12-Lead Electrocardiogram Change from Baseline (Safety Population)

9.3 Section 16 Data Listings

Note: Virology test results (Hepatitis and HIV) that are provided by the clinical laboratory will not be presented in subject data listings and will not be included in the database transfer. The date of sample collection only will be provided in the database and listings.

Data listings are numbered following the ICH structure but may be renumbered as appropriate during the compilation of the tables and figures for the CSR. The following is a list of appendix numbers and titles that will be included as data listings:

16.1 Study Information

Appendix 16.1.9 Statistical Methods

Appendix 16.1.7.2 Healthy Control Subjects Matched to Renal Function Groups

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

16.2. Subject Data Listings

16.2.1. Subject Discontinuation

Appendix 16.2.1 Subject Discontinuation (Safety Population)

16.2.2. Protocol Deviations

Appendix 16.2.2 Protocol Deviations

Note: Protocol deviations will be provided by the clinical study manager as Microsoft Excel file and read into the SDTM to generate the data listing.

16.2.3. Subjects Excluded from Pharmacokinetic Analysis

Appendix 16.2.3 Subjects Excluded from Pharmacokinetic Analysis

Note: Appendix 16.2.3 will be generated in MS Word for inclusion in the CSR.

16.2.4 Demographic Data

Appendix 16.2.4.1 Demographics (Safety Population)

Appendix 16.2.4.2 Physical Examination (Safety Population)

Appendix 16.2.4.3 Medical and Surgical History (Safety Population)

Appendix 16.2.4.4 Assessment of Renal Function (Safety Population)

16.2.5. Compliance and Drug Concentration Data

Appendix 16.2.5.1 Subject Eligibility (Safety Population)

Appendix 16.2.5.2 Test Compound Administration Times (Safety Population)

Appendix 16.2.5.3 PK Blood Draw Times and Protein Binding (Safety Population)

Appendix 16.2.5.4 Urine Collection Times (Safety Population)

Appendix 16.2.5.5 Follow-Up Phone Call (Safety Population)

Appendix 16.2.5.6 Prior and Concomitant Medications (Safety Population)

16.2.6 Individual Pharmacokinetic Response Data

Appendix 16.2.6.1 Individual Total and Unbound Plasma LOXO-292 Concentrations Versus Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 to Subject <#> (Linear and Semi-Log Scale)

Appendix 16.2.6.2 Individual Cumulative Amount of LOXO-292 Excreted Unchanged in Urine Following Administration of a Single Dose of 160 mg LOXO-292 to Subject <#> (Linear Scale)

Appendix 16.2.6.3 Individual Cumulative % Dose of LOXO-292 Excreted Unchanged in Urine Following Administration of a Single Dose of 160 mg LOXO-292 to Subject <#> (Linear Scale)

16.2.7 Adverse Events Listings

Appendix 16.2.7.1 Adverse Events (I of II) (Safety Population)

Appendix 16.2.7.2 Adverse Events (II of II) (Safety Population)

Appendix 16.2.7.3 Adverse Event Comments (Safety Population)

Appendix 16.2.7.4 Adverse Event Preferred Term Classification (Safety Population)

16.2.8 Listings of Individual Laboratory Measurements and Other Safety Observations

Appendix 16.2.8.1.1.1 Clinical Laboratory Report - Serum Chemistry (Conventional Units) (Safety Population)

Appendix 16.2.8.1.1.2 Clinical Laboratory Report - Serum Chemistry (SI Units) (Safety Population)

Appendix 16.2.8.1.2.1 Clinical Laboratory Report - Hematology and Coagulation (Conventional Units) (Safety Population)

Appendix 16.2.8.1.2.2 Clinical Laboratory Report - Hematology and Coagulation (SI Units) (Safety Population)

Appendix 16.2.8.1.3.1 Clinical Laboratory Report – Urinalysis (Conventional Units) (Safety Population)

Appendix 16.2.8.1.3.2 Clinical Laboratory Report – Urinalysis (SI Units) (Safety Population)

Appendix 16.2.8.1.4.1 Clinical Laboratory Report – Serum FSH (Conventional Units) (Safety Population)

Appendix 16.2.8.1.4.2 Clinical Laboratory Report – Serum FSH (SI Units) (Safety Population)

Appendix 16.2.8.1.5 Clinical Laboratory Report - Urine Drug Screening (Safety Population)

Appendix 16.2.8.1.6 Clinical Laboratory Report - Comments (Safety Population)

Appendix 16.2.8.1.7 Clinical Laboratory Serology Samples (Safety Population)

Appendix 16.2.8.2 Vital Signs (Safety Population)

Appendix 16.2.8.3 12-Lead Electrocardiogram (Safety Population)

10. TABLE AND FIGURE SHELLS

The following table shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the tables and figures that will be presented and included in the final CSR. Unless otherwise noted, all in-text tables will be presented in Times New Roman font size 8 and post-text tables in Courier New size font 9. These tables will be generated according to the ADaM Model 2.1 and ADaM implementation guide 1.1.

10.1 In-text Table Shells

Table 10-1 Summary of Disposition (Safety Population)

Disposition	Subjects with Mild RI	Subjects with Moderate RI	Subjects with Severe RI	Healthy Matched Control Subjects	Overall
Enrolled	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Completed Study	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Discontinued Early	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
<Reason1>	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
<Reason2>	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
RI = Renal impairment

Source: Table 14.1.1.1
CCI [redacted] DDMMMYYYY HH:MM

Table 11-1 Demographic Summary (Safety Population)

Trait		Subjects with Mild RI	Subjects with Moderate RI	Subjects with Severe RI	Healthy Matched Control Subjects	Overall
Sex	Male	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Female	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Race	Asian	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Black or African American	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	White	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Ethnicity	Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Not Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Age* (yr)	n	XX	XX	XX	XX	XX
	Mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	SD	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX
	Minimum	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Height (cm)	n	XX	XX	XX	XX	XX
	Mean	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XXX	XXX	XXX	XXX	XXX
	Median	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
	Maximum	XXX	XXX	XXX	XXX	XXX

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
RI = Renal impairment
* Age is calculated from the date of dosing.
BMI = Body mass index

Source: Table 14.1.1.2
CCI DDMMMYYYY HH:MM

Programmer Note: Weight (kg) and BMI (kg/m^2) will also be summarized in the table above. Weight, height, and BMI will be summarized at Screening.

In-text Tables 11-2, 11-9, and 11-16 will be in the following format:

Table 11-2 Summary of Total Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Pharmacokinetic Population)

Pharmacokinetic Parameters	Subjects with Mild RI	Subjects with Moderate RI	Subjects with Severe RI	Healthy Matched Control Subjects
Param1 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Param2 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Param3 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Param4 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
RI = Renal impairment

AUCs and Cmax values are presented as geometric mean (geometric CV%).
Tmax values are presented as median (min, max).
Other parameters are presented as arithmetic mean (± SD).
Source: Tables 14.2.1.5 to 14.2.1.8

Notes for Generating the Actual Table:

Presentation of Data:

- The following PK parameters will be presented in the following order:
  - Table 11-2 (plasma): AUC0-t, AUC0-inf, AUC%extrap, Cmax, Tmax, Kel, t½, CL/F, and Vz/F
    - Source: Tables 14.2.1.5 to 14.2.1.8
  - Table 11-9 (unbound plasma): AUC0-t,u, AUC0-inf,u, Cmax,u, CL/F,u, and Vz/F,u
    - Source: Tables 14.2.3.9 to 14.2.3.12
  - Table 11-16 (urine): Ae0-t, CLr, and Fe
    - Source: Tables 14.2.5.5 to 14.2.5.8
- n will be presented as an integer (with no decimal);
- Summary statistics will be presented with same precision as defined in post-text shells

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DDMMMYYYY HH:MM

In-text Tables 11-3 to 11-5 and 11-10 to 11-12 will be in the following format:

Table 11-3 Summary of Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild Renal Impairment Versus Corresponding Healthy Matched Control Subjects (Paired T-Test) (Pharmacokinetic Population)

Parameter	n	GMR (%)	90% Confidence Interval	p-value
param1 (units)	XX	XX.XX	XX.XX - XX.XX	X.XXXX
param2 (units)	XX	XX.XX	XX.XX - XX.XX	X.XXXX
param3 (units)	XX	XX.XX	XX.XX - XX.XX	X.XXXX

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
RI = Renal impairment
Parameters were ln-transformed prior to analysis and n is the number of paired differences (i.e, RI – Healthy).
Geometric Mean Ratio (GMR) and 90% confidence intervals (CIs) are calculated by exponentiating the mean difference (RI – healthy) and the associated 90 % confidence intervals derived from the paired t-test and multiplying by 100.

Source: Table 14.2.1.10

Notes for Generating the Actual Table:

Presentation of Data:

- The following PK parameters will be presented in the following order:
  - Table 11-3 through 11-5: AUC0-t, AUC0-inf, and Cmax
  - Table 11-10 through 11-12: AUC0-t,u, AUC0-inf,u, and Cmax,u
- n will be presented as an integer (with no decimal);
- All statistics will be presented with same precision as defined in post-text shells
- Source:
  - Table 11-3: Table 14.2.1.10
  - Table 11-4: Table 14.2.1.11
  - Table 11-5: Table 14.2.1.12
  - Table 11-10: Table 14.2.1.14
  - Table 11-11: Table 14.2.1.15
  - Table 11-12: Table 14.2.1.16

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In-text Tables 11-6 to 11-8 and 11-13 to 11-15 will be in the following format:

Table 11-6 Summary of Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild Renal Impairment Versus Healthy Matched Control Subjects (Pharmacokinetic Population)

	Subjects with Mild RI (Test)		Healthy Matched Control Subjects (Reference)		GMR (%)	90% Confidence Interval
Parameter	Geometric LSMs	n	Geometric LSMs	n		
param1 (units)	XXX.X	XX	XXX.X	XX	XX.XX	XX.XX - XX.XX
param2 (units)	XXX.X	XX	XXX.X	XX	XX.XX	XX.XX - XX.XX
param3 (units)	XXX.X	XX	XXX.X	XX	XX.XX	XX.XX - XX.XX

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
RI = Renal impairment
Parameters were ln-transformed prior to analysis.
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs derived from the ANCOVA.
Geometric Mean Ratio (GMR) = 100*(test/reference)

Source: Table 14.2.1.13

Notes for Generating the Actual Table:

Presentation of Data:

- The following PK parameters will be presented in the following order:
  - Table 11-3 through 11-5: AUC0-t, AUC0-inf, and Cmax
  - Table 11-13 through 11-5: AUC0-t,u, AUC0-inf,u, and Cmax,u
- n will be presented as an integer (with no decimal);
- All statistics will be presented with same precision as defined in post-text shells
- Source:
  - Table 11-3: Table 14.2.1.13
  - Table 11-4: Table 14.2.1.14
  - Table 11-5: Table 14.2.1.15
  - Table 11-13: Table 14.2.1.17
  - Table 11-14: Table 14.2.1.18
  - Table 11-15: Table 14.2.1.19

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Table 12-1 Treatment-Emergent Adverse Event Frequency by Cohort – Number of Subjects Reporting the Event (% of Subjects Dosed) (Safety Population)

Adverse Events*	Subjects with Mild RI	Subjects with Moderate RI s	Subjects with Severe RI	Healthy Matched Control Subjects	Overall
Number of Subjects Dosed	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Number of Subjects With TEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Number of Subjects Without TEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
System Organ Class 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
System Organ Class 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
RI = Renal impairment
* Adverse events are coded using MedDRA® Version 21.1 by System Organ Class and Preferred Term.
TEAE = Treatment-emergent Adverse event
Although a subject may have had 2 or more clinical adverse experiences, the subject is counted only once within a category. The same subject may appear in different categories.
If a TEAE decreased in severity grade, the new TEAE record with less severity was counted as the same TEAE event of the previous record with worse severity.

