Statistical Analysis Plan J2G-OX-JZJF

A Phase I, Single-Ascending Dose Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of LOXO-292 in Healthy Adult Subjects

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16.1.9 Documentation of Statistical Methods

16.1.9.1 Statistical Analysis Plan

Statistical Analysis Plan

A Phase I, Single-Ascending Dose Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of LOXO-292 in Healthy Adult Subjects

Protocol No: LOXO-RET-18057
Final Protocol Date: 25 January 2019
Compound Name: LOXO-292

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Statistical Analysis Plan Signature Page

Compound Name: LOXO-292

Protocol: LOXO-RET-18057

Study Title: A Phase I, Single-Ascending Dose Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of LOXO-292 in Healthy Adult Subjects

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1. INTRODUCTION

The following statistical analysis plan (SAP) provides the framework for the summarization of the data from this study. The SAP may change due to unforeseen circumstances. Any changes made from the planned analysis within protocol, after the unblinding, or 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 assess the safety and tolerability of single oral doses of LOXO-292 when administered to healthy adult subjects.

Secondary:

To assess the PK of single oral doses of LOXO-292 when administered to healthy adult subjects.

2.2 Endpoints

Safety:

Safety endpoints will include adverse events (AEs) including the subject incidence, number, and severity of treatment-emergent adverse events (TEAEs) following single oral doses of LOXO-292 in healthy adult subjects and safety markers for 12-lead electrocardiograms (ECGs), physical examinations, vital signs, and clinical laboratory tests.

Pharmacokinetics:

The plasma PK endpoints will include AUC0-t, AUC0-24, AUC0-inf, AUC%extrap, CL/F, Cmax, Tmax, Kel, t½, and Vz/F.

3. STUDY DESIGN

This will be a Phase I, safety, tolerability, and PK single ascending dose (SAD) study. Screening of subjects will occur within 28 days prior to dosing. The study will plan to enroll up to 18 healthy, adult male and female (of non-childbearing potential only) subjects. Every attempt will be made to enroll at least 1 female in each cohort.

Up to 3 cohorts will be planned for evaluation, with 6 healthy adult subjects in each cohort. Subjects will participate in only one cohort. In each cohort, subjects will receive a single oral dose of LOXO-292 on Day 1. Cohort 2 and Cohort 3 will include a sentinel group of 2 subjects who will dose at least 48 hours before the remaining 4 subjects. Blood samples will be collected for the PK assessment of LOXO-292 in plasma for 168 hours postdose.

Safety and tolerability will be assessed through end of treatment (EOT) or early termination (ET) by monitoring AEs, performing physical examinations and clinical laboratory tests, measuring vital signs, and recording ECGs.

Dose escalation to a higher dose level (i.e., next cohort) will not take place until the Principal Investigator (PI) and Loxo Oncology, Inc. reviewed all pertinent safety and tolerability data (e.g., physical examinations, ECGs, vital signs, clinical laboratory tests, and AEs) through a minimum of 48 hours (Day 3) postdose for Cohort 1 and through a minimum of 120 hours postdose (Day 5) for Cohort 2. Following their review, the PI and Loxo Oncology, Inc. will determine that adequate safety and tolerability from the previous, lower dose, cohort had been demonstrated to permit proceeding to the next cohort. Bioanalytical data, if available, may be used to guide the dose escalation decision. 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 (EOT) or 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 (FU)phone call. 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 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 the given treatment during the PK sampling period time course of the study for LOXO-292 may be excluded from the summary statistics for the given treatment and from the statistical comparison of PK parameters.
- Data from subjects who significantly violate a protocol inclusion or exclusion criteria, deviate significantly from the protocol, or have unavailable or incomplete data that may influence the PK analysis will be excluded from the PK Population.

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

All protocol deviations that occur during the study will be considered prior to database lock for their severity/impact and will be taken into consideration when subjects are assigned to analysis populations.

4.2 Preliminary Data and Interim Analysis

No interim analysis is planned for this study.

5. TREATMENT DESCRIPTIONS

LOXO 292 will be supplied as 80 mg capsules.

All study drugs will be administered orally after an overnight fast with approximately 240 mL of water. Additional water in increments of 50 mL up to a maximum of 100 mL may be administered if needed by the subject.

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

Table 5.1 Treatment Descriptions

Cohort	Short Description (text, tables headers, figures, listings, SAS output)	Abbreviated Description
1	320 mg	Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
2	640 mg	Administration of 640 mg (8 x 80 mg capsules) LOXO-292 on Day 1
3	720 mg	Administration of 720 mg (9 x 80 mg capsules) LOXO-292 on Day 1

Note: additional cohorts (6 subjects per cohort) may be enrolled if it is deemed appropriate to repeat any dose level, or to add an interim dose level(s) (lower than 720 mg), as determined by Loxo Oncology, Inc in consultation with the PI, depending on the safety and tolerability results from the prior cohort(s). Dosing will not exceed 720 mg in any subject. The dose increments will be based on a review of the safety and (potentially) PK data of previous cohorts; therefore, the doses listed in this table and TFL shells are subject to change. The actual doses used in the study will be depicted in the TFLs.

6. PHARMACOKINETIC ANALYSIS

6.1 Measurements and Collection Schedule

Blood samples for PK assessment of LOXO-292 will be taken at the following time points on Day 1 for each cohort: 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.

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 will be 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. All deviations and excluded data will be provided and discussed in the CSR.

6.2 Bioanalytical Method for LOXO-292

Plasma 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 range (lower limit of quantitation [LLOQ] – upper limit of quantitation [ULOQ]) for LOXO-292 is 1 – 1000 ng/mL. Samples that contain concentrations greater than 1000 ng/mL may be diluted up to 51-fold, 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 500 g/mol. LOXO-292 will be supplied as a powder-in-capsule containing 80 mg of drug substance (freebase) as a simple blend with excipients in a hard gelatin capsule.

6.4 Pharmacokinetic Concentrations

Plasma concentrations of LOXO-292 as determined at the collection times and per the bioanalytical method described in Section 6.1 and Section 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

The appropriate noncompartmental PK parameters will be calculated from the plasma LOXO-292 concentration-time data using Phoenix® WinNonlin® Version 7.0 or higher. Actual sample times will be used in the calculations of the PK parameters. The calculation of the actual time for LOXO-292 will be in respect to the dose administration time of LOXO-292 on Day 1. All 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 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, from time 0 to the last observed non-zero concentration	Calculated using the Linear Trapezoidal with Linear Interpolation Method

Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
AUC0-24	Area under the concentration-time curve from time 0 to 24 hours postdose on Day 1. If the 24-hour plasma concentration is missing, below limit of quantification (BLQ), or not reportable, then interpolation or extrapolation using the Kel will be conducted, as appropriate. If extrapolation cannot be performed, then this parameter cannot be calculated.	Calculated using the Linear Trapezoidal with Linear Interpolation Method
AUC0-inf	Area under the concentration-time curve from time 0 extrapolated to infinity	Calculated as AUC0-inf = 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 concentration	Taken directly from bioanalytical data
Tmax	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 by linear least squares regression analysis using the maximum number of points in the terminal log linear phase (e.g., three or more non zero plasma concentrations).
t½	Apparent first order terminal elimination half-life	Calculated as 0.693/Kel.
CL/F	Apparent total plasma clearance after oral (extravascular) administration	Calculated as Dose/(AUC0-inf)
Vz/F	Apparent volume of distribution during the terminal elimination phase after oral (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 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 AUC0-inf, AUC%extrap, t½, CL/F, and 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 (AUC0-inf, AUC%extrap, t½, CL/F, and Vz/F) may not be presented as judged appropriate and in accordance with Celerion SOPs.

6.6 Data Summarization and Presentation

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

The plasma concentrations of LOXO-292 will be listed and summarized by cohort and time point for all subjects in the PK Population. Plasma concentrations of LOXO-292 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. 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 concentration-time profiles will be presented on linear and semi-log scales. Linear mean plots will be presented with and without SD.

Plasma LOXO-292 PK parameters will be listed and summarized by cohort for all subjects in the PK Population. Pharmacokinetic parameters will be reported to 3 significant figures for individual parameters, with the exception of Tmax, which will be presented with 2 decimal places. Summary statistics (n, arithmetic mean, SD, CV%, SEM, minimum, median, maximum, geometric mean [Geom Mean], and geometric CV% [Geom CV%]) will be calculated for 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.

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/or parameter output,
- mean/median in one more level of precision than minimum/maximum,
- SD/SEM in one more level of precision than mean/median,
- n will be presented as an integer,
- CV% will be presented to the nearest tenth, and
- 90% CI will be presented with 2 decimals.

6.7 Statistical Analysis of PK Parameters

If all three cohorts are dosed using different dose levels, dose proportionality will be evaluated graphically and using a power model. A statistical linear relationship between ln-transformed LOXO-292 parameters AUC0-t, AUC0-inf, AUC0-24, and Cmax and the ln-transformed dose will be fitted by using a regression model with ln-transformed dose as a covariate.

$Ln(Y) = \beta_0 + \beta_1 \text{ Ln Dose} + \varepsilon$ (Model 1)

where Y represents the PK parameter AUC0-t, AUC0-inf, AUC0-24, and Cmax.

Dose proportionality requires that $\beta_1 = 1$ for dose-dependent parameters.

As a first step, a statistical linear relationship between the ln-transformed PK parameters AUC0-t, AUC0-inf, AUC0-24, and Cmax and the ln-transformed dose will be verified by including a quadratic $(\text{ln dose})^2$ term in model. A 5% level of significance will be used in sequential testing of the quadratic effect. The statistical linear relationship will be concluded if the quadratic term is not statistically significant at the 0.05 probability level. If the statistical linear relationship is established in step 1, a second step will be performed. An estimate of the slope with corresponding 90% confidence interval for the quadratic term will be obtained from the power model. And, a slope around unity indicates the quadratic term is found to be supported by data; the slope near zero implies the response y is independent of $(\text{ln dose})^2$. If the quadratic term is not suggested from the model in the first step, the linear effect in the second step will be evaluated. In the second step, the slope of ln dose around unit suggests dose-proportionality, and the model will be used to calculate the 90% CIs for the slope of the ln-transformed PK parameters AUC0-t, AUC0-inf, AUC0-24, and Cmax.

The above assessments of dose proportionality will be performed using the following SAS® PROC MIXED code:

Step 1: To evaluate a quadratic effect:

```
PROC MIXED;
MODEL ln(<PK Parameter>)  =  LDOSE LDOSE*LDOSE / HTYPE=1;
RUN;
```

If the quadratic term is found to be not supported by data in Step 1, and a second step will be performed to calculate the 90% CIs for the slope of the ln transformed AUC0-t, AUC0-inf, AUC0-24, and Cmax parameters. Calculation of the slope and associated 90% CI will be performed using the following SAS® PROC MIXED code:

Step 2: To evaluate a linear effect and to obtain a 90% for the slope parameter:

```
PROC MIXED;
MODEL LPARM = LDOSE / SOLUTION CL ALPHA=0.1 ddfm=kr outp=residuals;
RUN;
```

Distributional assumptions underlying the statistical analyses will be assessed by visual inspection of residual plots. Normality will be examined by normal probability plots, while homogeneity of variance will be assessed by plotting the residuals against the predicted values for the model (presented in SAS output). If the assumptions are grossly violated then alternative analyses will be performed.