Source: Table 14.3.1.1

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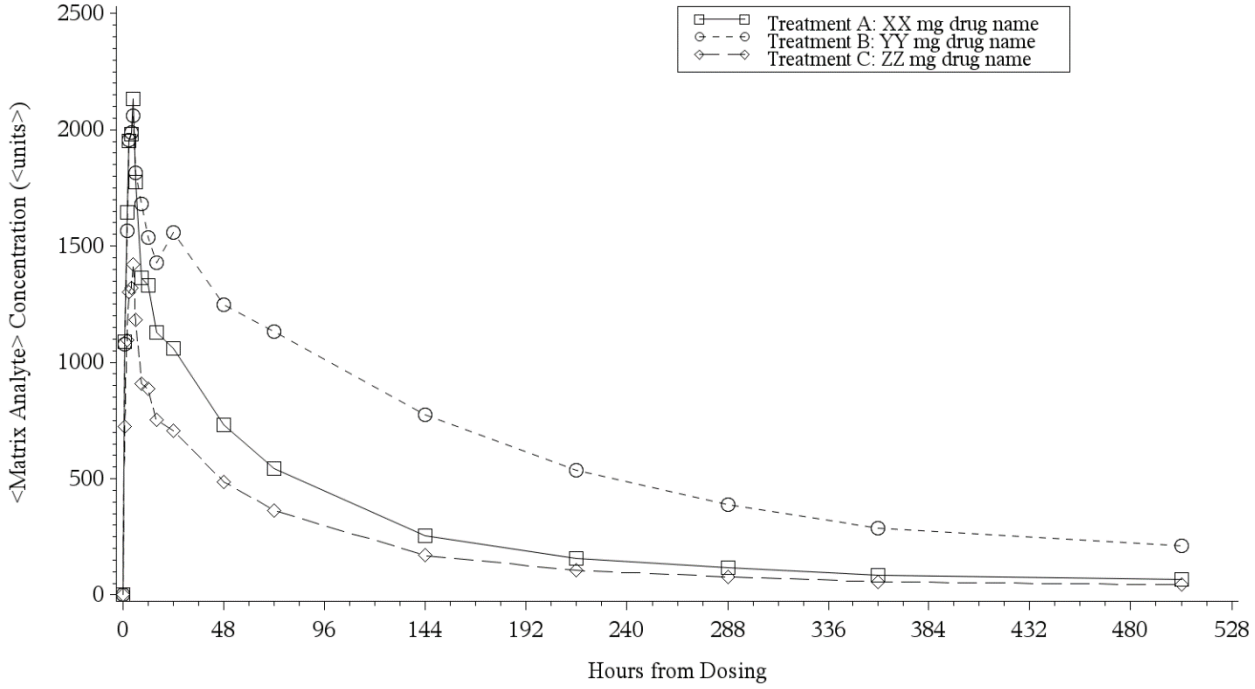
Programmer Note: Sort by decreasing frequency of system organ class and by preferred term within a system organ class of Overall column.

10.2 Figures Shells

In-text Figures 11-1, 11-5, and 11-9, Figures 14.2.2.2, 14.2.4.2, 14.2.6.2, and 14.2.6.4 will be in the following format:

Figure 11-1 Arithmetic Mean Total Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Pharmacokinetic Population)



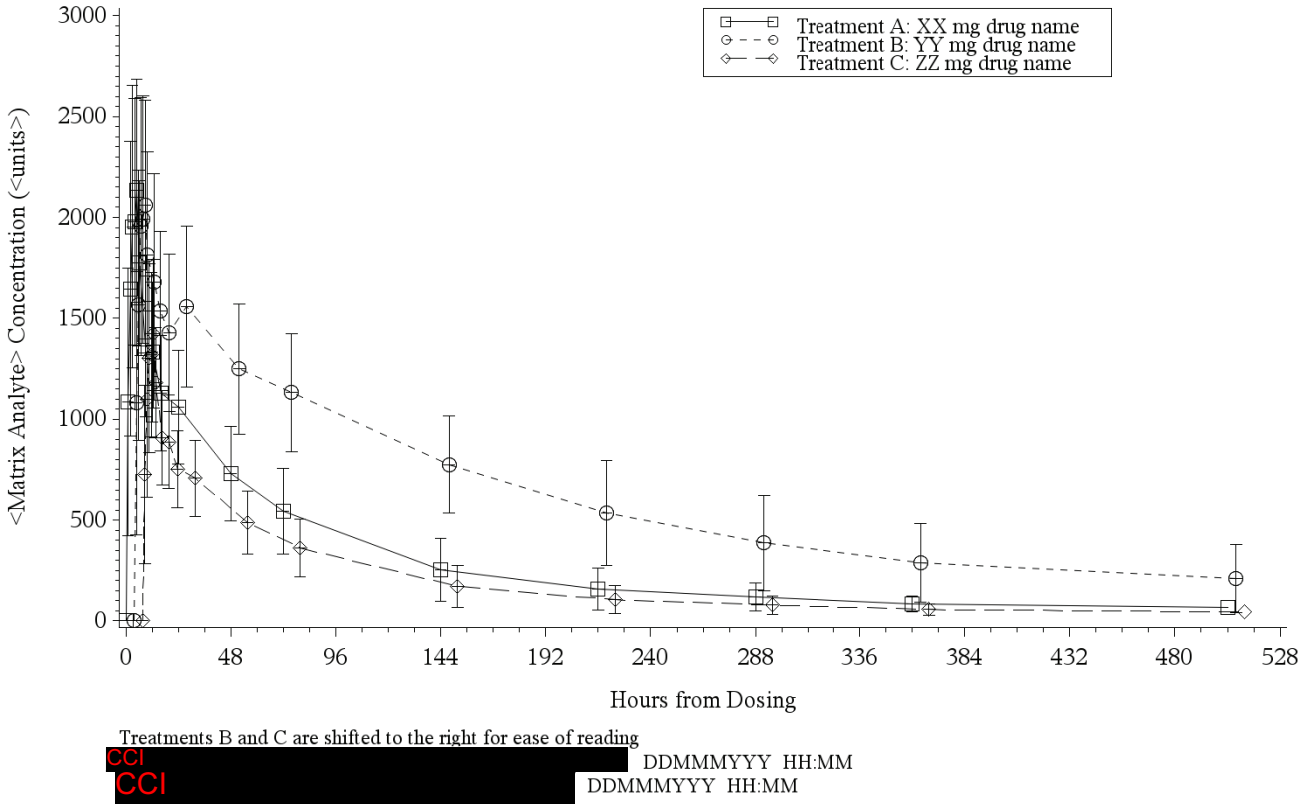
Notes for Generating the Actual Mean Figure:

- Figures 11-1 and 14.2.2.2:
  - Legend will be:
    - Subjects with Mild RI (n = X)
    - Subjects with Moderate RI (n = X)
    - Subjects with Severe RI (n = X)
    - Healthy Matched Control Subjects (n = X)
  - Y-axis label will be "Total Plasma LOXO-292 Concentration (ng/mL)"
  - X-axis label will be "Hours Postdose (hr) from LOXO-292 Dose"
  - Add in footnote: LLOQ value for LOXO-292 in plasma is 1.00 ng/mL.
- Figures 11-5 and 14.2.4.2:
  - Legend will be:
    - Subjects with Mild RI (n = X)
    - Subjects with Moderate RI (n = X)
    - Subjects with Severe RI (n = X)
    - Healthy Matched Control Subjects (n = X)
  - Y-axis label will be "Unbound Plasma LOXO-292 Concentration (ng/mL)"
  - X-axis label will be "Hours Postdose (hr) from LOXO-292 Dose"
  - Add in footnote: LLOQ value for LOXO-292 in plasma is 1.00 ng/mL.
- Figures 11-9 and 14.2.6.4:
  - Legend will be:
    - Subjects with Mild RI (n = X)
    - Subjects with Moderate RI (n = X)
    - Subjects with Severe RI (n = X)
    - Healthy Matched Control Subjects (n = X)
  - Y-axis label will be "Cumulative % Dose of LOXO-292 Excreted Unchanged (%)"
  - X-axis label will be "Interval End (hr)"
  - Add in footnote: LLOQ value for LOXO-292 in urine is 5.00 ng/mL.

- Figure 14.2.6.2:
  - Legend will be:
    - Subjects with Mild RI (n = X)
    - Subjects with Moderate RI (n = X)
    - Subjects with Severe RI (n = X)
    - Healthy Matched Control Subjects (n = X)
  - Y-axis label will be "Cumulative Amount of LOXO-292 Excreted Unchanged (ng)"
  - X-axis label will be "Interval End (hr)"
  - Add in footnote: LLOQ value for LOXO-292 in urine is 5.00 ng/mL.

Figures 14.2.2.1, 14.2.4.1, 14.2.6.1, and 14.2.6.3 will be in the following format:

Figure 14.2.2.1 Mean (SD) Total Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Linear Scale) (Pharmacokinetic Population)



Notes for Generating the Actual Mean Figure:

- Figure 14.2.2.1:
  - Legend will be:
    - Subjects with Mild RI (n = X)
    - Subjects with Moderate RI (n = X)
    - Subjects with Severe RI (n = X)
    - Healthy Matched Control Subjects (n = X)
  - Y-axis label will be "Total Plasma LOXO-292 Concentration (ng/mL)"
  - X-axis label will be "Hours Postdose (hr) from LOXO-292 Dose"
  - Add in footnote: LLOQ value for LOXO-292 in plasma is 1.00 ng/mL.
- Figure 14.2.4.1:
  - Legend will be:
    - Subjects with Mild RI (n = X)
    - Subjects with Moderate RI (n = X)
    - Subjects with Severe RI (n = X)
    - Healthy Matched Control Subjects (n = X)
  - Y-axis label will be "Unbound Plasma LOXO-292 Concentration (ng/mL)"
  - X-axis label will be "Hours Postdose (hr) from LOXO-292 Dose"
  - Add in footnote: LLOQ value for LOXO-292 in plasma is 1.00 ng/mL.
- Figure 14.2.6.1:
  - Legend will be:
    - Subjects with Mild RI (n = X)
    - Subjects with Moderate RI (n = X)
    - Subjects with Severe RI (n = X)
    - Healthy Matched Control Subjects (n = X)
  - Y-axis label will be "Cumulative Amount of LOXO-292 Excreted Unchanged (ng)"
  - X-axis label will be "Interval End (hr)"
  - Add in footnote: LLOQ value for LOXO-292 in urine is 5.00 ng/mL.

- Figure 14.2.6.3:
  - Legend will be:
    - Subjects with Mild RI (n = X)
    - Subjects with Moderate RI (n = X)
    - Subjects with Severe RI (n = X)
    - Healthy Matched Control Subjects (n = X)
  - Y-axis label will be "Cumulative % Dose of LOXO-292 Excreted Unchanged (%)"
  - X-axis label will be "Interval End (hr)"
  - Add in footnote: LLOQ value for LOXO-292 in urine is 5.00 ng/mL.

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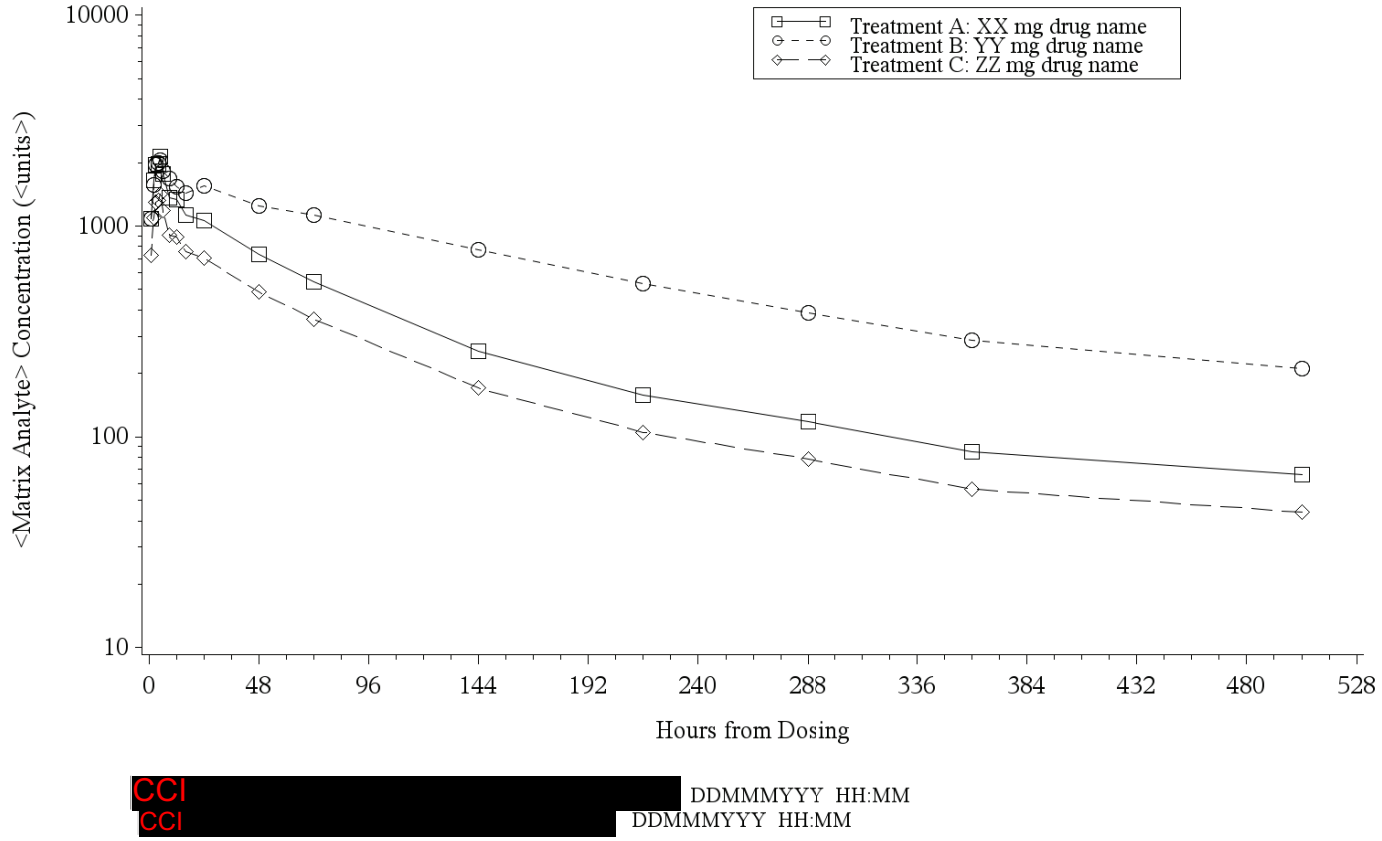
Figures 14.2.2.3 and 14.2.4.3 will be in the following format:

Figure 14.2.2.3 Mean Total Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Semi-Log Scale) (Pharmacokinetic Population)

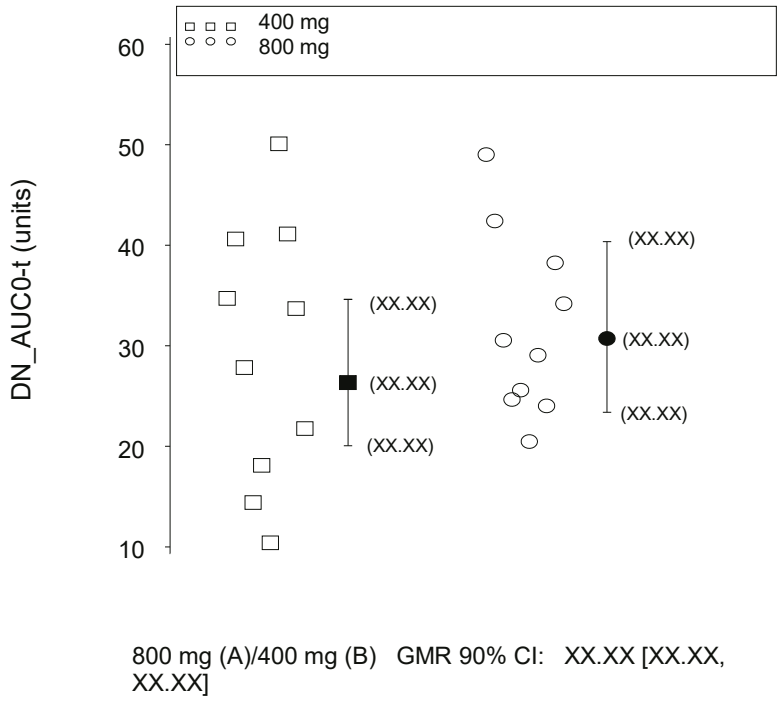


Notes for Generating the Actual Mean Figure:

- Figure 14.2.2.3:
  - Legend will be:
    - Subjects with Mild RI (n = X)
    - Subjects with Moderate RI (n = X)
    - Subjects with Severe RI (n = X)
    - Healthy Matched Control Subjects (n = X)
  - Y-axis label will be "Total Plasma LOXO-292 Concentration (ng/mL)"
  - X-axis label will be "Hours Postdose (hr) from LOXO-292 Dose"
  - Add in footnote: LLOQ value for LOXO-292 in plasma is 1.00 ng/mL.
- Figure 14.2.4.3:
  - Legend will be:
    - Subjects with Mild RI (n = X)
    - Subjects with Moderate RI (n = X)
    - Subjects with Severe RI (n = X)
    - Healthy Matched Control Subjects (n = X)
  - Y-axis label will be "Unbound Plasma LOXO-292 Concentration (ng/mL)"
  - X-axis label will be "Hours Postdose (hr) from LOXO-292 Dose"
  - Add in footnote: LLOQ value for LOXO-292 in plasma is 1.00 ng/mL.

In-text Figures 11-2 through 11-4, 11-6 through 11-8, and Figures 14.2.2.4 through 14.2.2.6 and 14.2.4.4 through 14.2.4.6 will be in the following format:

Figure 11-2 Individual Total Plasma LOXO-292 AUC0-t Values, Geometric Means With Corresponding 95% CIs, and GMR With Corresponding 90% CIs Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Pharmacokinetic Population)

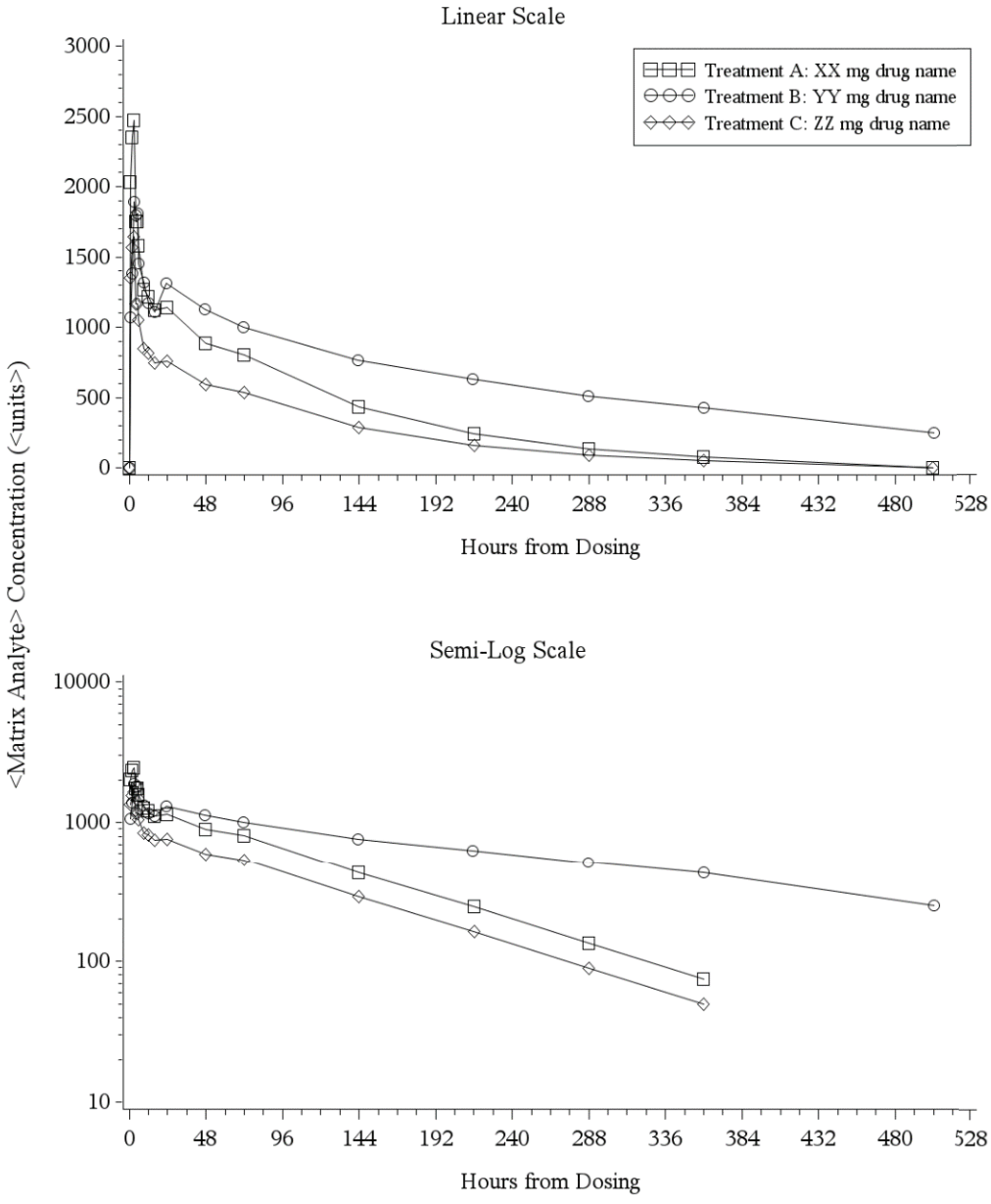


Notes for Generating the Actual Figure:

- The individual values by cohort will be presented in an almost vertical plane, and only staggered if there are some overlaps of symbols. The geometric mean and 95% CI will accompany each cohort. The GMR and 90% CI for each comparison from the paired t-test will be inserted below the x-axis as a footnote.
- Use different symbols for each cohort
- Legend will be:
    - Subjects with Mild RI (n = X)
    - Subjects with Moderate RI (n = X)
    - Subjects with Severe RI (n = X)
    - Healthy Matched Control Subjects (n = X)
- Y-axis label will be the PK parameter with the appropriate unit: AUC0-t, AUC0-t,u, AUC0-inf, AUC0-inf,u, Cmax, or Cmax,u
- X-axis label will be the cohorts: "Mild/Moderate/Severe/Healthy"

Appendices 16.2.6.1 through 16.2.6.3 will be in the following format:

Appendix 16.2.6.1
Individual Total and Unbound Plasma LOXO-292 Concentrations Versus Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 to Subject <#> (Linear and Semi-Log Scale)



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Notes for Generating the Actual Individual Figure:

- Appendix 16.2.6.1:
  - Legend will be one of the following:
    - Subjects with Mild RI
    - Subjects with Moderate RI
    - Subjects with Severe RI
    - Healthy Matched Control Subjects
  - Y-axis label will be "Total or Unbound Plasma LOXO-292 Concentration (ng/mL)"
  - X-axis label will be "Hours Postdose (hr) from LOXO-292 Dose"
  - Add in footnote: LLOQ value for LOXO-292 in plasma is 1.00 ng/mL.
- Appendix 16.2.6.2 (only linear scale presented):
  - Legend will be one of the following:
    - Subjects with Mild RI
    - Subjects with Moderate RI
    - Subjects with Severe RI
    - Healthy Matched Control Subjects
  - Y-axis label will be "Cumulative Amount of LOXO-292 Excreted Unchanged (ng)"
  - X-axis label will be "Interval End (hr)"
  - Add in footnote: LLOQ value for LOXO-292 in urine is 5.00 ng/mL.
- Appendix 16.2.6.3 (only linear scale presented):
  - Legend will be one of the following:
    - Subjects with Mild RI
    - Subjects with Moderate RI
    - Subjects with Severe RI
    - Healthy Matched Control Subjects
  - Y-axis label will be "Cumulative % Dose of LOXO-292 Excreted Unchanged (ng)"
  - X-axis label will be "Interval End (hr)"
  - Add in footnote: LLOQ value for LOXO-292 in urine is 5.00 ng/mL.

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10.3 Post-text Table Shells

Table 14.1.1.1 Summary of Disposition (Safety Population)

	Cohort				
Disposition	Mild	Moderate	Severe	Healthy	Overall
Enrolled	XX	XX	XX	XX	XX
Completed	XX	XX	XX	XX	XX
Discontinued Early	XX	XX	XX	XX	XX
Reason 1	XX	XX	XX	XX	XX
Reason 2	XX	XX	XX	XX	XX
Reason 3	XX	XX	XX	XX	XX
etc.					

Note: All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions:
Mild: Subjects with mild renal impairment
Moderate: Subjects with moderate renal impairment
Severe: Subjects with severe renal impairment
Healthy: Healthy matched control subjects

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Table 14.1.1.2 Demographic Summary (Safety Population)

Trait		Cohort: Mild	Moderate	Severe	Healthy	Overall
Sex	Male	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Female	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Race	Asian	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Black or African American	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	White	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Ethnicity	Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Not Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Age*(yr)	n	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX
Height (cm)	n	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX

Programmer Note: Also include weight (kg) and BMI (kg/m^2). Weight, height and BMI will be summarized at Screening.
Note: All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions:
Mild: Subjects with mild renal impairment
Moderate: Subjects with moderate renal impairment
Severe: Subjects with severe renal impairment
Healthy: Healthy matched control subjects
* Age is calculated from the date of dosing.
BMI = Body mass index

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Tables 14.2.1.1 through 14.2.1.4, and 14.2.3.5 through 14.2.3.8 will be in the following format:

Table 14.2.1.1 Total Plasma LOXO-292 Concentrations (ng/mL) Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild Renal Impairment (Pharmacokinetic Population)

	Sample Times (hr)								
Subject Number	Predose	XX	XX	XX	XX	XX	XX	XX	XX
XXX-XXX	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
XXX-XXX	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
XXX-XXX	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
n	XX	XX	XX	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%	.	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum	XX	XX	XX	XX	XX	XX	XX	XX	XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Maximum	XX	XX	XX	XX	XX	XX	XX	XX	XX

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 1.00 ng/mL are treated as 0 before the first quantifiable concentration and as missing elsewhere.
. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- Present the subject number in the following format: XXX-XXX
- Concentrations will be presented to same precision as in the bioanalytical data.
- Summary statistics presentation with respect to the precision of the bioanalytical data: n = integer; Mean and Median +1; SD and SEM +2, Min and Max +0, CV% to 1 decimal

Programmer Note:

- PK Time points are: predose and 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 12, 24, 36, 48, 72, 96, 120, 144, and 168 hours postdose.
- Tables 14.2.3.5 through 14.2.3.8: the unbound plasma LOXO-292 concentrations will be calculated by multiplying the measured LOXO-292 concentrations by the fraction of unbound LOXO-292 at each sampling time point for each subject. The fraction unbound will be calculated in Table 14.2.3.1 through 14.2.3.4.