The following SAS code will be used to plot residuals:

```
PROC UNIVARIATE DATA=RESIDUALS PLOT NORMAL;
VAR RESID;
HISTOGRAM RESID/NORMAL;
QQPLOT RESID;
```

If data support, plots will be provided showing individual subject values by treatment (dose) for each of the PK parameter, together with the predicted PK parameter value from the power model. For these plots, individual ln-transformed PK parameter values and ln-transformed dose values will be displayed in a scatterplot. The graph will display an estimated regression line and 90% CI. The estimated parameters of the linear regression (intercept and slope) and their 90% CIs will be included.

Dose proportionality will be concluded if a statistical linear relationship is demonstrated and if the 90% CIs around the slope estimate parameters include the value of 1 for dose dependent parameters (AUC0-t, AUC0-inf, AUC0-24, and Cmax).

7. SAFETY

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

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

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 assessment before dosing in Period 1, including unscheduled assessments, whichever is later. Unscheduled assessments and ET measurements taken after first dosing will not be used in the summarization.

Note: The term 'unscheduled' assessment used in this SAP also includes 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 treatment 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) for study overall. Weight, height and body mass index are summarized at screening. Age will be derived from the date of birth to the date of dosing in Period 1. Frequency counts will be provided for categorical variables (race, ethnicity, and sex) for overall. 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 according to the National Institution of Health's Common Terminology Criteria for Adverse Events (CTCAE, version 5.0) using a 5-point severity scale (Grade 1, 2, 3, 4 and 5). Not all grades are appropriate for all AEs. Therefore, some AEs may be 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 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 drugs to the AE will be described as Related or Unrelated to LOXO-292.

All AEs captured in the database will be listed in by-subject data listings including verbatim term, coded term, treatment group, severity grade, relationship to study drugs, 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 a 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 an AE decreases in severity grade, the new AE record with less severity will be considered and counted as the same AE event of

the previous record with worse severity under the same treatment group in the analysis and summary tables. If the severity grade of an AE remains the same, the AE will be kept open through to resolution.

If the onset time of an AE is missing and the onset date is the same as the treatment dosing date, then the AE will be considered treatment-emergent. If the onset date of an AE is missing, then the AE will be considered treatment-emergent. If the onset date of the AE is known to have occurred prior to dosing, then the AE will not be treated as a TEAE and will instead be captured as Medical History.

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 treatment and overall. Tables will also be presented by severity grade and relationship to study drugs. If a subject experienced the same TEAE more than once at a different severity grade for a given treatment, the TEAE will only be counted and presented once at the highest severity grade. Similarly, if a subject experienced the same TEAE more than once with different assessments of drug relationship for a given treatment, only the one considered 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.

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

Table 7.4 Lab Test Time Points

Study Day
Screening*
Day -1 (check-in)*
Day 2**
Day 5
Day 8** *
* performed following a fast of at least 12 hours ** performed following a fast of at least 8 hours *** performed prior to Clinic Discharge/EOT or ET

Out-of-normal range (OOR) flags will be recorded as follows: high (H) and low (L) for numerical results and did-not-match (*) for categorical results. If a value fails the reference range, it will automatically be compared to a computer clinically significant (CS) range suggested by the PIs (Celerion SOP GSOP.10.1028). If the value falls within the computer CS range, it will be noted as "N" for not clinically significant. If the value fails (i.e., falls outside of the CS range) the computer CS range, it will be flagged with a "Y" which prompts the PI after reviews all laboratory results to determine how the OOR value should be followed using 4 Investigator flags: "N", not clinically significant, "R", requesting a recheck, "^", checking at the next scheduled visit, or "Y", clinically significant. To distinguish the PI flag from the CS range flags, the PI flags "N" and "Y" will be presented as "-" and "+" in the data listings, respectively. Additionally, a derived flag based on a search of the PI comments for a comment of "CS" or "Clinically Significant" will be used. The derived flag will be populated with "+" if the positive clinically significant determination is found in the comments for cases when the PI flag is populated with a "^" or an "R". In addition, CTCAE, version 5.0 grading (found in NCI CTCAE guidance) will be applied to all out of range lab values deemed clinically significant by the Investigator (or designee) which are recorded as AEs.

Out-of-range values and corresponding recheck results will be listed. Other lab results within this panel and time point will also be listed for this subject. Results that are indicated as CS by the PI (either in the PI flag or in PI comments) will be listed in the table. Out-of-range values laboratory value results which are indicated as CS by PI will be reported as AEs.

For all laboratory values that are numeric, descriptive statistics (n, mean, SD, minimum, median, and maximum) will be presented for each laboratory test by treatment and time point. Change from baseline will be calculated and summarized using the Day -1 check-in value, or in the case of rechecks and unscheduled assessments the last non-missing predose measurement prior to dosing of LOXO-292. Postdose rechecks, unscheduled assessments, and ET results will not be used for calculation of descriptive statistics.

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.

All lab results, including unscheduled assessments (including rechecks), will be listed by subject.

7.5 Vital Signs (Blood Pressure, Heart Rate, and Temperature)

Vital signs measurements (Blood Pressure [BP], Heart Rate [HR], and Temperature [T]) will be taken at the following time points:

Table 7.6 Vital Signs Time Points

Study Day	Study Hour	Assessment
Screening		HR, HR, T†
Day -1	Check-in	HR, BP, T
Day 1	0*	HR, BP, T
Day 1	2	HR, BP
Day 1	4	HR, BP
Day 1	24	HR, BP
Day 3	48	HR, BP
Day 4	72	HR, BP
Day 5	96	HR, BP
Day 6	120	HR, BP
Day 7	144	HR, BP
Day 8	168**	HR, BP, T
* performed within 2 hours prior dosing on Day 1 ** performed prior to Clinic Discharge/EOT or ET †HR = heart rate, BP = blood pressure, T = temperature.		

Descriptive statistics will be reported for vital sign measurements (blood pressure and heart rate) and change from baseline by treatment and time point. Baseline is Day 1 predose value, or in the case of unscheduled assessments (including rechecks) is the last non-missing predose measurement prior to dosing. Postdose unscheduled assessments (including rechecks) 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 measurements will be taken at the following time points:

Table 7.7: ECG Time Points

Period Day	Study Hour
Screening	
Day -1	Check-in*
Day 1	3.5 (Cohorts 2 and 3 only)
Day 2	24
Day 5	96
Day 8	168**
* performed within 24 hours prior dosing on Day 1 ** performed prior to Clinic Discharge/EOT or ET	

Descriptive statistics will be reported for ECG parameters and change from baseline by treatment and time point. Baseline is Day -1 check-in assessment, or in the case of

unscheduled assessments (including rechecks) is the last non-missing predose measurement prior to dosing. Postdose unscheduled assessments (including rechecks) 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. All ECG results will be listed by subject.

7.7 Concomitant Medications

All concomitant medications recorded during the study will be coded with the WHO Dictionary, Version 01-Sep-2018 B3 and listed.

7.8 Physical Examination

A full physical examination will be performed at screening and at 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

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 Subject Disposition (Safety Population)

Section 11:

Table 11-1 Demographic Summary (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

14.2 Pharmacokinetic Data Summary Tables and Figures

14.2.1 Plasma LOXO-292 Tables

14.2.2 Plasma LOXO-292 Figures

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

Table 14.3.5.3 Clinical Laboratory Summary and Change from Baseline – Hematology (Safety Population)

Table 14.3.5.4 Clinical Laboratory Shift from Baseline – Hematology (Safety Population)

Table 14.3.5.5 Clinical Laboratory Summary and Change from Baseline – Urinalysis (Safety Population)

Table 14.3.5.6 Clinical Laboratory Shift from Baseline – Urinalysis (Safety Population)

Table 14.3.5.7 Vital Sign Summary and Change from Baseline (Safety Population)

Table 14.3.5.8 12-Lead Electrocardiogram Summary and 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.

Data listings are numbered following the ICH structure but may be renumbered as appropriate during the compilation of the TFLs 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 16.1.10.1 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

16.2.3 Subjects Excluded from <Pharmacokinetic/Efficacy> Analysis

Appendix 16.2.3 Subjects Excluded from <Pharmacokinetic/Efficacy> Analysis

<Note: Appendices 16.2.2 and 16.2.3 are generated in MS Word for inclusion in the study report.>

16.2.4 Demographic Data

Appendix 16.2.4.1 Demographics (Safety Population)
Appendix 16.2.4.2 Updated Informed Consent (Safety Population)
Appendix 16.2.4.3 Physical Examination (Safety Population)
Appendix 16.2.4.4 Medical and Surgical History (Safety Population)

16.2.5 Compliance and/or Drug Concentration Data

Appendix 16.2.5.1.1 Inclusion Criteria
Appendix 16.2.5.1.2 Exclusion Criteria
Appendix 16.2.5.2 Subject Eligibility (Safety Population)
Appendix 16.2.5.3 Check-in Criteria and Responses (Safety Population)
Appendix 16.2.5.4.1 Test Compound Description (Safety Population)
Appendix 16.2.5.4.2 Test Compound Administration Times (Safety Population)
Appendix 16.2.5.5 Blood Draw Times (Safety Population)
Appendix 16.2.5.6 Meal Times (Safety Population)
Appendix 16.2.5.7 Concomitant Medications (Safety Population)

16.2.6 Individual Pharmacokinetic Response Data

Appendix 16.2.6.1 Individual Plasma LOXO-292 Concentrations Versus Time Profiles Following Administration of a Single Dose of 320 mg LOXO-292 for Subject X (Cohort 1) (Linear and Semi-Log Scale)

Appendix 16.2.6.2 Individual Plasma LOXO-292 Concentrations Versus Time Profiles Following Administration of a Single Dose of 640 mg LOXO-292 for Subject X (Cohort 2) (Linear and Semi-Log Scale)

Appendix 16.2.6.3 Individual Plasma LOXO-292 Concentrations Versus Time Profiles Following Administration of a Single Dose of 720 mg LOXO-292 for Subject X (Cohort 3) (Linear and Semi-Log 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 Non-Drug Therapy (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	Clinical Laboratory Report - Serum Chemistry (Safety Population)
Appendix 16.2.8.1.2	Clinical Laboratory Report - Hematology (Safety Population)
Appendix 16.2.8.1.3	Clinical Laboratory Report - Urinalysis (Safety Population)
Appendix 16.2.8.1.4	Clinical Laboratory Report - Urine Drug Screening (Safety Population)
Appendix 16.2.8.1.5	Clinical Laboratory Report - Other (Safety Population)
Appendix 16.2.8.1.6	Clinical Laboratory Report - Comments (Safety Population)
Appendix 16.2.8.2	Vital Signs (Safety Population)
Appendix 16.2.8.3	12-Lead Electrocardiogram (Safety Population)
Appendix 16.2.8.4	Phone Call (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 Summary Tables Shells

Table 10-1 Summary of Disposition (Safety Population)

Disposition	320 mg	640 mg	720 mg	Overall
Enrolled	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Completed Study	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Discontinued Early	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
<Reason1>	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
<Reason2>	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)

320 mg LOXO-292: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg LOXO-292: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg LOXO-292: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

Source: Table 14.1.1.1
Program: /CAXXXXX/sas_prg/stsas/intext/t_disp.sas DDMMMYYYY HH:MM

Table 11-1 Demographic Summary (Safety Population)

Trait		320 mg	640 mg	720 mg	Study Overall
Sex	Male	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Female	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Race	Asian	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Black or African American	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	White	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Ethnicity	Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Not Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Age* (yr)	n	XX	XX	XX	XX
	Mean	XX.XX	XX.XX	XX.XX	XX.XX
	SD	XX.XXX	XX.XXX	XX.XXX	XX.XXX
	Minimum	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X
	Maximum	XX.XX	XX.XX	XX.XX	XX.XX
Height (cm)	n	XX	XX	XX	XX
	Mean	XXX.X	XXX.X	XXX.X	XXX.X
	SD	X.XX	X.XX	X.XX	X.XX
	Minimum	XXX	XXX	XXX	XXX
	Median	XXX.X	XXX.X	XXX.X	XXX.X
	Maximum	XXX	XXX	XXX	XXX