Per study design needs, the following changes are made to this table relative to Celerion standard:

1. Please remove the "Treatment Sequence" and "Study Period" columns

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Tables 14.2.1.5 through 14.2.1.8, and 14.2.3.9 through 14.2.3.12 will be in the following format:

Table 14.2.1.5 Total Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild Renal Impairment (Pharmacokinetic Population)

Subject Number	Parameters					
	param1 (units)	param2 (units)	param3 (units)	param4 (units)	param5 (units)	param6 (units)
XXX-XXX	XXX	X.XX	XXX	XXX	XX.X	X.XXX
XXX-XXX	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
XXX-XXX	XXX	X.XX	XXX	XXX	XX.X	X.XXX
XXX-XXX	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
XXX-XXX	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
XXX-XXX	X.XX	X.XX	XXX	XXX	XX.X	X.XXX
XXX-XXX	XXX	X.XX	XXX	XXX	XX.X	X.XXX
n	XX	XX	XX	XX	XX	XX
Mean	XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
Median	XX.XX	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Maximum	XXX	X.XX	XXX	XXX	XX.X	X.XXX
Geom Mean	XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Geom CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
L95% CI (Geom Mean)	XX.X	XX.X		XX.X		
U95% CI (Geom Mean)	XX.X	XX.X		XX.X		

. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- Present the subject number in the following format: XXX-XXX
- The following PK parameters will be presented in the following order:
  - Table 14.2.1.5 through 14.2.1.8: AUC0-t, AUC0-inf, AUC%extrap, Cmax, Tmax, Kel, t½, CL/F, and Vz/F
  - Table 14.2.3.9 through 14.2.3.12: AUC0-t,u, AUC0-inf,u, Cmax,u, CL/F,u, and Vz/F,u
- n will be presented as an integer (with no decimal);
- Parameter values for exposure-based parameters (i.e. AUCs, AUC%extrap, Cmax, CL/F, and Vz/F) will be presented with, at maximum, the precision of the bioanalytical data, and, at minimum, 3 significant figures (to be determined by the PKist once the bioanalytical data are received).
  - Summary statistics for exposure parameters will be presented as: Mean, Median, and Geom Mean +1; SD and SEM +2, Min and Max +0 with respect to the number of significant figures.
- Values for time-based parameters (i.e. Tmax, and t½) will be presented with 2 decimals.
  - Summary statistics for time-based parameters will be presented as: Mean, Median, and Geom Mean +1; SD and SEM +2, Min and Max +0 with respect to the number of decimals.
- Values for rate constants (i.e. Kel) will be presented with 3 significant figures.
  - Summary statistics for Kel will be presented as: Mean, Median, and Geom Mean +1; SD and SEM +2, Min and Max +0 with respect to the number of significant figures.
- CV% and Geom CV% for all parameters will be presented with 1 decimal
- 95% CI (Geom Mean) will be presented for AUC0-t, AUC0-inf and Cmax only
- 95% CI (Geom Mean) will be presented with 2 decimals
- Remove 'Treatment Sequence' and 'Study Period'

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Tables 14.2.1.9 and 14.2.3.13 will be in the following format:

Table 14.2.1.9 Intervals (Hours) Used for Determination of Total Plasma LOXO-292 Kel Values Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild, Moderate, and Severe Renal Impairment and to Healthy Matched Control Subjects (Pharmacokinetic Population)

Subject Number	Cohort	Interval	R2	n
XXX-XXX	X	XX.X - XX.X	X.XXX	X
XXX-XXX	X	XX.X - XX.X	X.XXX	X
XXX-XXX	X	XX.X - XX.X	X.XXX	X
XXX-XXX	X	XX.X - XX.X	X.XXX	X
XXX-XXX	X	XX.X - XX.X	X.XXX	X
XXX-XXX	X	XX.X - XX.X	X.XXX	X

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions:
Mild: Subjects with mild renal impairment
Moderate: Subjects with moderate renal impairment
Severe: Subjects with severe renal impairment
Healthy: Healthy matched control subjects
R2 = Coefficient of determination
n = Number of points used in Kel calculation
. = Kel value not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- Present the subject number in the following format: XXX-XXX
- Interval start and stop times will be presented to 1 decimal or 3 significant figures minimum;
- R2 will be presented to 3 decimals;
- n will be presented as an integer (with no decimal)

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Tables 14.2.1.10 through 14.2.1.12 and 14.2.3.14 through 14.2.3.16 will be in the following format:

Table 14.2.1.10 Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild Renal Impairment Versus Corresponding Healthy Matched Control Subjects (Paired t-test) (Pharmacokinetic Population)

Parameter	(unit)	n	Geometric Mean Ratio (%)	90% Confidence Intervals	p-value
Param1	(unit)	XX	XXX.XX	XXX.XX – XXX.XX	X.XXXX
Param2	(unit)	XX	XXX.XX	XXX.XX – XXX.XX	X.XXXX
Param3	(unit)	XX	XXX.XX	XXX.XX – XXX.XX	X.XXXX

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
RI = Renal impairment
Parameters were ln-transformed prior to analysis and n is the number of paired differences (i.e., RI - Healthy).
Geometric Mean Ratio (GMR) and 90% confidence intervals (CIs) are calculated by exponentiating the mean difference (RI - healthy) and the associated 90 % confidence intervals derived from the paired t-test and multiplying by 100

Notes for Generating the Actual Table:

Presentation of Data:

- p-value will be presented with 4 decimals.
- Geometric Mean Ratio and 90% CI will be presented to 2 decimal places.
- PK parameters to be presented are
  - Tables 14.2.1.10 through 14.2.1.12 : AUC0-t, AUC0-inf, and Cmax
  - Tables 14.2.3.14 through 14.2.3.16 : AUC0-t,u AUC0-inf,u, and Cmax,u

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Tables 14.2.1.13 through 14.2.1.15 and 14.2.3.17 through 14.2.3.19 will be in the following format:

Table 14.2.1.13 Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild Renal Impairment Versus Healthy Matched Control Subjects (Pharmacokinetic Population)

		Treatment Geometric LSMs				Geometric Mean	90%
Parameter	(unit)	Mild	(n)	Healthy	(n)	Ratio	Confidence Intervals
Param1	(unit)	X.XX	(n)	X.XX	(n)	XXX.XX	XXX.XX - XXX.XX
Param2	(unit)	X.XX	(n)	X.XX	(n)	XXX.XX	XXX.XX - XXX.XX
Param3	(unit)	X.XX	(n)	X.XX	(n)	XXX.XX	XXX.XX - XXX.XX

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions:
Mild: Subjects with mild renal impairment
Healthy: Healthy matched control subjects
Parameters were ln-transformed prior to analysis.
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs from ANCOVA.
Geometric Mean Ratio is calculated by exponentiating the LSM difference (Renal impaired - healthy) and multiplying by 100.

Notes for Generating the Actual Table:

Presentation of Data:

- Geometric LSMs will be presented to the same precision as the Mean in the PK parameter table.
- Geometric Mean Ratio and 90% CI will be presented to 2 decimal places.
- PK parameters to be presented are
  - Tables 14.2.1.13 through 14.2.1.15 : AUC0-t, AUC0-inf, and Cmax
  - Tables 14.2.3.17 through 14.2.3.19 : AUC0-t,u AUC0-inf,u, and Cmax,u

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Tables 14.2.3.1 through 14.2.3.4 will be presented in the following format:

Table 14.2.3.1 Concentrations of LOXO-292 (LOXO-292) (ng/mL), and Concentrations in the Buffer Chamber (LOXO-292 BC), and Concentrations in the Plasma Chamber (LOXO-292 PC), % Recovery, and Fraction Unbound Obtained Following the Plasma Protein Binding Assay in Subjects with Mild Renal Impairment (Pharmacokinetic Population)

Number	LOXO-292	LOXO-292 BC	LOXO-292 PC	Recovery (%)	Fraction Unbound
XXX-XXX	XXX	XX.X	XXX	XX.XX	X.XXX
XXX-XXX	XXX	XX.X	XXX	XX.XX	X.XXX
XXX-XXX	X	XX.X	XXX	XX.XX	X.XXX
n	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%	.	XX.X	XX.X	XX.X	XX.X
SEM	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum	XX	XX	XX	XX	XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Maximum	XX	XX	XX	XX	XX

LOXO-292: Total concentration, LOXO-292 concentration in matrix prior to dialysis
LOXO-292 BC: Buffer concentration, LOXO-292 concentration in the buffer chamber following dialysis
LOXO-292 PC: Plasma concentration, LOXO-292 concentration in the plasma chamber following dialysis
Recovery = (LOXO-292 BC + LOXO-292 PC) / LOXO-292
Fraction unbound = LOXO-292 BC / LOXO-292 PC
. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- Present the subject number in the following format: XXX-XXX
- Concentrations will be presented to same precision as in the bioanalytical data.
- Summary statistics presentation with respect to the precision of the bioanalytical data: n = integer; Mean and Median +1; SD and SEM +2, Min and Max +0, CV% to 1 decimal
- The 'Recovery' will be calculated as follow: (LOXO-292 BC + LOXO-292 PC) / LOXO-292
- The 'Fraction unbound' will be calculated as follow: LOXO-292 BC / LOXO-292 PC

Tables 14.2.5.1 through 15.2.5.4 will be presented in the following format:

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Table 14.2.5.1 Urinary Excretion of LOXO-292 Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild Renal Impairment (Pharmacokinetic Population)

	Parameters							
	Predose		t1 - t2 Hours			t2-t3 Hours		
Subject Number	Conc (units)	Vol (units)	Conc (units)	Vol (units)	Aet1-t2 (units)	Conc (units)	Vol (units)	Aet2-t3 (unit)
XXX-XXX	X.XX	X.XX	XX.XX	X.XX	X.XX	X.XX	X.XX	X.XX
XXX-XXX	X.XX	X.XX	XX.XX	X.XX	X.XX	X.XX	X.XX	X.XX
XXX-XXX	X.XX	X.XX	XX.XX	X.XX	X.XX	X.XX	X.XX	X.XX
n	X	X	X	X	X	X	X	X
Mean	X.XXX	X.XXX	XX.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
SD	X.XXXX	X.XXXX	XX.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
CV (%)	X.X	X.X	XX.X	X.X	X.X	X.X	X.X	X.X
SEM	X.XXXX	X.XXXX	XX.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
Minimum	X.XX	X.XX	XX.XX	X.XX	X.XX	X.XX	X.XX	X.XX
Median	X.XXX	X.XXX	XX.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Maximum	X.XX	X.XX	XX.XX	X.XX	X.XX	X.XX	X.XX	X.XX

. = Value missing or not reportable.
For the calculation of summary statistics and urinary excretion parameters, concentration values that are BLQ of 5.00 ng/mL are treated as 0.

Notes for Generating the Actual Table:

Presentation of Data:

- Present the subject number in the following format: XXX-XXX
- Intervals are: predose, and 0-4, 4-8, 8-12, 12-24, 24-48, 48-72, 72-96, 96-120, 120-144, and 144-168 hours postdose
- Parameters to be presented:
  - Predose: conc <unit> and volume <unit> only
  - Each postdose interval: conc <unit>, volume <unit>, Aet1-t2 <unit>
- Concentrations will be presented to same precision as in the bioanalytical data. Volume will be presented to the same precision as the CRF.
  - Note: If the amount of urine excreted was captured in the CRF as urine weight (g), it will be converted to volume (mL) using the assumed density of 1 g/mL
  - The units of Ae may be presented as mg if the overall cumulative value is more than 1 mg.
- Summary statistics presentation with respect to the precision of the bioanalytical data: n = integer; Mean and Median +1; SD and SEM +2, Min and Max +0, CV% to 1 decimal

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Table 14.2.5.5 through 14.2.5.8 will be presented as follow:

Table 14.2.5.5 Pharmacokinetic Parameters for Urinary Excretion of LOXO-292 Following Administration of a Single Dose of 160 mg LOXO-292 to Subjects with Mild Renal Impairment (Pharmacokinetic Population)

	Parameters		
Subject Number	Ae0-t (unit)	Fe (%)	CLr (unit)
XXX-XX	X.XX	X.XX	X.XX
XXX-XX	X.XX	X.XX	X.XX
XXX-XX	X.XX	X.XX	X.XX
n	X	X	X
Mean	X.XXX	X.XXX	X.XXX
SD	X.XXXX	X.XXXX	X.XXXX
CV%	X.X	X.X	X.X
SEM	X.XXXX	X.XXXX	X.XXXX
Minimum	X.XX	X.XX	X.XX
Median	X.XXX	X.XXX	X.XXX
Maximum	X.XX	X.XX	X.XX
Geom Mean	X.XXX	X.XXX	X.XXX
Geom CV%	X.X	X.X	X.X

. = Value missing or not reportable.
For the calculation of summary statistics and urinary excretion parameters, concentration values that are BLQ of 5.00 ng/mL are treated as 0.

Notes for Generating the Actual Table:

Presentation of Data:

- Present the subject number in the following format: XXX-XXX
- PK parameters to present: Ae0-t <unit>, Fe <%>, CLr <unit>
    - Ae0-t is CumAe in Celerion standard programs, where t is the end time of the last interval with concentration data available
    - Fe is CumFe in Celerion standard programs
- Ae0-t will be presented to the same precision as the bioanalytical data; Fe will be presented to 3 decimal places; CLr will be presented to 3 significant figures.
- Note: If the amount of urine excreted was captured in the CRF as urine weight (g), it will be converted to volume (mL) using the assumed density of 1 g/mL
- Summary statistics: n = integer; Mean, Median, and Geom Mean +1; SD and SEM +2; Min and Max +0; CV% and Geom CV% to 1 decimal

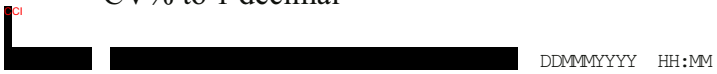

Table 14.3.1.1 Treatment-emergent Adverse Event Frequency by Cohort - Number of Subjects Reporting Events (% of Subject Dosed) (Safety Population)

	Cohort				
TE Adverse Event*	Mild	Moderate	Severe	Healthy	Overall
Number of Subjects Dosed	X (100%)	X (100%)	X(100%)	X(100%)	X(100%)
Number of Subjects with TE Adverse Events	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Number of Subjects without TE Adverse Events	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Nervous system disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dizziness	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Headache	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Presyncope	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Respiratory, thoracic and mediastinal disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dry throat	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Oropharyngeal pain	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sinus congestion	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sneezing	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
General disorders and administration site conditions	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Fatigue	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Thirst	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
etc.					

Note: * Adverse events are classified according to the MedDRA Version 21.1 by System Organ Class and Preferred Term.
TE = Treatment-emergent
If a TEAE decreased in severity grade, the new TEAE record with less severity was counted as the same TEAE event of the previous record with worse severity.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions:
Mild: Subjects with mild renal impairment
Moderate: Subjects with moderate renal impairment
Severe: Subjects with severe renal impairment
Healthy: Healthy matched control subjects

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Programmer Note: Sort by decreasing frequency of system organ class and by preferred term within a system organ class of Overall column. For each subject, please sort the AEs with same verbatim and preferred term by onset date/time. For any pair (e.g., AE_S1, AE_S2) of these AEs (for same subject, same verbatim and preferred term), if the onset date/time of AE_S2 = resolved date/time of AE_S1 and the grade of AE_S2 < the grade level of AE_S1, then mark the AE_S2 with a flag like EVAUL_FLG =”N”. Then, for AE analysis (summary tables), please exclude the ones with EVAUL_FLG =”N”. Won’t repeat this comment again.

Table 14.3.1.2 Treatment-emergent Adverse Event Frequency by Cohort – Number of Adverse Events (% of Total Adverse Events) (Safety Population)

	Cohort				
TE Adverse Event*	Mild	Moderate	Severe	Healthy	Overall
Number of TE Adverse Events	X (100%)	X (100%)	X(100%)	X(100%)	X(100%)
Nervous system disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dizziness	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Headache	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Presyncope	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Respiratory, thoracic and mediastinal disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dry throat	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Oropharyngeal pain	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sinus congestion	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sneezing	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
General disorders and administration site conditions	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Fatigue	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Thirst	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
etc.					

Note: * Adverse events are classified according to the MedDRA Version 21.1 by System Organ Class and Preferred Term.
TE = Treatment-emergent
If a TEAE decreased in severity grade, the new TEAE record with less severity was counted as the same TEAE event of the previous record with worse severity.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

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Programmer Note: Sort by decreasing frequency of system organ class and by preferred term within a system organ class of Overall column.

Table 14.3.1.3 Treatment-Emergent Adverse Event Frequency by Cohort, Severity Grade, and Relationship to Study Drug – Number of Subjects Reporting Events (Safety Population)

TE Adverse Event*	Cohort	Number of Subjects with Adverse Events	Severity Grade					Relationship to Study Drug	
			1	2	3	4	5	Related	Not Related
Dizziness	XXXX	X	X	X	X	X	X	X	X
Dry eye	XXXX	X	X	X	X	X	X	X	X
Dry mouth	XXXX	X	X	X	X	X	X	X	X
	XXXX	X	X	X	X	X	X	X	X
Dry throat	XXXX	X	X	X	X	X	X	X	X
Ear pain	XXXX	X	X	X	X	X	X	X	X
Fatigue	XXXX	X	X	X	X	X	X	X	X
Mild RI Subjects		XX	X	X	X	X	X	X	X
Moderate RI Subjects		XX	X	X	X	X	X	X	X
Severe RI Subjects		XX	X	X	X	X	X	X	X
Healthy Matched Subjects		XX	X	X	X	X	X	X	X
Overall		XX	X	X	X	X	X	X	X

Note: * Adverse events are classified according to MedDRA Version 21.1 by System Organ Class and Preferred Term.
TE = Treatment-emergent; AE = Adverse event
Severity Grade: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe or medically significant but not immediately life-threatening; Grade 4 = Life-threatening consequences; Grade 5 = Death related to AE
Not all grades are appropriate for all AEs, therefore some AEs are listed in the CTCAE with fewer than 5 options for grade selection.
If a TEAE decreased in severity grade, the new TEAE record with less severity was counted as the same TEAE event of the previous record with worse severity.
When a subject experienced the same TEAE at more than one level of severity, only the most severe one was counted.
When a subject experienced the same TEAE at more than one level of drug relationship, only the one related to study drug was counted.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

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Table 14.3.1.4 Treatment-Emergent Adverse Event Frequency by Cohort, Severity Grade, and Relationship to Study Drug – Number of Adverse Events (Safety Population)

TE Adverse Event*	Cohort	Number of Adverse Events	Severity Grade					Relationship to Study Drug	
			1	2	3	4	5	Related	Not Related
Dizziness	XXXX	X	X	X	X	X	X	X	X
Dry eye	XXXX	X	X	X	X	X	X	X	X
Dry mouth	XXXX	X	X	X	X	X	X	X	X
	XXXX	X	X	X	X	X	X	X	X
Dry throat	XXXX	X	X	X	X	X	X	X	X
Ear pain	XXXX	X	X	X	X	X	X	X	X
Fatigue	XXXX	X	X	X	X	X	X	X	X
Mild RI Subjects		XX	X	X	X	X	X	X	X
Moderate RI Subjects		XX	X	X	X	X	X	X	X
Severe RI Subjects		XX	X	X	X	X	X	X	X
Healthy Matched Subjects		XX	X	X	X	X	X	X	X
Overall		XX	X	X	X	X	X	X	X

Note: * Adverse events are classified according to MedDRA Version 21.1 by System Organ Class and Preferred Term.
TE = Treatment-emergent; AE = Adverse event
Severity Grade: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe or medically significant but not immediately life-threatening; Grade 4 = Life-threatening consequences; Grade 5 = Death related to AE
Not all grades are appropriate for all AEs, therefore some AEs are listed in the CTCAE with fewer than 5 options for grade selection.
If a TEAE decreased in severity grade, the new TEAE record with less severity was counted as the same TEAE event of the previous record with worse severity.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

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Table 14.3.2.1 Serious Adverse Events (Safety Population)

Cohort	Subject Number	TE?^	Adverse Event	PT*/ SOC	Onset/Resolution Day	Onset/Resolution Date	Onset/Resolution Time	Freq*	Severity Grade	Ser*	Outcome	Action for Study Drug	Other Action	Relationship To Study Drug
XXXX	XXX-XXX	Yes	XXXXXXX	XXXXXXX/ XXXXXXXX	XX/ XX	DDMMMYYYY/ DDMMMYYYY	XX:XX/ XX:XX	Inter.	X	NS	Resolved	XXXXXXXXX	XXXXXX	XXXXXXXXX

Note: * Adverse events are classified according to MedDRA Version 21.1 by System Organ Class and Preferred Term.
TE = Treatment-emergent; PT = Preferred Term; SOC = System Organ Class, Onset day is relative to Day 1.
Freq* represents Frequency: SE = Single Episode, Inter. = Intermittent, Cont. = Continuous
Ser* represents Serious: NS = Not Serious
Severity/Intensity: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe or medically significant but not immediately life-threatening; Grade 4 = Life-threatening consequences; Grade 5 = Death related to AE
Not all grades are appropriate for all AEs.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

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Programmer Note: if there are no serious adverse events reported, there will be just one table (Table 14.3.2.1) with the statement "There was no serious adverse event recorded during the study."

Tables 14.3.4.2-14.3.4.3 will have the following format.

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Table 14.3.4.1 Out-of-Range Values and Unscheduled Results – Serum Chemistry (Safety Population)

Cohort	Site-Subject Number	Age$/ Sex	Visit	Time Point	Date	Parameter1 (Unit)	Parameter2 (Unit)	Parameter3 (Unit)	Parameter4 (Unit)	Parameter5 (Unit)
XXX	XXX-XXX	XX/M	XXXXX		DDMMMYYYY	XX HN	XX	XX	XX	XX HN
			XXXXX	XXXXXXX	DDMMMYYYY	XX	XX	XX	XX	XX
			XXXXX	XXXXXXX	DDMMMYYYY	XX	XX	XX	XX HN	XX
					DDMMMYYYY	XX	XX	XX	XX	XX
					DDMMMYYYY	XX LY-	XX LN	XX	XX LY-	XX

Programmer Notes: Clinical laboratory results will be presented in SI units. Please include flags as appropriate next to each value if present in the database and add a footer with the flag definition. The ranges will not be presented in the header given that there is more than one site involved in the study and the following footnote will be added: 'Refer to appendix 16.1.10.1 for site specific reference ranges.'. Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early termination records chronologically with other scheduled assessments. Arrange alphabetically by lab test name.

Clinically significant lab values generally will be captured as AEs, some of which the PI may indicate in Appendix 16.2.8.1.6 lab comments (as per GPG.03.0028 sections 2.9 and 2.10). Derive an additional flag for PI flag –/+ based on comments (i.e. NCS/CS). Present this derived 4th column in all tables, and list only PI-determined out-of-range clinically significant lab values in Table 14.3.4.4.

Note: $ Age is calculated from the date of dosing.
Abnormal flag: H = Above Reference Range, L = Below Reference Range
Computer Clinical significance: N = Not Clinically Significant, Y = Clinically Significant
PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event
Refer to appendix 16.1.10.1 for site specific reference ranges.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

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Table 14.3.4.4 Clinically Significant Laboratory and Corresponding Results (Safety Population)

Cohort	Subject Number	Age$/ Sex	Visit	Time Point	Date	Time	Department	Test	Result		Reference Range	Unit
XXXXXX	XXX-XXX	XX/X	XXXXX	XXXXX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX		X - X	mg/dL
			XXXXX	XXXXX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HYR+	X - X	mg/dL
			XXXXX	XXXXX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HY-	X - X	mg/dL
			XXXXX	XXXXX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HN	X - X	mg/dL

Programmer Notes: Clinical laboratory results will be presented in SI units. Please include flags as appropriate next to each value if present in the database and add a footer with the flag definition. All time points for a subject/test with at least one value deemed as CS by the PI will be presented in this table. If there were no CS values as deemed by PI (i.e., no "CS" or "Clinically Significant" in the PI comment field in the laboratory dataset), then this table will contain the following statement: "There were no laboratory values documented as clinically significant by the PI in the study."

Note: $ Age is calculated from the date of dosing.
H = Above Reference Range, L = Below Reference Range
Computer: N = Not Clinically Significant, Y = Clinically Significant
PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

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Tables 14.3.5.1, 14.3.5.2, 14.3.5.4, 14.3.5.5, 14.3.5.7, and 14.3.5.8 will have the following format.

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Table 14.3.5.1 Clinical Laboratory Summary – Serum Chemistry (Safety Population)

Laboratory Test (unit)	Time Point	Statistic	Cohort			
			Mild	Moderate	Severe	Healthy
Testname (unit)	Screening	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	Day -1	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	Day 2	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX

Programmer note: Similar for remaining laboratory tests. Sort alphabetically by lab test name. SI units will be used in the summarization of all clinical laboratory results. For the change from baseline tables, please remove the screening and Day -1 time points, keep the baseline definition footnote and change the 'Cohort' header to 'Change From Baseline'.

Note: Baseline is the last non-missing predose measurement prior to dosing (Day -1), including unscheduled assessments.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

[redacted] DDMMMYYYY HH:MM

Tables 14.3.5.3, 14.3.5.6, and 14.3.5.9 will have the following format:

Page 1 of X

Table 14.3.5.3 Clinical Laboratory Shift from Baseline – Serum Chemistry (Safety Population)

Laboratory Test (units)	Cohort	Time Point	Baseline L: Postdose L	Baseline L: Postdose N	Baseline L: Postdose H	Baseline N: Postdose L	Baseline N: Postdose N	Baseline N: Postdose H	Baseline H: Postdose L	Baseline H: Postdose N	Baseline H: Postdose H
Testname(unit)	Mild	Day 2	X	XX	X	X	XX	X	X	XX	X
		Day 5	X	XX	X	X	XX	X	X	XX	X
		Day 8	X	XX	X	X	XX	X	X	XX	X

Programmer note: Similar for remaining laboratory tests. Use N = Within Normal Range, O = Outside Normal Range for urinalysis shift table.

Note: N = Within Normal Range, L = Below Normal Range, H= Above Normal Range.
Baseline is the last non-missing predose measurement prior to dosing (Day -1), including unscheduled assessments.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Tables 14.3.5.10 and 14.3.5.11 will have the following format:

Table 14.3.5.10 Vital Sign Summary (Safety Population)

Vital Sign Parameter (unit)	Time Point	Statistic	Cohort: Mild	Moderate	Severe	Healthy
Parameter1 (unit)	Screening	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	Day -1	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	Day 1 Predose	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX

<Programmer note: Similar for remaining vital sign parameters and time points. For the change from baseline tables, please remove the screening, Day -1, and Day 1 Predose time points, keep the baseline definition footnote and change the 'Cohort' header to 'Change From Baseline'.