320 mg LOXO-292: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg LOXO-292: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg LOXO-292: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1
* Age is calculated from the date of first dosing.
BMI = Body mass index

Source: Table 14.1.1.3
Program: /CAXXXXX/sas_prg/stsas/intexttest/t_dem.sas DDMMMYYYY HH:MM

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

Table 11-2 will be in the following format:

Table 11-2 Summary of Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of Single Ascending Doses of LOXO-292 (Cohorts 1 – 3) (PK Population)

Pharmacokinetic Parameters	320 mg	640 mg	720 mg
Param1 (units)	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]
Param3 (units)	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]
320 mg LOXO-292: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1 640 mg LOXO-292: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1 720 mg LOXO-292: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1 AUCs and Cmax values are presented as geometric mean and geometric CV%. Tmax values are presented as median (min, max). Other parameters are presented as arithmetic mean (± SD). Source: Tables 14.2.1.4 through 14.2.1.6			

Notes for Generating the Actual Table:

Presentation of Data:

- The following PK parameters will be presented in the following order and with following units: AUC0-24 (ng*hr/mL), AUC0-t (ng*hr/mL), AUC0-inf (ng*hr/mL), AUC%extrap (%), Cmax (ng/mL), Tmax (hr), Kel (1/hr), t½ (hr), CL/F (L/hr), and Vz/F (L)
- n will be presented as an integer (with no decimal);
- Summary statistics will be presented with same precision as defined in post-text shells

Celerion Note: Per study design needs, the following changes are made to this table relative to Celerion's standard shell:
1. Add the third treatment column to this table and update title

Program: /CAXXXXX/sas_prg/pksas/intext-pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_intext_pkparam.sas DDMMMYYYY HH:MM

Table 11-3 will be in the following format:

Table 11-3 Dose Proportionality Analysis of Plasma LOXO-292 Following Administration of Single Ascending Doses of LOXO-292 (Cohorts 1 – 3) (PK Population)

Pharmacokinetic Parameters	**Estimate of Slope (b)**	**Standard error**	**90% Confidence Interval for Slope**
param1	X.XXXX	X.XXXX	X.XXXX - X.XXXX
param2	X.XXXX	X.XXXX	X.XXXX - X.XXXX
param3	X.XXXX	X.XXXX	X.XXXX - X.XXXX
param4	X.XXXX	X.XXXX	X.XXXX - X.XXXX
Parameters were ln-transformed prior to analysis. The following statistical model using PROC MIXED of SAS was used to test dose proportionality: Parameter = a * Dose^b which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)] Dose proportionality is not rejected if the 90% CI for b contains 1. Source: Table 14.2.1.6			

Notes for Generating the Actual Table:

PK Parameters are AUC0-24, AUC0-t, AUC0-inf, and Cmax

Please use the footnote below:

Parameters were ln-transformed prior to analysis.
The following statistical model using PROC MIXED of SAS was used to test dose proportionality: Parameter = a * Dose^b which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)]
Dose proportionality is not rejected if the 90% CI for b contains 1.

Presentation of Data:

- Slope will be presented to 4 decimal places
- Standard error will be presented to 4 decimal places
- 90% CI will be presented to 4 decimal places

Program: /CAXXXXX/sas_prg/pksas/doseprop-mixed.sas DDMMMYYYY HH:MM

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

Adverse Events*	Treatment			Overall
	320 mg	640 mg	720 mg	
Number of Subjects Dosed	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Number of Subjects With TEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Number of Subjects Without TEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
System Organ Class 1	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 1	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 2	X (X%)	X (X%)	X (X%)	X (X%)
System Organ Class 2	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 1	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 2	X (X%)	X (X%)	X (X%)	X (X%)

320 mg LOXO-292: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg LOXO-292: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg LOXO-292: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1
* 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.
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.

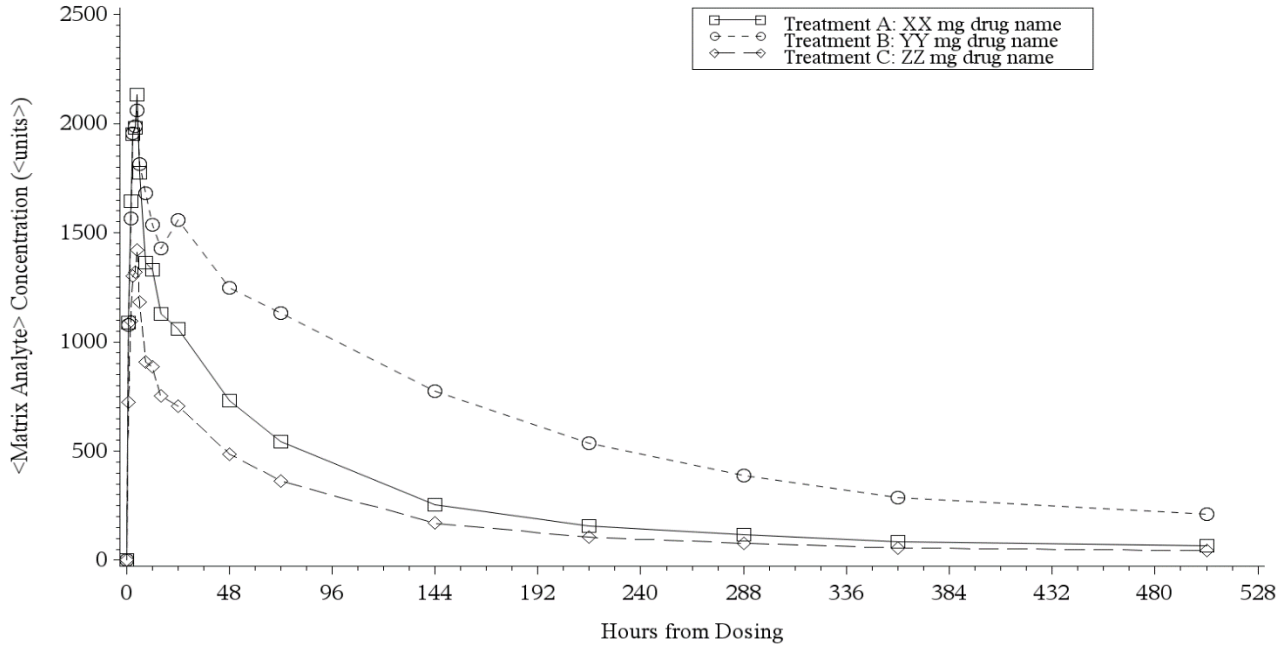
Source: Table 14.3.1.1
Program: /CAXXXXX/sas_prg/stsas/intexttest/t_ae.sas DDMMMYYYY HH:MM

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

Figures 11-1 and 14.2.2.2 will be in the following format:

Figure 11-1 Mean Plasma LOXO-292 Concentrations-Time Profiles Following Administration of Single Ascending Doses of LOXO-292 (Cohorts 1 – 3) (Linear Scale) (PK Population)



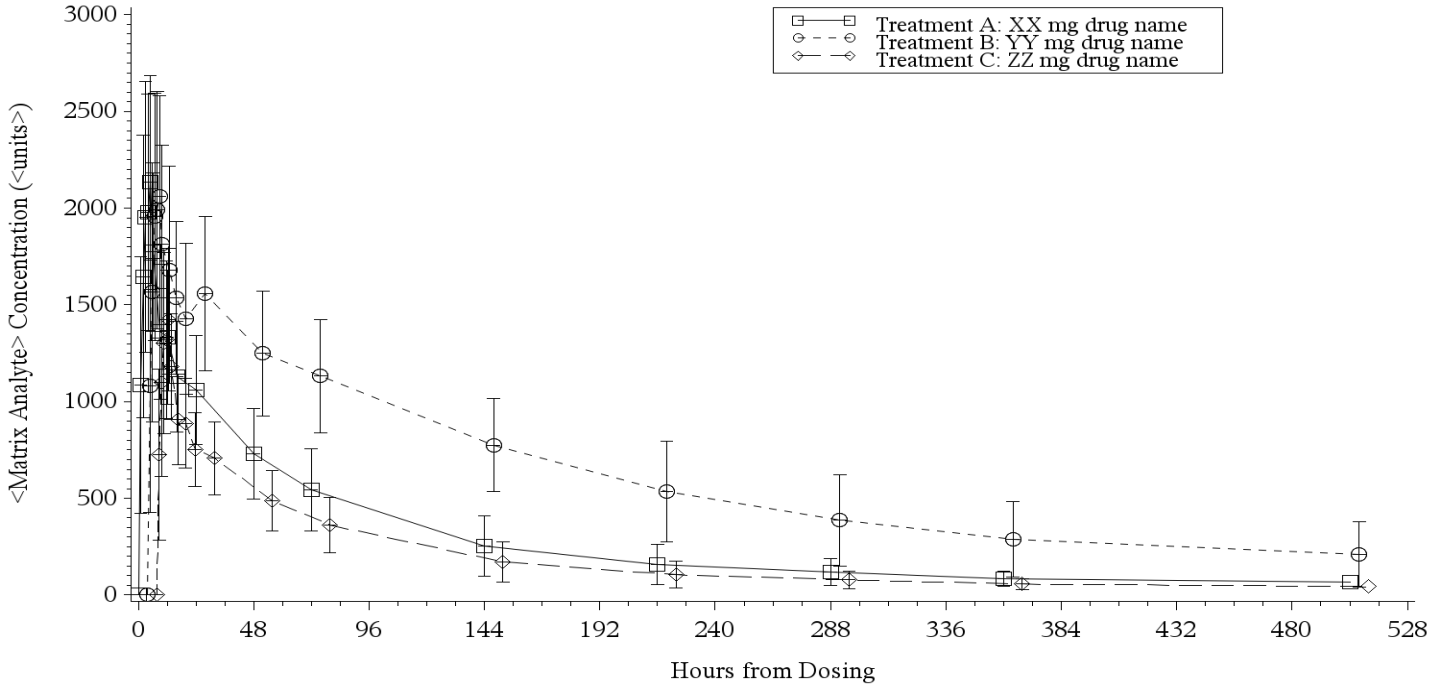
Notes for Generating the Actual Mean Figure:

- Legend will be "320 mg LOXO-292", "640 mg LOXO-292", and "720 mg LOXO-292"
- Y axis label will be "Plasma LOXO-292 Concentration (ng/mL)"
- X axis label will be "Time (hr)"
- Add in footnote: LLOQ value for LOXO-292 in plasma is 1.00 ng/mL

```
Program:  /CAXXXXX/sas_prg/pksas/meangraph.sas        DDMMMYYYY  HH:MM
Program:  /CAXXXXX/sas_prg/pksas/adam_meangraph.sas      DDMMMYYYY  HH:MM
```

Figure 14.2.2.1 will be in the following format:

Figure 14.2.2.1 Mean (SD) Plasma LOXO-292 Concentration-Time Profiles Following Administration of Single Ascending Doses of LOXO-292 (Linear Scale) (PK Population)



Treatments B and C are shifted to the right for ease of reading
Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYY HH:MM