Note: Baseline is the last non-missing predose measurement prior to dosing (Day 1 Predose), including unscheduled assessments.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Tables 14.3.5.12 and 14.3.5.13 will have the following format:

Page 1 of X

Table 14.3.5.12 12-Lead Electrocardiogram Summary (Safety Population)

ECG Parameter (unit)	Time Point	Statistic	Cohort: Mild	Moderate	Severe	Healthy
Parameter1 (unit)	Screening	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	Day -1	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	Day 8	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX

Programmer note: Similar for remaining ECG parameters. For the change from baseline tables, please remove the Screening and Day -1 time points, keep the baseline definition footnote and change the 'Cohort' header to 'Change From Baseline'.

Note: Baseline is the last non-missing predose measurement prior to dosing (Day -1), including unscheduled assessments.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

11. LISTING SHELLS

The following listing shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the listings that will be presented and included in the final CSR. These listings will be generated off of the Celerion SDTM Tabulation Model 1.4 mapped in accordance with SDTM Implementation Guide 3.2. All listings will be presented in Courier New size font 9.

Note: The visit and time point variables will be presented as recorded in the datasets and can be added and removed as appropriate from the listings.

Appendix 16.1.7.2 Healthy Control Subjects Matched to Renal Function Groups

Subject Number	Assigned Renal Function Group	Healthy MatchedSubject Number
XXX-XXX	XXXXXXXXXX	XXX-XXX
XXX-XXX	XXXXXXXXXX	XXX-XXX
XXX-XXX	XXXXXXXXXX	XXX-XXX
XXX-XXX	XXXXXXXXXX	XXX-XXX
XXX-XXX	XXXXXXXXXX	XXX-XXX
XXX-XXX	XXXXXXXXXX	XXX-XXX

Note: All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

Site	Laboratory Group	Test Name	Sex	Age Category	Conventional Normal Range	Conventional Unit	SI Normal Range	SI Units
XXX	Serum Chemistry	Test Name	XXXXXX	XX	XX – XX	units	XX – XX	units
		Test Name	XXXXXX	XX	XX – XX	units	XX – XX	units
		Test Name	XXXXXX	XX	XX – XX	units	XX – XX	units
		Test Name	XXXXXX	XX	XX – XX	units	XX – XX	units
		Test Name	XXXXXX	XX	XX – XX	units	XX – XX	units
		Test Name	XXXXXX	XX	XX – XX	units	XX – XX	units
	Hematology	Test Name	XXXXXX	XX	XX – XX	units	XX – XX	units
		Test Name	XXXXXX	XX	XX – XX	units	XX – XX	units
		Test Name	XXXXXX	XX	XX – XX	units	XX – XX	units
		Test Name	XXXXXX	XX	XX – XX	units	XX – XX	units
		Test Name	XXXXXX	XX	XX – XX	units	XX – XX	units

Programmer note: Sort alphabetically by lab test name within each lab group.

<similar for remaining Laboratory Groups and Test Names>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.1 Subject Discontinuation (Safety Population)

Cohort	Site/ Subject Number	Date of Study Completion/ End of Study or Date of Discontinuation	Completed Study?	Primary Discontinuation Reason	Specify
XXXXXX	XXX-XXX	DDMMMYYYY	YES		
	XXX-XXX	DDMMMYYYY	YES		
	XXX-XXX	DDMMMYYYY	YES		
	XXX-XXX	DDMMMYYYY	YES		
	XXX-XXX	DDMMMYYYY	NO	Adverse Event	XXXXXXXXXX
	XXX-XXX	DDMMMYYYY	YES		
	XXX-XXX	DDMMMYYYY	YES		
	XXX-XXX	DDMMMYYYY	YES		

Note: All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.4.1 Demographics (Safety Population)

Cohort	Site/ Subject Number	Date of Birth	Age* (yrs)	Reproductive Status	Sex	Race	Ethnicity	Height (cm)	Weight (kg)	Body Mass Index (kg/m^2)	Informed Consent Signed Date	Protocol Version
XXXX	XXX-XXX	DDMMMYYYY	XX	AAAAAAAA	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	AAAAAAAAA
	XXX-XXX	DDMMMYYYY	XX	AAAAAAAA	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	AAAAAAAAA
	XXX-XXX	DDMMMYYYY	XX	AAAAAAAA	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	AAAAAAAAA
	XXX-XXX	DDMMMYYYY	XX	AAAAAAAA	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	AAAAAAAAA

Programmer note: Please also include re-consent signed date and re-consent version.

Note: * Age is calculated from the date of dosing.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.4.2 Physical Examination (Safety Population)

Cohort	Site/ Subject Number	Visit	Time Point	Date	Body System	Answer or Result	Comment
XXXXXX	XXX-XXX	XXXXX	XXXXXX	DDMMMYYYY	Was PE performed?	Yes	
					General	Normal	
					HEENT	Normal	
					< >	< >	
		XXXXX	XXXXX	DDMMMYYYY	Was PE performed?	Yes	
					HEENT	Normal	
					< >	< >	

Programmer Note: The 'comment' column will present any data that is recorded in the 'Reason not done' or 'If Abnormal, Specify' fields of the CRF.

Note: All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.4.3 Medical and Surgical History (Safety Population)

Cohort	Site/ Subject Number	Any History?	Category	Body system	Date Start	Date End	Ongoing?	Condition or Events
XXXXX	XXX-XXX	XXX	Medical	XXXXXXXXXXX	DDMMMYYYY	DDMMMYYYY	YES	XXXXXXX XXXXXX XXXXXXXX
			Surgical		DDMMMYYYY	DDMMMYYYY		
	XXX-XXX	XXX	Medical	XXXXXXXXXXX	DDMMMYYYY	DDMMMYYYY	NO	

Note: All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.4.4 Assessment of Renal Function (Safety Population)

		eGFR #1			eGFR #2				Creatinine clearance	
Cohort	Site/ Subject Number	Date	Time	Value (unit)	Date	Time	Value (Unit)	Mean eGFR (unit)	Date	Result (Unit)
XXXXX	XXX-XXX	DDMMMYYYY	HH:MM	XXXXX	DDMMMYYYY	HH:MM	XXXXX	XXXXXX	DDMMMYYYY	XXXXX
	XXX-XXX	DDMMMYYYY	HH:MM	XXXXX	DDMMMYYYY	HH:MM	XXXXX	XXXXXX	DDMMMYYYY	XXXXX
	XXX-XXX	DDMMMYYYY	HH:MM	XXXXX	DDMMMYYYY	HH:MM	XXXXX	XXXXXX	DDMMMYYYY	XXXXX

Note: All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.5.1 Subject Eligibility (Safety Population)

Cohort	Site/ Subject Number	Did subject meet all eligibility criteria?	Specify
XXXXXX	XXX-XXX	YES	
	XXX-XXX	NO	<this column is only presented if data is present>

Note: All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.5.2 Test Compound Administration Times (Safety Population)

Cohort	Site/ Subject Number	Visit	Time Point	Was Subject Fasted for at least 2 hours prior to dosing?	Was LOXO-292 Administered?	If no, Reason Why?	Date Dispensed	Time	Dosage (Unit)	Route	Formulation	Comments
XXXXX	XXX-XXX	XXXXX	XXXXX	XXXXXX	XXXXXXX	XXXXXXXX	DDMMMYYYY	XX:XX	XXXXXXX	XXXXX	XXXXXXXX	<This column prints only if data is present>

Note: All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.5.3 PK Blood Draw Times and Protein Binding (Safety Population)

Cohort	Site/ Subject Number	Visit	Time Point	Was PK Sample Collected?	If Not Done, Specify	Predose Plasma Protein Binding Sample?	Collection Date	Collection Time	Comments
XXXX	XXX-XXX	XXXXX	XXXXXXXXX	XXXXXXXX		XXXXX	DDMMMYYYY	X:XX	
				XXXXXXXX			DDMMMYYYY	X:XX	
				XXXXXXXX			DDMMMYYYY	X:XX	
				XXXXXXXX			DDMMMYYYY	X:XX	

Programmer note: If appropriate, please add the 'flag for programming' column if present to the database.

Note: All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.5.4 Urine Collection Times (Safety Population)

					Urine Collection								
					Start		Stop						
Cohort	Site/ Subject Number	Day	Hour	Sample Collected?	Date	Time	Date	Time	Volume (mL)	Weight (g)	Unable to Void?	Subject is Anuric?	Comments
XXXX	XXX-XXX	XX	XXXX	XXXX	DDMMMYYYY	X:XX:XX	DDMMMYYYY	X:XX:XX	XXX	XXX	XXXXX	XXXXX	XXXXXXXXXX
		XX	XXXX	XXXX	DDMMMYYYY	X:XX:XX	DDMMMYYYY	X:XX:XX	XXX	XXX	XXXXX	XXXXX	XXXXXXXXXX

Programmer note: If appropriate, please add the 'flag for programming' column if present to the database.

Note: All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.5.5 Follow-Up Phone Call (Safety Population)

Cohort	Site/ Subject Number	Was a Telephone Call Performed? (Yes/No)	Date	If No, Reason*	Any AE Since Last Visit?	Any new concomitant medication or change in concomitant medication Since last visit ?
XXXX	XXX-XXX	YES	DDMMMYYYY	XXXXXXXXXXXXX	XXXXXXX	XXXXXXXX

Note: * Reason options: 3 call attempts with no subject return call; Phone Disconnected; Wrong Number
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.5.6 Prior and Concomitant Medications (Safety Population)

Cohort	Site/ Subject Number	Any Med^?	Prior to Study?	Medication (WHO* Term)	Dosage	Route	Frequency	Start Day/Date/Time	Stop Day/Date/Time	Indi- cation	AE Term (If Due to AE)	MH Term (If Due to AE)	Conti- nuing Med^?
XXXXX	XXX-XXX	No		None									
	XXX-XXX	Yes	Yes	ACETAMINOPHEN (ACETAMINOPHEN)	620 mg	BY MOUTH	AS NEEDED	XX/DDMMMYYYY/ HH:MM	XX/DDMMYYYY/ HH:MM	XXXXX	NA	NA	YES

Note: * Concomitant medications are coded with WHO Dictionary Version 01Sep2018 B3.
^ Med = Medication; UNK = Unknown; AE = Adverse Event; MH = Medical History; NA = Not Applicable
Prior medication was medication taken prior to study drug administration.
Start and stop day is relative to Day 1.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.7.1 Adverse Events (I of II) (Safety Population)

Cohort	Site/ Subject Number	TE?^	Adverse Event/ Preferred Term*	Time from Last Dose (DD:HH:MM)	Onset Day	Onset Date	Onset Time	Resolved Day	Resolved Date	Resolved Time	Duration (DD:HH:MM)
XXX	XXX-XXX		None								
	XXX-XXX	Yes	XXXXXXXXXXXXX/ XXXXXXXXXX	XX:XX:XX	XX	DDMMMYYYY	X:XX	XX	DDMMMYYYY	X:XX	XX:XX:XX
		No	XXXXXXXXXXXXX/ XXXXXXXXXX	XX:XX:XX	XX	DDMMMYYYY	X:XX	XX	DDMMMYYYY	X:XX	XX:XX:XX

Note: * Adverse events are classified according to MedDRA Version 21.1 by System Organ Class and Preferred Term.
^ TE = Treatment-emergent, Onset and resolved day is relative to Day 1.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.7.2 Adverse Events (II of II) (Safety Population)

Cohort	Site/ Subject Number	Treat-ment	Adverse Event	Onset Day	Onset Date	Onset Time	Freq*	Severity	Ser*	Outcome	Action for Study Drug	Other Action Taken	Relationship to Study Drug
XXXX	XXX-XXX		None										
	XXX-XXX	X	XXXXXXX	XX	DDMMMYYYY	XX:XX	Inter.	Grade 1	NS	Recovered or Resolved	Dose Not Changed	XXXXXXXX	Not Related

Note: Ser* represents Serious: NS = Not Serious
Freq* represents Frequency: SE = Single Episode, Inter. = Intermittent, Cont. = Continuous
Severity/Intensity: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe or medically significant but not immediately life-threatening; Grade 4 = Life-threatening consequences; Grade 5 = Death related to AE
Onset and resolved day is relative to Day 1.
Not all grades are appropriate for all AEs, therefore some AEs are listed in the CTCAE with fewer than 5 options for grade selection.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.7.3 Adverse Event Comments (Safety Population)

Cohort	Site/ Subject Number	Adverse Event	Onset Day	Onset Date	Onset Time	Resolved Day	Resolved Date	Resolved Time	Comments
XXXXX	XXX-XXX	DRY LIPS	XX	DDMMMYYYY	X:XX	XX	DDMMMYYYY	X:XX	XXXXXXXXXXX

Note: Onset and resolved day is relative to Day 1.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.7.4 Adverse Event Preferred Term Classification (Safety Population)

Cohort	Site/ Subject Number	Adverse Event	Preferred Term*	System Organ Class*	Onset Day	Onset Date	Onset Time
XXXX	XXX-XXX	XXXXXX XXXXX XXXX XXXXXX	XXXXXXXXXX XXXXXXX	XXXXXXXXXXXXXXXXXXXX	XX	DDMMMYYYY	X:XX

Note: * Adverse events are classified to MedDRA Version 21.1 by System Organ Class and Preferred Term.
Onset day is relative to Day 1.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendices 16.2.8.1.1-16.2.8.1.5 will have the following format.