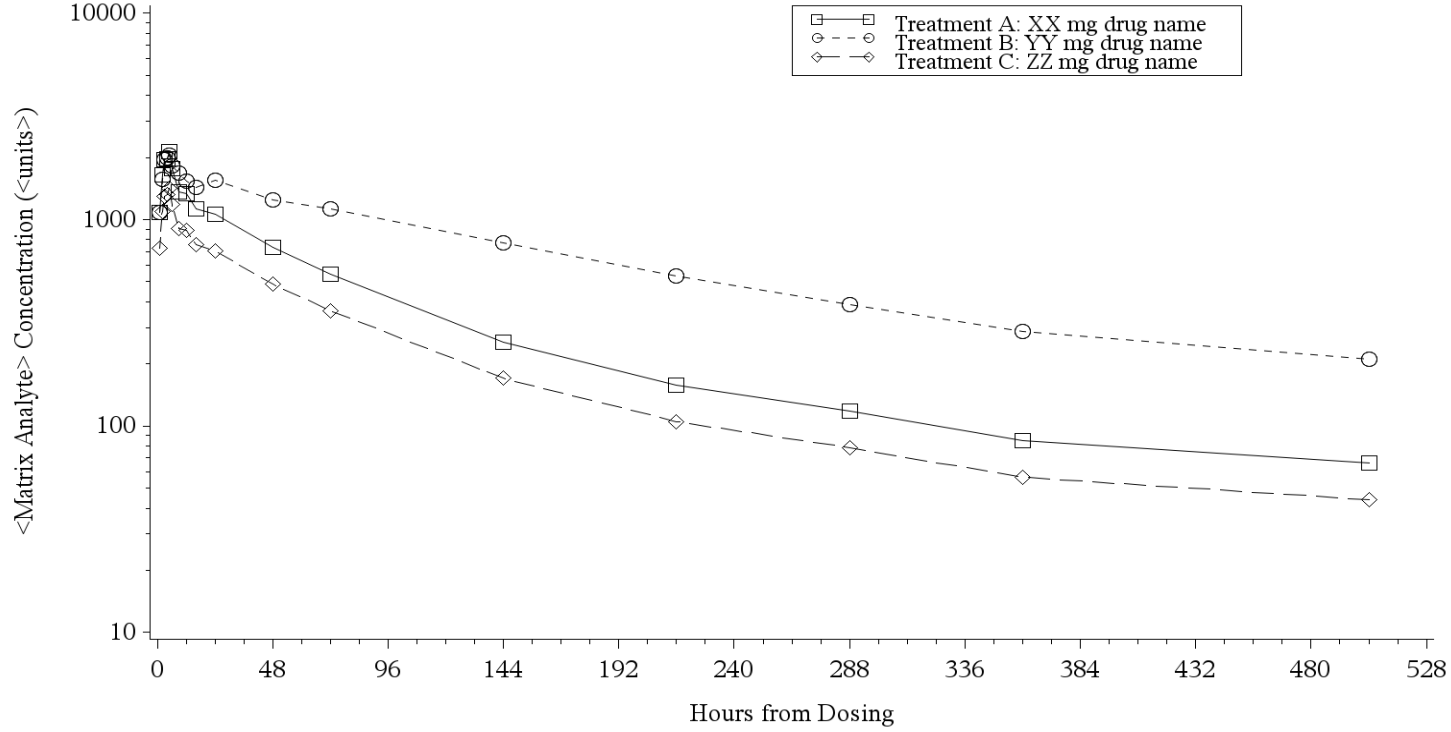
Notes for Generating the Actual Mean Figure:

- Legend will be "320 mg LOXO-292", "640 mg LOXO-292", and "720 mg LOXO-292"
- Y axis label will be "Plasma LOXO-292 Concentration (ng/mL)"
- X axis label will be "Time (hr)"
- Add the following footnote: "640 mg LOXO-292 and 720 mg LOXO-292 are shifted to the right for ease of reading"
- Add in footnote: LLOQ value for LOXO-292 in plasma is 1.00 ng/mL

Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYYY HH:MM

Figure 14.2.2.3 will be in the following format:

Figure 14.2.2.3 Mean Plasma LOXO-292 Concentration-Time Profiles Following Administration of Single Ascending Doses of LOXO-292 (Semi-Log Scale) (PK Population)



Notes for Generating the Actual Mean Figure:

- Legend will be "320 mg LOXO-292", "640 mg LOXO-292", and "720 mg LOXO-292"
- Y axis label will be "Plasma LOXO-292 Concentration (ng/mL)"
- X axis label will be "Time (hr)"
- Add in footnote: LLOQ value for LOXO-292 in plasma is 1.00 ng/mL

```
Program:  /CAXXXXX/sas_prg/pksas/meangraph.sas        DDMMMYYYY  HH:MM
Program:  /CAXXXXX/sas_prg/pksas/adam_meangraph.sas      DDMMMYYYY  HH:MM
```

Figures 11-2 through 11-5 and 14.2.2.4 through 14.2.2.7 will be in the following format:

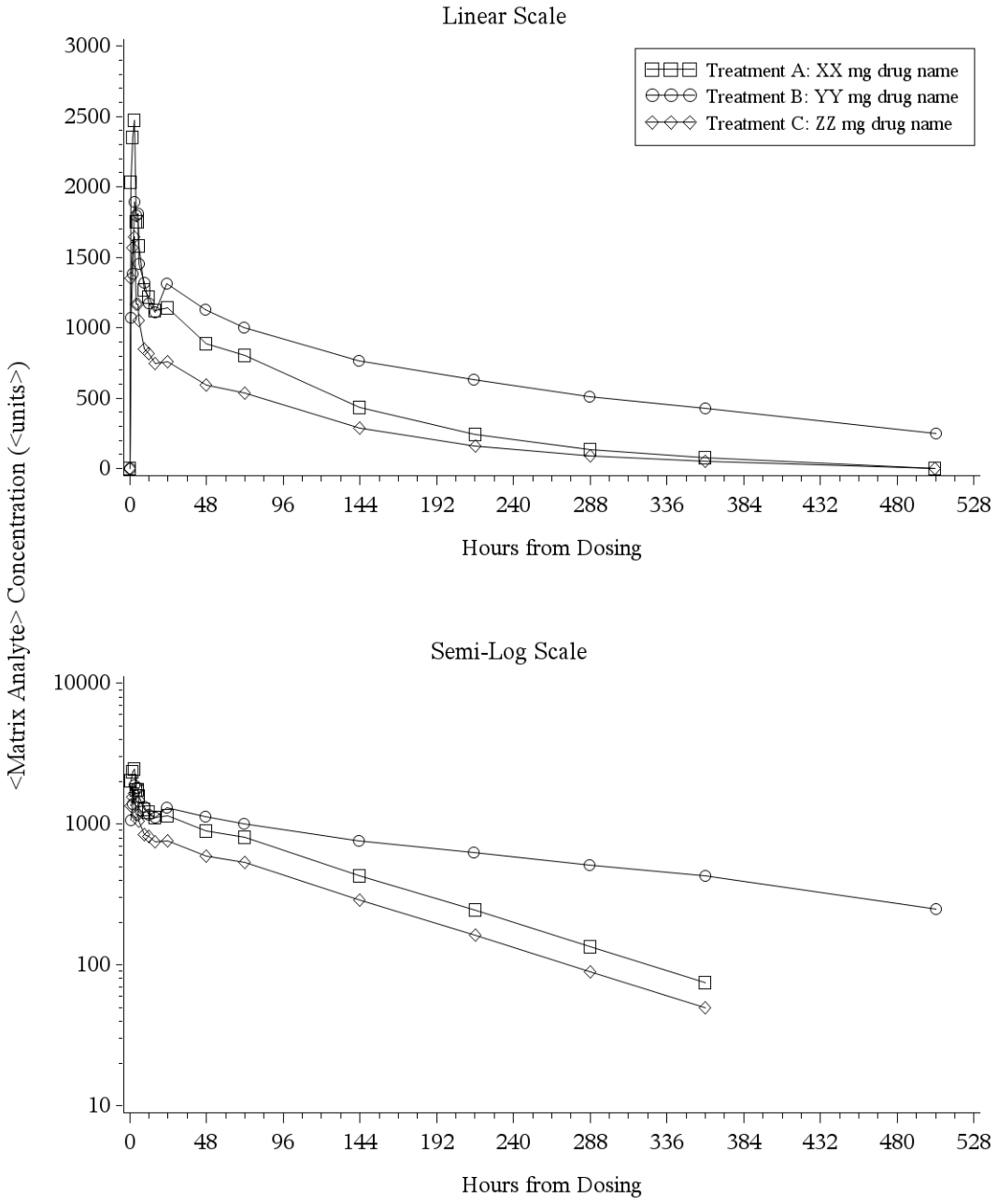
Figure 11-2 Dose Proportionality of Plasma LOXO-292 AUC0-t Following Administration of Single Ascending Doses of LOXO-292 (PK Population) (Log Scale)

***** Note: this is not a Celerion standard figure *****

Notes for Generating the Actual Mean Figure:

- Legend will be "320 mg LOXO-292", "640 mg LOXO-292", and "720 mg LOXO-292"
- Y axis label will be "AUC0-24 (ng*hr/mL), AUC0-t (ng*hr/mL), AUC0-inf (ng*hr/mL), and Cmax (ng/mL)" as appropriate (Log scale)
- X axis will be "LOXO-292 Dose (mg)" (Log scale)

Appendix 16.2.6.1
Individual Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 320 mg LOXO-292 for Subject X (Cohort 1) (Linear and Semi-Log Scale)



Program: /CAXXXXX/sas_prg/pksas/adam_indgraph.sas DDMMMYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/indgraph-all.sas DDMMMYYY HH:MM

Notes for Generating the Actual Individual Figure:

- Use same format for Appendix 16.2.6.1 through 16.2.6.3
- Legend will be "320 mg LOXO-292" for Appendix 16.2.6.1
- Legend will be "640 mg LOXO-292" for Appendix 16.2.6.2
- Legend will be "720 mg LOXO-292" for Appendix 16.2.6.3
- Y axis label will be "Plasma LOXO-292 Concentration (ng/mL)"
- X axis label will be "Hours"
- Add in footnote: LLOQ value for LOXO-292 in plasma is 1.00 ng/mL

Program: /CAXXXXX/sas_prg/pksas/indgraph-all.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_indgraph.sas DDMMMYYYY HH:MM

10.3 Section 14 Summary Tables Shells

Page X of X

Table 14.1.1 Summary of Disposition (Safety Population)

Disposition	320 mg	640 mg	720 mg	Overall
Enrolled	X	X	X	XX
Completed	X	X	X	XX
Discontinued Early	X	X	X	XX
Reason 1	X	X	X	XX
Reason 2	X	X	X	XX
Reason 3	X	X	X	XX
etc.				

Note: 320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Table 14.1.2 Disposition of Subjects (Safety Population)

Subject Number	Treatment	Dosed	Completed	Study Completion Status	Study Completion Date
XXX-XXX	XXX mg	Yes	Yes	Completed Study	DDMMYYYY
XXX-XXX	XXX mg	Yes	No	Withdrew Consent	DDMMYYYY

Note: 320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Table 14.1.3 Demographic Summary (Safety Population)

Trait		320 mg	640 mg	720 mg	Study Overall
Sex	Male	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Female	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Race	Asian	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Black or African American	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	White	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Ethnicity	Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Not Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Age*(yr)	n	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX
Height (cm)	n	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX

Programmer Note: Also include weight (kg) and BMI (kg/m^2)

Note: * Age is calculated from the date of first dosing.
BMI = Body mass index
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Tables 14.2.1.1 through 14.2.1.3 will be in the following format:

Table 14.2.1.1 Plasma LOXO-292 Concentrations (ng/mL) Following Administration of a Single Dose of 320 mg LOXO-292 (Cohort 1) (PK Population)

Subject	Sample Times (hr)								
Number	Predose	XX	XX	XX	XX	XX	XX	XX	XX
X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
X	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 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:
Concentrations will be presented to same precision as in bio data.
Summary statistics presentation with respect to the precision of the bio 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.

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 from all tables.

Program: [redacted]pk-conc-tables.sas DDMMMYYYY HH:MM
Program: [redacted]pk-conc-tables-sig.sas DDMMMYYYY HH:MM
[redacted]

Tables 14.2.1.4 through 14.2.1.6 will be in the following format:

Table 14.2.1.4 Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 320 mg LOXO-292 (Cohort 1) (PK Population)

	Parameters					
Subject Number	param1 (units)	param2 (units)	param3 (units)	param4 (units)	param5 (units)	param6 (units)
X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	X.XX	X.XX	XXX	XXX	XX.X	X.XXX
X	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

. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- PK Parameters will be presented in the following order and with following units: AUC0-24 (ng*hr/mL), AUC0-t (ng*hr/mL), AUC0-inf (ng*hr/mL), AUC%extrap (%), Cmax (ng/mL), Tmax (hr), Kel (1/hr), t1/2 (hr), CL/F (L/hr), and Vz/F (L)
- n will be presented as an integer (with no decimal);
- Parameter values for exposure based parameters (i.e. AUCs, Cmax, Vz/F, and CL/F) will be presented with, at maximum, the precision of the bio data, and, at minimum, 3 significant figures (to be determined by the PKist once bio 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.
- Values for time-based parameters (i.e. Tmax and t1/2) will be presented with 2 decimals. Summary statistics for time-based parameters will be presented as: Mean, Median, and Geom Mean +1; SD +2, Min and Max +0.
- 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.
- CV% and Geom CV% for all parameters will be presented with 1 decimal

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.

Program: /CAXXXXX/sas_prg/pksas/pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_pkparam.sas DDMMMYYYY HH:MM

Table 14.2.1.7 will be in the following format:

Table 14.2.1.7 Intervals (Hours) Used for Determination of Plasma LOXO-292 Kel Values Following Administration of a Single Dose of LOXO-292 (Cohorts 1 – 3) (PK Population)

Subject Number	Treatment	Interval	R2	n
X	X	XX.X – XX.X	X.XXX	X
X	X	XX.X – XX.X	X.XXX	X
X	X	XX.X – XX.X	X.XXX	X
X	X	XX.X – XX.X	X.XXX	X
X	X	XX.X – XX.X	X.XXX	X
X	X	XX.X – XX.X	X.XXX	X

320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 640 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 720 mg (9 x 80 mg capsules) LOXO-292 on Day 1
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:

- Interval start and stop times will be presented to 1 decimal or 3 sig figures min;
- R2 will be presented to 3 decimals;
- n will be presented as an integer (with no decimal)

Program: /CAXXXXX/sas_prg/pksas/kel-tables-parallel.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_kel.sas DDMMMYYYY HH:MM

Table 14.2.1.8 will be in the following format:

Table 14.2.1.8 Dose Proportionality Analysis of Plasma LOXO-292 Following Administration of Single Ascending Doses of LOXO-292 (Cohorts 1 – 3) (PK Population)

Pharmacokinetic Parameters	Estimate of Slope (b)	Standard Error	90% Confidence Interval for Slope
Param1	X.XXXX	X.XXXX	X.XXXX – X.XXXX
Param2	X.XXXX	X.XXXX	X.XXXX – X.XXXX
Param3	X.XXXX	X.XXXX	X.XXXX – X.XXXX

Presentation of Data:

- Slope will be presented to 4 decimal places
- Standard error will be presented to 4 decimal places
- 90% CI will be presented to 4 decimal places

Notes for Generating the Actual Table:

Programmers Note:
PK Parameters are AUC0-24, AUC0-t, AUC0-inf, and Cmax

Please use the footnote below:
Parameters were ln-transformed prior to analysis.
The following statistical model using PROC MIXED of SAS was used to test dose proportionality: Parameter = a * Dose^b which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)]
Dose proportionality is not rejected if the 90% CI for b contains 1.

Program: [redacted]doseprop-mixed.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_dosepropmixed.sas DDMMMYYYY HH:MM

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

TE Adverse Event*	320 mg	640 mg	720 mg	Overall
Number of Subjects Dosed	X (100%)	X (100%)	X (100%)	X(100%)
Number of Subjects with TE Adverse Events	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Number of Subjects without TE Adverse Events	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Nervous system disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dizziness	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Headache	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Presyncope	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Respiratory, thoracic and mediastinal disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dry throat	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Oropharyngeal pain	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sinus congestion	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sneezing	X (XX%)	X (XX%)	X (XX%)	X (XX%)
etc.				

Note: * Adverse events are classified according to MedDRA Version 21.1 by System Organ Class and Preferred Term.
TE = Treatment-emergent
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.
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

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 Treatment, Severity Grade, and Relationship to Study Drugs – Number of Subjects Reporting Events (Safety Population)

TE Adverse Event*	Treatment	Number of Subjects with Adverse Events	Severity Grade					Relationship to Study Drug		
			1	2	3	4	5	Related	Not Related	
Dizziness	320 mg	X	X	X	X	X	X	X	X	
Dry eye	640 mg	X	X	X	X	X	X	X	X	
Dry mouth	XXX mg	X	X	X	X	X	X	X	X	
		X	X	X	X	X	X	X	X	
Dry throat	XXX mg	X	X	X	X	X	X	X	X	
Ear pain	XXX mg	X	X	X	X	X	X	X	X	
Fatigue	XXX mg	X	X	X	X	X	X	X	X	
Treatment 320 mg		XX	X	X	X	X	X	X	X	
Treatment 640 mg		XX	X	X	X	X	X	X	X	
Treatment 720 mg		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.
AEs are graded according to NCI CTCAE version 5.0 grading scale. 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 under the same treatment group.
When a subject experienced the same TEAE at more than one level of severity during a treatment period, only the most severe one was counted.
When a subject experienced the same TEAE at more than one level of drug relationship during a treatment period, only the one related to study drugs was counted.
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Table 14.3.2.1 Serious Adverse Events (Safety Population)

Subject Number	Treatment	TE?^	Adverse Event	PT*/ SOC	Onset/Resolution Day	Onset/Resolution Date	Onset/Resolution Time	Freq*	Severity Grade	Ser*	Outcome	Action	Other Action Taken	Relationship
XXX-XXX	640 mg	Yes	XXXXXXX	XXXXXXX/ XXXXXXXX	XX/ XX	DDMMMYYYY/ DDMMMYYYY	XX:XX/ XX:XX	Inter.	X	NS	Recovered or resolved	XXXXXXXXX XXXXXXXXX	None XXXX	XXXXXXXXX/ 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 Period 1 Day 1.
Freq* represents Frequency: SI = 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
AEs are graded according to NCI CTCAE version 5.0 grading scale. Not all grades are appropriate for all AEs, therefore some AEs are listed in the CTCAE with fewer than 5 options for grade selection.
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

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 14.3.4.1-14.3.4.3 will have the following format.

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

Subject Number	Treatment	Age$/ Sex	Study Period	Day	Hour	Date	Parameter1 < Range> (Unit)	Parameter2 < Range> (Unit)	Parameter3 < Range> (Unit)	Parameter4 < Range> (Unit)	Parameter5 < Range> (Unit)
XXX-XXX	XXX mg	XX/M	Screen			DDMMMYYYY	XX HN	XX	XX	XX	XX HN
			1	-X	Check-in	DDMMMYYYY	XX	XX	XX	XX	XX
			1	X	X	DDMMMYYYY	XX	XX	XX	XX HN	XX
				X	X	DDMMMYYYY	XX	XX	XX	XX	XX
				X	X	DDMMMYYYY	XX LY-	XX LN	XX	XX LY-	XX

Programmer Note: Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for. Arrange alphabetically by lab test name.

Note: $ Age is calculated from the date of first 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
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

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

Subject Number	Treatment	Age$/ Sex	Study Period	Day	Hour	Date	Time	Department	Test	Result	Reference Range	Unit
XXX-XXX	XXX mg	XX/X	X	X	X.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	X - X	mg/dL
				X	XX.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX HYR+	X - X	mg/dL
				X	XX.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX HY-	X - X	mg/dL
				X	XX.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX HN	X - X	mg/dL

Programmer Note: 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 flag or comment field in the laboratory dataset), then this table will contain only the statement: "There were no laboratory values deemed clinically significant by the PI in the study."

Note: $ Age is calculated from the date of first 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
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

Program : /CAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.3.5.1, 14.3.5.3, and 14.3.5.5 will have the following format.

Table 14.3.5.1 Clinical Laboratory Summary and Change from Baseline – Serum Chemistry (Safety Population)

				Treatment			Change From Baseline		
Laboratory Test (unit)	Normal Range#	Time Point	Statistic	320 mg	640 mg	720 mg	320 mg	640 mg	720 mg
Parameter1 (unit)	XX – XX	Day –1	n	XX	XX				
			Mean	XX.XX	XX.XX				
			SD	X.XXX	X.XXX				
			Minimum	XX.X	XX.X				
			Median	XX.XX	XX.XX				
			Maximum	XX.X	XX.X				
		Day 2	n	XX	XX	XX	XX	XX	XX
			Mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
			SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
			Minimum	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
			Median	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
			Maximum	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
		Day 5	n	XX	XX	XX	XX	XX	XX
			Mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
			SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
			Minimum	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
			Median	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
			Maximum	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

<Programmer note: Similar for remaining laboratory tests. Also need to add Day 8 time point. Sort alphabetically by lab test name.>

Note: # Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
Baseline is Day –1 check-in and is the last non-missing predose measurement prior to dosing, including rechecks and unscheduled assessments.
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Tables 14.3.5.2, 14.3.5.4, and 14.3.5.6 will have the following format.

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

Laboratory Test (units)	Treatment	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)	XXX mg	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 Day -1 check-in and is the last non-missing predose measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments.
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Table 14.3.5.7 Vital Sign Summary and Change from Baseline (Safety Population)

Vital sign Paramater (unit)	Time Point	Statistic	Treatment 320 mg	Treatment 640 mg	Treatment 720 mg	Change From Baseline 320 mg	Change From Baseline 640 mg	Change From Baseline 720 mg
Parameter1 (unit)	Day -1 Check-in	n	XX	XX				
		Mean	XX.XX	XX.XX				
		SD	X.XXX	X.XXX				
		Minimum	XX.X	XX.X				
		Median	XX.XX	XX.XX				
		Maximum	XX.X	XX.X				
	Day 1 Predose	n	XX	XX				
		Mean	XX.XX	XX.XX				
		SD	X.XXX	X.XXX				
		Minimum	XX.X	XX.X				
		Median	XX.XX	XX.XX				
		Maximum	XX.X	XX.X				
	Day 1 Hour 2	n	XX	XX	XX	XX	XX	XX
		Mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
		Median	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

<Programmer note: Similar for remaining vital sign parameters. Also need to add additional time points: Day 1 Hour 4, Day 2, Day 3, Day 4, Day 5, Day 6, Day 7, and Day 8.