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Appendix 16.2.8.1.1.1 Clinical Laboratory Report – Serum Chemistry (Conventional Units)(Safety Population)

Cohort	Site/ Subject Number	Age$/ Sex	Visit	Time Point	Date	Parameter1 (Unit)	Parameter2 (Unit)	Parameter3 (Unit)	Parameter4 (Unit)	Parameter5 (Unit)
XXXXX	XXX-XXX	XX/M	XXXXXX	XXXXXXXXX	DDMMMYYYY	XX HN	XX	XX	XX	XX HN
			XXXXXX	XXXXXXXXX	DDMMMYYYY	XX	XX	XX	XX	XX
			XXXXXX	XXXXXXXXX	DDMMMYYYY	XX	XX	XX	XX HN	XX

Programmer Notes: Please also include the following columns in the listings as appropriate for each department: 'Was Sample Collected?', 'If no, reason', 'Was the subject fasting?', 'Any clinically significant results?'. These columns will be presented before the individual test results. Clinical laboratory results will be presented in SI and conventional units. Please include flags as appropriate next to each value if present in the database and add a footer with the flag definition. The ranges will not be presented in the header since there is more than one site involved in the study and the following footnote will be added: 'Refer to appendix 16.1.10.1 for site specific reference ranges.'. Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early term chronologically with other scheduled assessments. The reproductive status will also be included in the serum FSH listings.

Clinically significant lab values generally will be captured as AEs, some of which the PI may indicate in Appendix 16.2.8.1.6 lab comments (as per GPG.03.0028 sections 2.9 and 2.10). Derive an additional flag for PI flag (+) based on positive CS/Clinically Significant comments. Present this derived 4th column in all tables, and list only PI-determined out-of-range clinically significant lab values in Table 14.3.4.4. Arrange alphabetically by lab test name.

Note: $ Age is calculated from the date of dosing.
H = Above Reference Range, L = Below Reference Range
Computer Clinical Significance: N = Not Clinically Significant, Y = Clinically Significant
PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event
Refer to appendix 16.1.10.1 for site specific reference ranges.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.1.6 Clinical Laboratory Report – Comments (Safety Population)

Cohort	Subject Number	Visit	Time Point	Date	Department	Test	SI Result	SI Unit	Comment
XXXX	XXX-XXX	XXX	XXXXXX	DDMMMYYYY	Other Tests	Fibrinogen	XXX	mg/dL	Not significant in the context of this study.

Programmer Note: Results will be presented in SI units.

Note: All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

Appendix 16.2.8.1.7 Clinical Laboratory Serology Samples(Safety Population)

Cohort	Site/ Subject Number	Age$/ Sex	Visit	Date	Was the Sample Collected?
XXXXX	XXX-XXX	XX/M	XXXXXX	DDMMMYYYY	XX
			XXXXXX	DDMMMYYYY	XX
			XXXXXX	DDMMMYYYY	XX

Note: $ Age is calculated from the date of dosing.
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.8.2 Vital Signs (Safety Population)

Cohort	Subject Number	Visit	Time Point	Date	Time	Position	Supine for at least 5 minutes?	Blood Pressure (mmHg) Systolic/Diastolic	Pulse (bpm)	Respiration (rpm)	Temperature (°C)	Weight (kg)	Comments
XXX	XXX-XXX	XXXXX	XXXXXX	DDMMMYYYY	X:XX							XXX.X	
		XXXXX	XXXXXX	DDMMMYYYY	X:XX	SIT	XXXX	XXX/ XX	XX	XX	XX.X		
		XXXXX	XXXXXX	DDMMMYYYY	XX:XX							XXX.X	
		XXXXX	XXXXXX	DDMMMYYYY	XX:XX	SIT	XXXX	XXX/ XX	XX	XX			

Programmer note: Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Please also include 'Not Done' if populated by 'Yes' in the database. If appropriate, please add the 'flag for programming' column if present to the database.

Note: SIT = Sitting
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

Appendix 16.2.8.3 12-Lead Electrocardiogram (Safety Population)

Cohort	Subject Number	Visit	Time Point	Date	Time	Was Subject supine for at least 10 minutes?	Result	Heart Rate (bpm)	PR (msec)	RR (msec)	QRS (msec)	QT (msec)	QTcF* (msec)	Comments
XXXX	XXX-XXX	XXXXX	XXXXXXX	DDMMMYYYY	X:XX	XXX	Normal	XX	XXX.X	XX.X	XX.X	XXX.X	XXX.X	
		XXXXX	XXXXXXX	DDMMMYYYY	X:XX	XXX	ANCS	XX	XXX.X	XX.X	XX.X	XXX.X	XXX.X	
		XXXXX	XXXXXXX	DDMMMYYYY	X:XX	XXX	Normal	XX	XXX.X	XX.X	XX.X	XXX.X	XXX.X	
			XXXXXXX	DDMMMYYYY	X:XX	XXX	Normal	XX	XXX.X	XX.X	XX.X	XXX.X	XXX.X #	
			XXXXXXX	DDMMMYYYY	X:XX	XXX	Normal	XX	XXX.X	XX.X	XX.X	XXX.X	XXX.X @	

Programmer note: Sort unscheduled assessment and early term chronologically with other scheduled assessments. Please also include 'Not Done' if populated by 'Yes' in the database. If appropriate, please add the 'flag for programming' column if present to the database.

Note: ANCS = Abnormal, Not Clinically Significant
QTcF* = QT corrected for heart rate using Fridericia's correction.
= QTcF > 450, @ = QTcF change from baseline greater than 30 msec
All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.
Cohort Descriptions: <description>

CCI [redacted] DDMMMYYYY HH:MM

16.1.9.2 Statistical Outputs

Statistical Comparisons of Pharmacokinetic Parameter: AUC0-t
for Table 14.2.1.10 (Paired t-test)

The TTEST Procedure

Difference: Mild - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	0.0396	0.3774	0.1334	-0.4846	0.5254

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.0396	-0.2132	0.2924	0.3774	0.2662	0.6782

DF	t Value	Pr > |t|
7	0.30	0.7752

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:41

Statistical Comparisons of Pharmacokinetic Parameter: AUC0-inf
for Table 14.2.1.10 (Paired t-test)

The TTEST Procedure

Difference: Mild - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	0.0378	0.3766	0.1331	-0.4833	0.5235

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.0378	-0.2144	0.2900	0.3766	0.2656	0.6768

DF	t Value	Pr > |t|
7	0.28	0.7847

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:41

Statistical Comparisons of Pharmacokinetic Parameter: Cmax
for Table 14.2.1.10 (Paired t-test)

The TTEST Procedure

Difference: Mild - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	0.2328	0.5220	0.1846	-0.4454	1.1183

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.2328	-0.1169	0.5824	0.5220	0.3682	0.9381

DF	t Value	Pr > |t|
7	1.26	0.2477

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:41

Statistical Comparisons of Pharmacokinetic Parameter: AUC0-t
for Table 14.2.1.11 (Paired t-test)

The TTEST Procedure

Difference: Moderate - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	0.5415	0.5311	0.1878	-0.3158	1.2106

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.5415	0.1858	0.8972	0.5311	0.3746	0.9544

DF	t Value	Pr > |t|
7	2.88	0.0235

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:41

Statistical Comparisons of Pharmacokinetic Parameter: AUC0-inf
for Table 14.2.1.11 (Paired t-test)

The TTEST Procedure

Difference: Moderate - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	0.5434	0.5311	0.1878	-0.3113	1.2110

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.5434	0.1877	0.8992	0.5311	0.3747	0.9545

DF	t Value	Pr > |t|
7	2.89	0.0232

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:41

Statistical Comparisons of Pharmacokinetic Parameter: Cmax
for Table 14.2.1.11 (Paired t-test)

The TTEST Procedure

Difference: Moderate - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	0.4204	1.0211	0.3610	-0.6931	2.5017

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.4204	-0.2635	1.1043	1.0211	0.7203	1.8350

DF	t Value	Pr > |t|
7	1.16	0.2824

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:41

Statistical Comparisons of Pharmacokinetic Parameter: AUC0-t
for Table 14.2.1.12 (Paired t-test)

The TTEST Procedure

Difference: Severe - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	0.2045	0.5711	0.2158	-0.3914	0.9839

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.2045	-0.2150	0.6239	0.5711	0.3942	1.0938

DF	t Value	Pr > |t|
6	0.95	0.3801

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:41

Statistical Comparisons of Pharmacokinetic Parameter: AUC0-inf
for Table 14.2.1.12 (Paired t-test)

The TTEST Procedure

Difference: Severe - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	0.2167	0.5742	0.2170	-0.3721	0.9847

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.2167	-0.2050	0.6385	0.5742	0.3964	1.0999

DF	t Value	Pr > |t|
6	1.00	0.3566

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:41

Statistical Comparisons of Pharmacokinetic Parameter: Cmax
for Table 14.2.1.12 (Paired t-test)

The TTEST Procedure

Difference: Severe - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	-0.1780	0.6735	0.2546	-1.4332	0.6119

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
-0.1780	-0.6727	0.3167	0.6735	0.4649	1.2901

DF	t Value	Pr > |t|
6	-0.70	0.5105

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

30APR2020 18:41

Statistical Comparisons of Pharmacokinetic Parameter: AUC0-t,u
for Table 14.2.3.14 (Paired t-test)

The TTEST Procedure

Difference: Mild - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	0.0662	0.3302	0.1167	-0.2769	0.6432

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.0662	-0.1550	0.2874	0.3302	0.2329	0.5935

DF	t Value	Pr > |t|
7	0.57	0.5886

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:43

Statistical Comparisons of Pharmacokinetic Parameter: AUC0-inf,u
for Table 14.2.3.14 (Paired t-test)

The TTEST Procedure

Difference: Mild - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	0.0643	0.3298	0.1166	-0.2794	0.6393

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.0643	-0.1566	0.2853	0.3298	0.2327	0.5928

DF	t Value	Pr > |t|
7	0.55	0.5983

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:43

Statistical Comparisons of Pharmacokinetic Parameter: Cmax,u
for Table 14.2.3.14 (Paired t-test)

The TTEST Procedure

Difference: Mild - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	0.2593	0.5317	0.1880	-0.4629	0.9349

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.2593	-0.0969	0.6155	0.5317	0.3751	0.9556

DF	t Value	Pr > |t|
7	1.38	0.2102

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:43

Statistical Comparisons of Pharmacokinetic Parameter: AUC0-t,u
for Table 14.2.3.15 (Paired t-test)

The TTEST Procedure

Difference: Moderate - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	0.6333	0.5204	0.1840	-0.0706	1.3654

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.6333	0.2847	0.9819	0.5204	0.3671	0.9353

DF	t Value	Pr > |t|
7	3.44	0.0108

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:43

Statistical Comparisons of Pharmacokinetic Parameter: AUC0-inf,u
for Table 14.2.3.15 (Paired t-test)

The TTEST Procedure

Difference: Moderate - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	0.6353	0.5202	0.1839	-0.0685	1.3653

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.6353	0.2868	0.9837	0.5202	0.3669	0.9348

DF	t Value	Pr > |t|
7	3.45	0.0106

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:43

Statistical Comparisons of Pharmacokinetic Parameter: Cmax,u
for Table 14.2.3.15 (Paired t-test)

The TTEST Procedure

Difference: Moderate - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	0.5122	1.0347	0.3658	-0.5627	2.4730

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.5122	-0.1809	1.2053	1.0347	0.7299	1.8595

DF	t Value	Pr > |t|
7	1.40	0.2042

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:43

Statistical Comparisons of Pharmacokinetic Parameter: AUC0-t,u
for Table 14.2.3.16 (Paired t-test)

The TTEST Procedure

Difference: Severe - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	0.4172	0.7358	0.2781	-0.2507	1.5224

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.4172	-0.1233	0.9576	0.7358	0.5079	1.4094

DF	t Value	Pr > |t|
6	1.50	0.1843

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:43

Statistical Comparisons of Pharmacokinetic Parameter: AUC0-inf,u
for Table 14.2.3.16 (Paired t-test)

The TTEST Procedure

Difference: Severe - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	0.4294	0.7403	0.2798	-0.2414	1.5622

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.4294	-0.1143	0.9732	0.7403	0.5111	1.4181

DF	t Value	Pr > |t|
6	1.53	0.1758

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:43

Statistical Comparisons of Pharmacokinetic Parameter: Cmax,u
for Table 14.2.3.16 (Paired t-test)

The TTEST Procedure

Difference: Severe - Healthy

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	0.0347	0.8208	0.3102	-1.2926	0.9587

Mean	90% CL Mean		Std Dev	90% CL Std Dev	
0.0347	-0.5682	0.6375	0.8208	0.5666	1.5722

DF	t Value	Pr > |t|
6	0.11	0.9147

All subjects received a single oral dose of 160 mg LOXO-292 following a 2-hour fast.