Note: Baseline is Day 1 predose and is the last non-missing predose measurement prior to dosing, including rechecks and unscheduled assessments.>

320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Table 14.3.5.8 12-Lead Electrocardiogram Summary and Change from Baseline (Safety Population)

			Treatment			Change From Baseline		
ECG Paramater (unit)	Time Point	Statistic	320 mg	640 mg	720 mg	320 mg	640 mg	720 mg
Parameter1 (unit)	Day -1	n	XX	XX				
		Mean	XX.XX	XX.XX				
		SD	X.XXX	X.XXX				
		Minimum	XX.X	XX.X				
		Median	XX.XX	XX.XX				
		Maximum	XX.X	XX.X				
	Day 2	n	XX	XX	XX	XX	XX	XX
		Mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
		Median	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Day 5	n	XX	XX	XX	XX	XX	XX
		Mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
		Median	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

<Programmer note: Similar for remaining ECG parameters. Also need to add Day 8 time point.>

Note: Baseline is Day -1 check-in assessment and is the last non-missing predose measurement prior to dosing, including rechecks and unscheduled assessments.
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas 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.

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

Laboratory Group	Test Name	Sex	Age Category	Normal Range	Unit
Serum Chemistry	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
Hematology	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units

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

<similar for remaining Laboratory Groups and Test Names>

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

Appendix 16.2.1 Subject Discontinuation (Safety Population)

Treatment	Subject Number	Study Period	Date	Completed Study?	Primary Discontinuation Reason
XXX mg	XXX-XXX	Post	DDMMMYYYY	YES	
XXX mg	XXX-XXX	Post	DDMMMYYYY	YES	
XXX mg	XXX-XXX	Post	DDMMMYYYY	YES	
XXX mg	XXX-XXX	Post	DDMMMYYYY	NO	Adverse Event
XXX mg	XXX-XXX	Post	DDMMMYYYY	YES	
XXX mg	XXX-XXX	Post	DDMMMYYYY	YES	

Note: 320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.4.1 Demographics (Safety Population)

Treatment	Subject Number	Date of Birth	Age* (yrs)	Sex	Race	Ethnicity	Height (cm)	Weight (kg)	Body Mass Index (kg/m^2)	Informed Consent Date	Informed Consent Version Date
XXX mg	XXX-XXX	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	DDMMMYYYY
XXX mg	XXX-XXX	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	DDMMMYYYY
XXX mg	XXX-XXX	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	DDMMMYYYY
XXX mg	XXX-XXX	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	DDMMMYYYY
XXX mg	XXX-XXX	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	DDMMMYYYY
XXX mg	XXX-XXX	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	DDMMMYYYY
XXX mg	XXX-XXX	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	DDMMMYYYY

Note: * Age is calculated form the date of first dosing.
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.4.2 Updated Informed Consent (Safety Population)

Treatment	Subject Number	Date Subject Signed Informed Re-Consent	Informed Re-Consent Version Date	Reason for Re-Consent
XXX mg	XXX-XXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXXXX
XXX mg	XXX-XXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXXXX
XXX mg	XXX-XXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXXXX
XXX mg	XXX-XXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXXXX
XXX mg	XXX-XXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXXXX
XXX mg	XXX-XXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXXXX
XXX mg	XXX-XXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXXXX

Note: 320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.4.3 Physical Examination (Safety Population)

Subject Number	Treatment	Period	Study Day	Study Hour	Date	Body System	Answer or Result	Comment
XXX-XXX	XXX mg	Screen			DDMMMYYYY	Was PE performed?	Yes	
						General	Normal	
						HEENT	Normal	
						< >	< >	
		1	-1	Check-in	DDMMMYYYY	Was PE performed?	Yes	
						HEENT	Unchanged	
						< >	< >	

Note: 320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.4.4 Medical and Surgical History (Safety Population)

Treatment	Subject Number	Any History?	Study Period	Category	Body system	Date		Ongoing?	Condition or Events
						Start	End		
XXX mg	XXX-XXX	XXX	Screen	Medical	XXXXXXXXXXX	DDMMMYYYY	DDMMMYYYY	YES	XXXXXXX XXXXXX XXXXXXXX
				Surgical		DDMMMYYYY	DDMMMYYYY		
XXX mg	XXX-XXX	XXX	Screen	Medical	XXXXXXXXXXX	DDMMMYYYY	DDMMMYYYY	NO	

Note: 320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.5.1.1 Inclusion Criteria

1. Healthy, adult, male or female (of non-childbearing potential only), 18–55 years of age, inclusive, at screening.
2. < >
3. < >
4. < >
5. < >

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

Appendix 16.2.5.1.2 Exclusion Criteria

1. Is mentally of legally incapacitated or has significant emotional problems at the time of the screening visit or expected during the conduct of the study.
2. < >
3. < >
4. < >
5. < >
6. < >
7. < >

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

Appendix 16.2.5.2 Subject Eligibility (Safety Population)

Treatment	Subject Number	Study Period	Did subject meet all eligibility criteria?	Specify
XXX mg	XXX-XXX	Screen	YES	
XXX mg	XXX-XXX	Screen	NO	<this column is only presented if data is present>

Note: 320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.5.3.1 Check-in Criteria

1. Did the Subject report any study restriction violations since the last study visit?

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

Appendix 16.2.5.3.2 Check-in Responses (Safety Population)

Treatment	Subject Number	Study Period	Day	Hour	Date	Time	Check-in Criteria	Specify
XXX mg	XXX-XXX	1	X	Check-in	DDMMMYYYY	hh:mm	YES	<this column prints only if data is present>

Note: 320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.5.4.1 Test Compound Description

Compound	Form	Route
XXXXXXXXXXXXX	< >	XXXX
XXXXXXXXXXXXX	< >	XXXX

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

Appendix 16.2.5.4.2 Test Compound Administration Times (Safety Population)

Treatment	Subject Number	Study Period	Day	Hour	Start Date	Start Time	Compound	Dosage	Comments
XXX mg	XXX-XXX	1	X	0	DDMMMYYYY	HH:MM:SS	XXXXXXXXX	< >	<Only populate if there are comments present in the data>

Note: 320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.5.5 PK Blood Draw Times (Safety Population)

Subject Number	Treatment	Study Period	Day	Hour	Date	Actual Time	Bioassay	Comments
XXX-XXX	XXX mg	1	1	-X.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXX	
				XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXX	
				XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXX	
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
			2	XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXX	
				XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXX	
				XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
			3	XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXX	

Note: 320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.5.6 Meal Times (Safety Population)

Subject Number	Treatment	Study Period	Day	Hour	Event	Date	Start Time	Stop Time	Comments
XXX-XXX	XXX mg	1	-X	-XX.XX	LUNCH	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				-XX.XX	DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				-XX.XX	SNACK	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
			X	XX.XX	LUNCH	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				-XX.XX	DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				-XX.XX	SNACK	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
			X	XX.XX	BREAKFAST	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				-XX.XX	LUNCH	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				-XX.XX	DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	

Note: 320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.5.7 Prior and Concomitant Medications (Safety Population)

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

Note: * Concomitant medications are coded with WHO Dictionary Version 01SEP2018.
^ Med = Medication; UNK = Unknown
Prior medication was medication taken prior to study drug administration.
Start and stop day is relative to Period 1 Day 1.
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

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

Subject Number	Treatment	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 mg	None									
XXX-XXX	XXX mg	Yes	XXXXXXXXXXXX/ XXXXXXXXXX	XX:XX:XX	XX	DDMMMYYYY	X:XX	XX	DDMMMYYYY	X:XX	XX:XX:XX
		No	XXXXXXXXXXXX/ 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 Period 1 Day 1.
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

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

Subject Number	Treatment	Adverse Event	Onset Day	Onset Date	Onset Time	Freq*	Severity	Ser*	Outcome	Action	Other Action Taken	Relationship to Study Drug
XXX-XXX	XXX mg	None										
XXX-XXX	XXX mg	XXXXXXX	XX	DDMMMYYYY	XX:XX	Inter.	Grade 1	NO	Resolved	Dose Not Changed	None	

Note: Ser* = Serious; Freq* represents Frequency: SI = 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
AEs are graded according to NCI CTCAE version 5.0 grading scale. Not all grades are appropriate for all AEs, therefore some AEs are listed in the CTCAE with fewer than 5 options for grade selection.
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.7.3 Adverse Event Non-Drug Therapy (Safety Population)

Subject Number	Treatment	Adverse Event	Onset Day	Onset Date	Onset Time	Resolved Day	Resolved Date	Resolved Time	Therapy Date	Therapy Time	Therapy Description
XXX-XXX	XXX mg	DRY LIPS	XX	DDMMMYYYY	X:XX	XX	DDMMMYYYY	X:XX	DDMMMYYYY	XX:XX	PETROLEUM JELLY

Note: Onset and resolved day is relative to Period 1 Day 1.
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.7.4 Adverse Event Preferred Term Classification (Safety Population)

Subject Number	Treatment	Adverse Event	Preferred Term*	Body System	Onset Day	Onset Date	Onset Time
XXX-XXX	XXX mg	XXXXXXX 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 Period 1 Day 1.
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendices 16.2.8.1.2-16.2.8.1.5 will have the following format.

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Appendix 16.2.8.1.1 Clinical Laboratory Report - Serum Chemistry (Safety Population)

Cohort	Subject Number	Age$/ Sex	Study Period	Day	Hour	Date	Parameter1 < Range> (Unit)	Parameter2 < Range> (Unit)	Parameter3 < Range> (Unit)	Parameter4 < Range> (Unit)	Parameter5 < Range> (Unit)
X	XXX-XXX	XX/M	Screen 1	-X	Check-in	DDMMMYYYY	XX HN	XX	XX	XX	XX HN
				X	0	DDMMMYYYY	XX	XX	XX	XX HN	XX
				X	0	DDMMMYYYY	XX	XX	XX	XX	XX
				X	0	DDMMMYYYY	XX LY-	XX LN	XX	XX LY-	XX

Programmer Note: Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for. Arrange alphabetically by lab test name.

Note: $ Age is calculated from the date of first 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
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.8.1.6 Clinical Laboratory Report – Comments (Safety Population)

Subject Number	Treatment	Study Period	Day	Hour	Date	Department	Test	Result	Unit	Comment
XXX-XXX	XXX mg	X	X	-X.X	DDMMMYYYY	Other Tests	Fibrinogen	XXX	mg/dL	Not significant in the context of this study.

Note: 320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.8.2 Vital Signs (Safety Population)

Subject Number	Treat-ment	Study Period	Day	Hour	Date	Time	Blood Pressure (mmHg) Test	Arm	Sys/Dia	Heart rate (bpm)	Temper-ature (°C)	Weight (kg)	Comments
XXX-XXX	XXX mg	Screen			DDMMMYYYY	X:XX:XX						XXX.X	
					DDMMMYYYY	X:XX:XX	SUPX	Right	XXX/ XX	XX	XX.X		
		1	-X	Check-in	DDMMMYYYY	XX:XX:XX						XXX.X	
					DDMMMYYYY	XX:XX:XX	SUPX	Right	XXX/ XX	XX			
			X	X.X	DDMMMYYYY	XX:XX:XX	SUPX	Right					
				X.X	DDMMMYYYY	XX:XX:XX	SUPX	Right					
				X.X	DDMMMYYYY	X:XX:XX	SUPX	Right	XXX/ XX	XX			
				X.X	DDMMMYYYY	X:XX:XX	SUPX	Right	XXX/ XX	XX			
				X.X	DDMMMYYYY	X:XX:XX	SUPX	Right	XXX/ XX	XX			
				R	DDMMMYYYY	XX:XX:XX	SUPX	Right	XXX/ XX	XX			
				X.X	DDMMMYYYY	XX:XX:XX	SUPX	Right					

Programmer note: Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.

Note: SUPX = X-minute supine, R = Recheck Value, Sys/Dia = Systolic/Diastolic
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.8.3 12-Lead Electrocardiogram (Safety Population)

Subject Number	Treatment	Study Period	Day	Hour	Date	Time	Result	Heart Rate (bpm)	PR (msec)	QRS (msec)	QT (msec)	QTcF* (msec)	Comments
XXX-XXX	XXX mg	Screen 1	.		DDMMMYYYY	X:XX:XX	NORMAL	XX	XXX.X	XX.X	XXX.X	XXX.X	
			-1	Check-in	DDMMMYYYY	X:XX:XX	NORMAL	XX	XXX.X	XX.X	XXX.X	XXX.X	
				X.XX	DDMMMYYYY	X:XX:XX	NORMAL	XX	XXX.X	XX.X	XXX.X	XXX.X	
			X	X.XX	DDMMMYYYY	X:XX:XX	NORMAL	XX	XXX.X	XX.X	XXX.X	XXX.X	
				X.XX	DDMMMYYYY	X:XX:XX	NORMAL	XX	XXX.X	XX.X	XXX.X	XXX.X	
			X	X.XX	DDMMMYYYY	X:XX:XX	NORMAL	XX	XXX.X	XX.X	XXX.X	XXX.X	#
			X	X.XX	DDMMMYYYY	X:XX:XX	NORMAL	XX	XXX.X	XX.X	XXX.X	XXX.X	@

Programmer note: Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.

Note: NCS = Abnormal, Not Clinically Significant
QTcF* = QT corrected for heart rate using Fridericia's correction.
= QTcF > 450, @ = QTcF change from baseline greater than 30 msec
320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

Appendix 16.2.8.4 Phone Call (Safety Population)

Subject Number	Treatment	Study Period	Day	Phone Call Completed?	Date	Time	If no, reason
XXX-XXX	XXX mg	X	X	Yes/No	DDMMMYYYY	HH:MM	Wrong number

Note: 320 mg: Administration of 320 mg (4 x 80 mg capsules) LOXO-292 on Day 1
640 mg: Administration of 320 mg (8 x 80 mg capsules) LOXO-292 on Day 1
720 mg: Administration of 320 mg (9 x 80 mg capsules) LOXO-292 on Day 1

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

16.1.9.2 Statistical Outputs

Dose Proportionality Analysis for Plasma LOXO-292 PK Parameter AUC0-24
for Table 14.2.1.8 (Quadratic)

The Mixed Procedure

Model Information

Data Set	WORK.TOTAL
Dependent Variable	LAUC24
Covariance Structure	Diagonal
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Residual

Dimensions

Covariance Parameters	1
Columns in X	3
Columns in Z	0
Subjects	1
Max Obs Per Subject	18

Number of Observations

Number of Observations Read	18
Number of Observations Used	18
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.3375

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 PK Parameter AUC0-24
for Table 14.2.1.8 (Quadratic)

The Mixed Procedure

Fit Statistics

-2 Res Log Likelihood	26.2
AIC (smaller is better)	28.2
AICC (smaller is better)	28.5
BIC (smaller is better)	28.9

Type 1 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
LDOSE	1	15	2.60	0.1279
LDOSE*LDOSE	1	15	0.09	0.7681

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-24
for Table 14.2.1.8 (Linear)

The Mixed Procedure

Model Information

Data Set	WORK.TOTAL
Dependent Variable	LAUC24
Covariance Structure	Diagonal
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Residual

Dimensions

Covariance Parameters	1
Columns in X	2
Columns in Z	0
Subjects	1
Max Obs Per Subject	18

Number of Observations

Number of Observations Read	18
Number of Observations Used	18
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.3183

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-24
for Table 14.2.1.8 (Linear)

The Mixed Procedure

Fit Statistics

-2 Res Log Likelihood	30.8
AIC (smaller is better)	32.8
AICC (smaller is better)	33.1
BIC (smaller is better)	33.6

Solution for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
Intercept	6.3992	2.3343	16	2.74	0.0145	0.1	2.3238	10.4746
LDOSE	0.6169	0.3717	16	1.66	0.1165	0.1	-0.03208	1.2658

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
LDOSE	1	16	2.75	0.1165

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-24
for Table 14.2.1.8 (Linear)

Parameter	Estimate	Lower Limit	Upper Limit
Intercept	6.3992	2.3238	10.4746
Slope	0.6169	-0.03208	1.2658

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 PK Parameter AUC0-t
for Table 14.2.1.8 (Quadratic)

The Mixed Procedure

Model Information

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

Dimensions

Covariance Parameters	1
Columns in X	3
Columns in Z	0
Subjects	1
Max Obs Per Subject	18

Number of Observations

Number of Observations Read	18
Number of Observations Used	18
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.2431

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 PK Parameter AUC0-t
for Table 14.2.1.8 (Quadratic)

The Mixed Procedure

Fit Statistics

-2 Res Log Likelihood	21.3
AIC (smaller is better)	23.3
AICC (smaller is better)	23.6
BIC (smaller is better)	24.0

Type 1 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
LDOSE	1	15	3.38	0.0859
LDOSE*LDOSE	1	15	0.18	0.6797

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-t
for Table 14.2.1.8 (Linear)

The Mixed Procedure

Model Information

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

Dimensions

Covariance Parameters	1
Columns in X	2
Columns in Z	0
Subjects	1
Max Obs Per Subject	18

Number of Observations

Number of Observations Read	18
Number of Observations Used	18
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.2306

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-t
for Table 14.2.1.8 (Linear)

The Mixed Procedure

Fit Statistics

-2 Res Log Likelihood	25.7
AIC (smaller is better)	27.7
AICC (smaller is better)	27.9
BIC (smaller is better)	28.4

Solution for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
Intercept	7.0351	1.9866	16	3.54	0.0027	0.1	3.5667	10.5035
LDOSE	0.5970	0.3163	16	1.89	0.0774	0.1	0.04475	1.1493

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
LDOSE	1	16	3.56	0.0774

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-t
for Table 14.2.1.8 (Linear)

Parameter	Estimate	Lower Limit	Upper Limit
Intercept	7.0351	3.5667	10.5035
Slope	0.5970	0.04475	1.1493

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 PK Parameter AUC0-inf
for Table 14.2.1.8 (Quadratic)

The Mixed Procedure

Model Information

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

Dimensions

Covariance Parameters	1
Columns in X	3
Columns in Z	0
Subjects	1
Max Obs Per Subject	18

Number of Observations

Number of Observations Read	18
Number of Observations Used	18
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.2437

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 PK Parameter AUC0-inf
for Table 14.2.1.8 (Quadratic)

The Mixed Procedure

Fit Statistics

-2 Res Log Likelihood	21.3
AIC (smaller is better)	23.3
AICC (smaller is better)	23.6
BIC (smaller is better)	24.0

Type 1 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
LDOSE	1	15	3.39	0.0854
LDOSE*LDOSE	1	15	0.18	0.6790

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-inf
for Table 14.2.1.8 (Linear)

The Mixed Procedure

Model Information

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

Dimensions

Covariance Parameters	1
Columns in X	2
Columns in Z	0
Subjects	1
Max Obs Per Subject	18

Number of Observations

Number of Observations Read	18
Number of Observations Used	18
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.2312

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-inf
for Table 14.2.1.8 (Linear)

The Mixed Procedure

Fit Statistics

-2 Res Log Likelihood	25.7
AIC (smaller is better)	27.7
AICC (smaller is better)	28.0
BIC (smaller is better)	28.5

Solution for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
Intercept	7.0292	1.9893	16	3.53	0.0028	0.1	3.5561	10.5023
LDOSE	0.5990	0.3168	16	1.89	0.0769	0.1	0.04592	1.1520

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
LDOSE	1	16	3.58	0.0769

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-inf
for Table 14.2.1.8 (Linear)

Parameter	Estimate	Lower Limit	Upper Limit
Intercept	7.0292	3.5561	10.5023
Slope	0.5990	0.04592	1.1520

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 PK Parameter Cmax
for Table 14.2.1.8 (Quadratic)

The Mixed Procedure

Model Information

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

Dimensions

Covariance Parameters	1
Columns in X	3
Columns in Z	0
Subjects	1
Max Obs Per Subject	18

Number of Observations

Number of Observations Read	18
Number of Observations Used	18
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.3736

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 PK Parameter Cmax
for Table 14.2.1.8 (Quadratic)

The Mixed Procedure

Fit Statistics

-2 Res Log Likelihood	27.7
AIC (smaller is better)	29.7
AICC (smaller is better)	30.1
BIC (smaller is better)	30.5

Type 1 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
LDOSE	1	15	2.12	0.1662
LDOSE*LDOSE	1	15	0.02	0.8827

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 - Cmax
for Table 14.2.1.8 (Linear)

The Mixed Procedure

Model Information

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

Dimensions

Covariance Parameters	1
Columns in X	2
Columns in Z	0
Subjects	1
Max Obs Per Subject	18

Number of Observations

Number of Observations Read	18
Number of Observations Used	18
Number of Observations Not Used	0

Covariance Parameter Estimates

Cov Parm	Estimate
Residual	0.3508

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 - Cmax
for Table 14.2.1.8 (Linear)

The Mixed Procedure

Fit Statistics

-2 Res Log Likelihood	32.4
AIC (smaller is better)	34.4
AICC (smaller is better)	34.7
BIC (smaller is better)	35.1

Solution for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
Intercept	4.3482	2.4504	16	1.77	0.0950	0.1	0.07012	8.6262
LDOSE	0.5860	0.3902	16	1.50	0.1526	0.1	-0.09519	1.2673

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
LDOSE	1	16	2.26	0.1526

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 - Cmax
for Table 14.2.1.8 (Linear)

Parameter	Estimate	Lower Limit	Upper Limit
Intercept	4.3482	0.07012	8.6262
Slope	0.5860	-0.09519	1.2673

Program: /CA27486/sas_prg/pksas/adam_doseprop-mixed.sas 19JUN2019 4:22

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-t
for Figure 14.2.2.7

Model: MODEL1
Dependent Variable: AVAL Analysis Value

Number of Observations Read	18
Number of Observations Used	18

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.82125	0.82125	3.56	0.0774
Error	16	3.68893	0.23056		
Corrected Total	17	4.51018			

Root MSE	0.48016	R-Square	0.1821
Dependent Mean	10.77842	Adj R-Sq	0.1310
Coeff Var	4.45487		

Program: /CA27486/sas_prg/pksas/adam_parm_dose_scattergraph.sas 19JUN2019 4:34

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-t
for Figure 14.2.2.7

Model: MODEL1
Dependent Variable: AVAL Analysis Value

Parameter Estimates

Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	Intercept	1	7.03512	1.98661	3.54	0.0027
LDOSE	Log Value of Actual Treatment Dose	1	0.59705	0.31635	1.89	0.0774

Program: /CA27486/sas_prg/pksas/adam_parm_dose_scattergraph.sas 19JUN2019 4:34

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-t
for Figure 14.2.2.7

Model: MODEL1
Dependent Variable: AVAL Analysis Value

Output Statistics

Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	90% CL Predict		Residual
1	10.4651	10.4791	0.1948	9.5744	11.3838	-0.0140
2	11.1581	10.4791	0.1948	9.5744	11.3838	0.6791
3	10.9136	10.4791	0.1948	9.5744	11.3838	0.4345
4	9.5716	10.4791	0.1948	9.5744	11.3838	-0.9075
5	10.2653	10.4791	0.1948	9.5744	11.3838	-0.2138
6	10.5566	10.4791	0.1948	9.5744	11.3838	0.0775
7	10.8621	10.8929	0.1284	10.0252	11.7607	-0.0308
8	11.4083	10.8929	0.1284	10.0252	11.7607	0.5154
9	10.5419	10.8929	0.1284	10.0252	11.7607	-0.3511
10	11.2988	10.8929	0.1284	10.0252	11.7607	0.4059
11	10.3294	10.8929	0.1284	10.0252	11.7607	-0.5635
12	10.5328	10.8929	0.1284	10.0252	11.7607	-0.3601
13	10.5899	10.9633	0.1497	10.0852	11.8413	-0.3733
14	10.5752	10.9633	0.1497	10.0852	11.8413	-0.3881
15	11.7530	10.9633	0.1497	10.0852	11.8413	0.7898
16	11.0174	10.9633	0.1497	10.0852	11.8413	0.0541
17	11.4140	10.9633	0.1497	10.0852	11.8413	0.4508
18	10.7584	10.9633	0.1497	10.0852	11.8413	-0.2049