CCI [redacted] 30APR2020 18:43

Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-t
for Tables 14.2.1.13 - 14.2.1.15

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDLOXO292LAUCLST
Dependent Variable	AVAL
Covariance Structure	Diagonal
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Residual

Class Level Information

Class	Levels	Values
COHORT	4	A B C D
SEX	2	F M

Dimensions

Covariance Parameters	1
Columns in X	9
Columns in Z	0
Subjects	1
Max Obs per Subject	33

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-t
for Tables 14.2.1.13 - 14.2.1.15

The Mixed Procedure

Number of Observations

Number of Observations Read	33
Number of Observations Used	33
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.1767

Fit Statistics

-2 Res Log Likelihood	52.4
AIC (Smaller is Better)	54.4
AICC (Smaller is Better)	54.6
BIC (Smaller is Better)	55.7

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
rment

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Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-t
for Tables 14.2.1.13 - 14.2.1.15

The Mixed Procedure

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
COHORT	3	26	1.38	0.2697
SEX	1	26	4.76	0.0384
AGE	1	26	0.98	0.3312
BMIBL	1	26	0.39	0.5375

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
cohort A versus cohort D	0.1993	0.2003	26	0.99	0.3289	0.1	-0.1424	0.5410
cohort B versus cohort D	0.4060	0.2044	26	1.99	0.0577	0.1	0.05734	0.7546
cohort C versus cohort D	0.1103	0.2218	26	0.50	0.6233	0.1	-0.2681	0.4886

Least Squares Means

Effect	Cohort	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
COHORT	A	10.1248	0.1512	26	66.98	<.0001	0.1	9.8669	10.3826
COHORT	B	10.3315	0.1585	26	65.17	<.0001	0.1	10.0611	10.6018
COHORT	C	10.0357	0.1704	26	58.91	<.0001	0.1	9.7452	10.3263

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

CCI [redacted] 30APR2020 18:47

Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-t
for Tables 14.2.1.13 - 14.2.1.15

The Mixed Procedure

Least Squares Means

Effect	Cohort	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
COHORT	D	9.9255	0.1364	26	72.79	<.0001	0.1	9.6929	10.1580

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

CCI 30APR2020 18:47

Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-inf
for Tables 14.2.1.13 - 14.2.1.15

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDLOXO292LAUCIFO
Dependent Variable	AVAL
Covariance Structure	Diagonal
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Residual

Class Level Information

Class	Levels	Values
COHORT	4	A B C D
SEX	2	F M

Dimensions

Covariance Parameters	1
Columns in X	9
Columns in Z	0
Subjects	1
Max Obs per Subject	33

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-inf
for Tables 14.2.1.13 - 14.2.1.15

The Mixed Procedure

Number of Observations

Number of Observations Read	33
Number of Observations Used	33
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.1779

Fit Statistics

-2 Res Log Likelihood	52.6
AIC (Smaller is Better)	54.6
AICC (Smaller is Better)	54.8
BIC (Smaller is Better)	55.9

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

CCI [redacted] 30APR2020 18:47

Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-inf
for Tables 14.2.1.13 - 14.2.1.15

The Mixed Procedure

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
COHORT	3	26	1.36	0.2755
SEX	1	26	4.70	0.0395
AGE	1	26	1.05	0.3155
BMIBL	1	26	0.33	0.5695

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
cohort A versus cohort D	0.1969	0.2010	26	0.98	0.3364	0.1	-0.1460	0.5397
cohort B versus cohort D	0.4065	0.2051	26	1.98	0.0581	0.1	0.05668	0.7563
cohort C versus cohort D	0.1184	0.2226	26	0.53	0.5994	0.1	-0.2613	0.4980

Least Squares Means

Effect	Cohort	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
COHORT	A	10.1284	0.1517	26	66.77	<.0001	0.1	9.8697	10.3871
COHORT	B	10.3381	0.1591	26	64.99	<.0001	0.1	10.0668	10.6094
COHORT	C	10.0499	0.1709	26	58.80	<.0001	0.1	9.7584	10.3415

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

CCI [redacted] 30APR2020 18:47

Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-inf
for Tables 14.2.1.13 - 14.2.1.15

The Mixed Procedure

Least Squares Means

Effect	Cohort	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
COHORT	D	9.9315	0.1368	26	72.58	<.0001	0.1	9.6982	10.1649

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

CCI [redacted] 30APR2020 18:47

Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameter: Cmax
for Tables 14.2.1.13 - 14.2.1.15

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDLOXO292LCMAX
Dependent Variable	AVAL
Covariance Structure	Diagonal
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Residual

Class Level Information

Class	Levels	Values
COHORT	4	A B C D
SEX	2	F M

Dimensions

Covariance Parameters	1
Columns in X	9
Columns in Z	0
Subjects	1
Max Obs per Subject	33

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

CCI [redacted] 30APR2020 18:47

Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameter: Cmax
for Tables 14.2.1.13 - 14.2.1.15

The Mixed Procedure

Number of Observations

Number of Observations Read	33
Number of Observations Used	33
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.4786

Fit Statistics

-2 Res Log Likelihood	78.3
AIC (Smaller is Better)	80.3
AICC (Smaller is Better)	80.5
BIC (Smaller is Better)	81.6

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

CCI [redacted] 30APR2020 18:47

Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameter: Cmax
for Tables 14.2.1.13 - 14.2.1.15

The Mixed Procedure

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
COHORT	3	26	1.42	0.2596
SEX	1	26	3.34	0.0793
AGE	1	26	0.19	0.6679
BMIBL	1	26	1.11	0.3026

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
cohort A versus cohort D	0.5248	0.3297	26	1.59	0.1236	0.1	-0.03759	1.0871
cohort B versus cohort D	0.2591	0.3364	26	0.77	0.4481	0.1	-0.3147	0.8329
cohort C versus cohort D	-0.1592	0.3651	26	-0.44	0.6664	0.1	-0.7819	0.4635

Least Squares Means

Effect	Cohort	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
COHORT	A	7.7901	0.2488	26	31.31	<.0001	0.1	7.3657	8.2144
COHORT	B	7.5244	0.2609	26	28.84	<.0001	0.1	7.0795	7.9694
COHORT	C	7.1061	0.2804	26	25.35	<.0001	0.1	6.6279	7.5843

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Total Plasma LOXO-292 Pharmacokinetic Parameter: Cmax
for Tables 14.2.1.13 - 14.2.1.15

The Mixed Procedure

Least Squares Means

Effect	Cohort	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
COHORT	D	7.2653	0.2244	26	32.37	<.0001	0.1	6.8825	7.6481

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

CCI [redacted] 30APR2020 18:47

Statistical Comparisons of Unbound Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-t,u
for Tables 14.2.3.17 - 14.2.3.19

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDLOXO292LAUCLST
Dependent Variable	AVAL
Covariance Structure	Diagonal
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Residual

Class Level Information

Class	Levels	Values
COHORT	4	A B C D
SEX	2	F M

Dimensions

Covariance Parameters	1
Columns in X	9
Columns in Z	0
Subjects	1
Max Obs per Subject	33

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Unbound Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-t,u
for Tables 14.2.3.17 - 14.2.3.19

The Mixed Procedure

Number of Observations

Number of Observations Read	33
Number of Observations Used	33
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.2142

Fit Statistics

-2 Res Log Likelihood	57.4
AIC (Smaller is Better)	59.4
AICC (Smaller is Better)	59.6
BIC (Smaller is Better)	60.7

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Unbound Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-t,u
for Tables 14.2.3.17 - 14.2.3.19

The Mixed Procedure

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
COHORT	3	26	1.40	0.2641
SEX	1	26	3.42	0.0757
AGE	1	26	2.77	0.1080
BMIBL	1	26	0.03	0.8656

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
cohort A versus cohort D	0.2337	0.2206	26	1.06	0.2991	0.1	-0.1425	0.6099
cohort B versus cohort D	0.4555	0.2251	26	2.02	0.0534	0.1	0.07161	0.8393
cohort C versus cohort D	0.2739	0.2442	26	1.12	0.2724	0.1	-0.1427	0.6904

Least Squares Means

Effect	Cohort	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
COHORT	A	6.5687	0.1664	26	39.47	<.0001	0.1	6.2849	6.8526
COHORT	B	6.7905	0.1745	26	38.91	<.0001	0.1	6.4928	7.0882
COHORT	C	6.6089	0.1876	26	35.24	<.0001	0.1	6.2890	6.9288

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Unbound Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-t,u
for Tables 14.2.3.17 - 14.2.3.19

The Mixed Procedure

Least Squares Means

Effect	Cohort	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
COHORT	D	6.3350	0.1501	26	42.20	<.0001	0.1	6.0790	6.5911

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Unbound Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-inf,u
for Tables 14.2.3.17 - 14.2.3.19

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDLOXO292LAUCIFO
Dependent Variable	AVAL
Covariance Structure	Diagonal
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Residual

Class Level Information

Class	Levels	Values
COHORT	4	A B C D
SEX	2	F M

Dimensions

Covariance Parameters	1
Columns in X	9
Columns in Z	0
Subjects	1
Max Obs per Subject	33

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Unbound Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-inf,u
for Tables 14.2.3.17 - 14.2.3.19

The Mixed Procedure

Number of Observations

Number of Observations Read	33
Number of Observations Used	33
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.2155

Fit Statistics

-2 Res Log Likelihood	57.6
AIC (Smaller is Better)	59.6
AICC (Smaller is Better)	59.7
BIC (Smaller is Better)	60.8

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Unbound Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-inf,u
for Tables 14.2.3.17 - 14.2.3.19

The Mixed Procedure

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
COHORT	3	26	1.40	0.2640
SEX	1	26	3.38	0.0775
AGE	1	26	2.87	0.1025
BMIBL	1	26	0.05	0.8331

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
cohort A versus cohort D	0.2312	0.2213	26	1.05	0.3056	0.1	-0.1461	0.6086
cohort B versus cohort D	0.4560	0.2258	26	2.02	0.0538	0.1	0.07092	0.8410
cohort C versus cohort D	0.2820	0.2450	26	1.15	0.2603	0.1	-0.1359	0.6998

Least Squares Means

Effect	Cohort	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
COHORT	A	6.5724	0.1670	26	39.37	<.0001	0.1	6.2876	6.8571
COHORT	B	6.7971	0.1751	26	38.82	<.0001	0.1	6.4985	7.0957
COHORT	C	6.6231	0.1881	26	35.20	<.0001	0.1	6.3022	6.9440

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Unbound Plasma LOXO-292 Pharmacokinetic Parameter: AUC0-inf,u
for Tables 14.2.3.17 - 14.2.3.19

The Mixed Procedure

Least Squares Means

Effect	Cohort	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
COHORT	D	6.3411	0.1506	26	42.10	<.0001	0.1	6.0843	6.5980

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Unbound Plasma LOXO-292 Pharmacokinetic Parameter: Cmax,u
for Tables 14.2.3.17 - 14.2.3.19

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDLOXO292LCMAX
Dependent Variable	AVAL
Covariance Structure	Diagonal
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Residual

Class Level Information

Class	Levels	Values
COHORT	4	A B C D
SEX	2	F M

Dimensions

Covariance Parameters	1
Columns in X	9
Columns in Z	0
Subjects	1
Max Obs per Subject	33

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Unbound Plasma LOXO-292 Pharmacokinetic Parameter: Cmax,u
for Tables 14.2.3.17 - 14.2.3.19

The Mixed Procedure

Number of Observations

Number of Observations Read	33
Number of Observations Used	33
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.5746

Fit Statistics

-2 Res Log Likelihood	83.1
AIC (Smaller is Better)	85.1
AICC (Smaller is Better)	85.2
BIC (Smaller is Better)	86.3

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Unbound Plasma LOXO-292 Pharmacokinetic Parameter: Cmax,u
for Tables 14.2.3.17 - 14.2.3.19

The Mixed Procedure

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
COHORT	3	26	1.03	0.3974
SEX	1	26	2.52	0.1247
AGE	1	26	0.75	0.3959
BMIBL	1	26	0.26	0.6150

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
cohort A versus cohort D	0.5591	0.3612	26	1.55	0.1338	0.1	-0.05701	1.1753
cohort B versus cohort D	0.3086	0.3686	26	0.84	0.4101	0.1	-0.3201	0.9373
cohort C versus cohort D	0.004353	0.4000	26	0.01	0.9914	0.1	-0.6779	0.6866

Least Squares Means

Effect	Cohort	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
COHORT	A	4.2340	0.2726	26	15.53	<.0001	0.1	3.7691	4.6990
COHORT	B	3.9835	0.2859	26	13.94	<.0001	0.1	3.4959	4.4711
COHORT	C	3.6792	0.3072	26	11.98	<.0001	0.1	3.1553	4.2032

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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Statistical Comparisons of Unbound Plasma LOXO-292 Pharmacokinetic Parameter: Cmax,u
for Tables 14.2.3.17 - 14.2.3.19

The Mixed Procedure

Least Squares Means

Effect	Cohort	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
COHORT	D	3.6749	0.2459	26	14.94	<.0001	0.1	3.2555	4.0943

Cohort Descriptions:
A: Subjects with mild renal impairment
B: Subjects with moderate renal impairment
C: Subjects with severe renal impairment

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