Sum of Residuals	0
Sum of Squared Residuals	3.68893
Predicted Residual SS (PRESS)	4.77330

Program: /CA27486/sas_prg/pksas/adam_parm_dose_scattergraph.sas 19JUN2019 4:34

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-24
for Figure 14.2.2.8

Model: MODEL1
Dependent Variable: AVAL Analysis Value

Number of Observations Read	18
Number of Observations Used	18

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.87671	0.87671	2.75	0.1165
Error	16	5.09307	0.31832		
Corrected Total	17	5.96979			

Root MSE	0.56420	R-Square	0.1469
Dependent Mean	10.26685	Adj R-Sq	0.0935
Coeff Var	5.49532		

Program: /CA27486/sas_prg/pksas/adam_parm_dose_scattergraph.sas 19JUN2019 4:34

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-24
for Figure 14.2.2.8

Model: MODEL1
Dependent Variable: AVAL Analysis Value

Parameter Estimates

Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	Intercept	1	6.39921	2.33428	2.74	0.0145
LDOSE	Log Value of Actual Treatment Dose	1	0.61688	0.37171	1.66	0.1165

Program: /CA27486/sas_prg/pksas/adam_parm_dose_scattergraph.sas 19JUN2019 4:34

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-24
for Figure 14.2.2.8

Model: MODEL1
Dependent Variable: AVAL Analysis Value

Output Statistics

Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	90% CL Predict		Residual
1	9.8894	9.9576	0.2289	8.8945	11.0206	-0.0681
2	10.6905	9.9576	0.2289	8.8945	11.0206	0.7329
3	10.5971	9.9576	0.2289	8.8945	11.0206	0.6396
4	8.9243	9.9576	0.2289	8.8945	11.0206	-1.0333
5	9.3860	9.9576	0.2289	8.8945	11.0206	-0.5716
6	10.3050	9.9576	0.2289	8.8945	11.0206	0.3474
7	10.3395	10.3852	0.1509	9.3655	11.4048	-0.0456
8	11.0223	10.3852	0.1509	9.3655	11.4048	0.6371
9	10.0003	10.3852	0.1509	9.3655	11.4048	-0.3848
10	10.7864	10.3852	0.1509	9.3655	11.4048	0.4012
11	9.8830	10.3852	0.1509	9.3655	11.4048	-0.5022
12	9.9566	10.3852	0.1509	9.3655	11.4048	-0.4286
13	9.9191	10.4578	0.1759	9.4261	11.4896	-0.5387
14	10.0936	10.4578	0.1759	9.4261	11.4896	-0.3642
15	11.3690	10.4578	0.1759	9.4261	11.4896	0.9112
16	10.5137	10.4578	0.1759	9.4261	11.4896	0.0559
17	10.8764	10.4578	0.1759	9.4261	11.4896	0.4186
18	10.2511	10.4578	0.1759	9.4261	11.4896	-0.2067

Sum of Residuals	0
Sum of Squared Residuals	5.09307
Predicted Residual SS (PRESS)	6.67982

Program: /CA27486/sas_prg/pksas/adam_parm_dose_scattergraph.sas 19JUN2019 4:34

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-inf
for Figure 14.2.2.9

Model: MODEL1
Dependent Variable: AVAL Analysis Value

Number of Observations Read	18
Number of Observations Used	18

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.82655	0.82655	3.58	0.0769
Error	16	3.69893	0.23118		
Corrected Total	17	4.52548			

Root MSE	0.48082	R-Square	0.1826
Dependent Mean	10.78453	Adj R-Sq	0.1316
Coeff Var	4.45838		

Program: /CA27486/sas_prg/pksas/adam_parm_dose_scattergraph.sas 19JUN2019 4:34

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-inf
for Figure 14.2.2.9

Model: MODEL1
Dependent Variable: AVAL Analysis Value

Parameter Estimates

Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	Intercept	1	7.02918	1.98930	3.53	0.0028
LDOSE	Log Value of Actual Treatment Dose	1	0.59897	0.31677	1.89	0.0769

Program: /CA27486/sas_prg/pksas/adam_parm_dose_scattergraph.sas 19JUN2019 4:34

Dose Proportionality Analysis for Plasma LOXO-292 - AUC0-inf
for Figure 14.2.2.9

Model: MODEL1
Dependent Variable: AVAL Analysis Value

Output Statistics

Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	90% CL Predict		Residual
1	10.4696	10.4842	0.1951	9.5783	11.3902	-0.0147
2	11.1650	10.4842	0.1951	9.5783	11.3902	0.6808
3	10.9144	10.4842	0.1951	9.5783	11.3902	0.4302
4	9.5750	10.4842	0.1951	9.5783	11.3902	-0.9092
5	10.2787	10.4842	0.1951	9.5783	11.3902	-0.2056
6	10.5587	10.4842	0.1951	9.5783	11.3902	0.0745
7	10.8661	10.8994	0.1286	10.0305	11.7684	-0.0333
8	11.4174	10.8994	0.1286	10.0305	11.7684	0.5180
9	10.5468	10.8994	0.1286	10.0305	11.7684	-0.3527
10	11.3095	10.8994	0.1286	10.0305	11.7684	0.4101
11	10.3349	10.8994	0.1286	10.0305	11.7684	-0.5645
12	10.5363	10.8994	0.1286	10.0305	11.7684	-0.3631
13	10.6012	10.9700	0.1499	10.0907	11.8492	-0.3688
14	10.5779	10.9700	0.1499	10.0907	11.8492	-0.3921
15	11.7593	10.9700	0.1499	10.0907	11.8492	0.7894
16	11.0231	10.9700	0.1499	10.0907	11.8492	0.0532
17	11.4232	10.9700	0.1499	10.0907	11.8492	0.4532
18	10.7646	10.9700	0.1499	10.0907	11.8492	-0.2054

Sum of Residuals	0
Sum of Squared Residuals	3.69893
Predicted Residual SS (PRESS)	4.78441

Program: /CA27486/sas_prg/pksas/adam_parm_dose_scattergraph.sas 19JUN2019 4:34

Dose Proportionality Analysis for Plasma LOXO-292 - Cmax
for Figure 14.2.2.10

Model: MODEL1
Dependent Variable: AVAL Analysis Value

Number of Observations Read 18
Number of Observations Used 18

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.79125	0.79125	2.26	0.1526
Error	16	5.61220	0.35076		
Corrected Total	17	6.40345			

Root MSE	0.59225	R-Square	0.1236
Dependent Mean	8.02245	Adj R-Sq	0.0688
Coeff Var	7.38243		

Program: /CA27486/sas_prg/pksas/adam_parm_dose_scattergraph.sas 19JUN2019 4:34

Dose Proportionality Analysis for Plasma LOXO-292 - Cmax
for Figure 14.2.2.10

Model: MODEL1
Dependent Variable: AVAL Analysis Value

Parameter Estimates

Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	Intercept	1	4.34816	2.45036	1.77	0.0950
LDOSE	Log Value of Actual Treatment Dose	1	0.58604	0.39019	1.50	0.1526

Program: /CA27486/sas_prg/pksas/adam_parm_dose_scattergraph.sas 19JUN2019 4:34

Dose Proportionality Analysis for Plasma LOXO-292 - Cmax
for Figure 14.2.2.10

Model: MODEL1
Dependent Variable: AVAL Analysis Value

Output Statistics

Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	90% CL Predict		Residual
1	7.3715	7.7286	0.2403	6.6127	8.8445	-0.3571
2	8.4764	7.7286	0.2403	6.6127	8.8445	0.7477
3	8.4805	7.7286	0.2403	6.6127	8.8445	0.7519
4	6.7405	7.7286	0.2403	6.6127	8.8445	-0.9881
5	7.0901	7.7286	0.2403	6.6127	8.8445	-0.6386
6	8.2375	7.7286	0.2403	6.6127	8.8445	0.5088
7	8.1519	8.1348	0.1584	7.0645	9.2052	0.0171
8	8.7499	8.1348	0.1584	7.0645	9.2052	0.6150
9	7.8861	8.1348	0.1584	7.0645	9.2052	-0.2488
10	8.6827	8.1348	0.1584	7.0645	9.2052	0.5479
11	7.7187	8.1348	0.1584	7.0645	9.2052	-0.4162
12	7.4501	8.1348	0.1584	7.0645	9.2052	-0.6848
13	7.8120	8.2039	0.1846	7.1208	9.2869	-0.3919
14	7.9725	8.2039	0.1846	7.1208	9.2869	-0.2314
15	9.2301	8.2039	0.1846	7.1208	9.2869	1.0263
16	8.1017	8.2039	0.1846	7.1208	9.2869	-0.1022
17	8.2865	8.2039	0.1846	7.1208	9.2869	0.0826
18	7.9655	8.2039	0.1846	7.1208	9.2869	-0.2383

Sum of Residuals	0
Sum of Squared Residuals	5.61220
Predicted Residual SS (PRESS)	7.38988

Program: /CA27486/sas_prg/pksas/adam_parm_dose_scattergraph.sas 19JUN2019 4:34

16.1.9.3 Normality Assessments

Normality Assessment for Plasma LOXO-292 - AUC0-24 for Table 14.2.1.8

Variable: Resid
(Residual)

Moments			
N	18	**Sum Weights**	18
Mean	0	**Sum Observations**	0
Std Deviation	0.54735048	**Variance**	0.29959255
Skewness	0.03401098	**Kurtosis**	-0.9501699
Uncorrected SS	5.09307327	**Corrected SS**	5.09307327
Coeff Variation	.	**Std Error Mean**	0.12901174

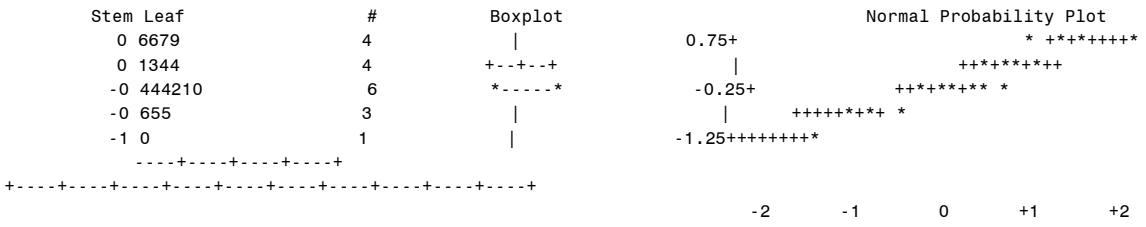
Basic Statistical Measures			
Location		**Variability**	
Mean	0.00000	**Std Deviation**	0.54735
Median	-0.05687	**Variance**	0.29959
Mode	.	**Range**	1.94447
		Interquartile Range	0.84716

Tests for Location: Mu0=0				
Test	**Statistic**		**p Value**	
Student's t	**t**	0	**Pr > |t|**	1.0000
Sign	**M**	-1	**Pr >= |M|**	0.8145
Signed Rank	**S**	0.5	**Pr >= |S|**	1.0000

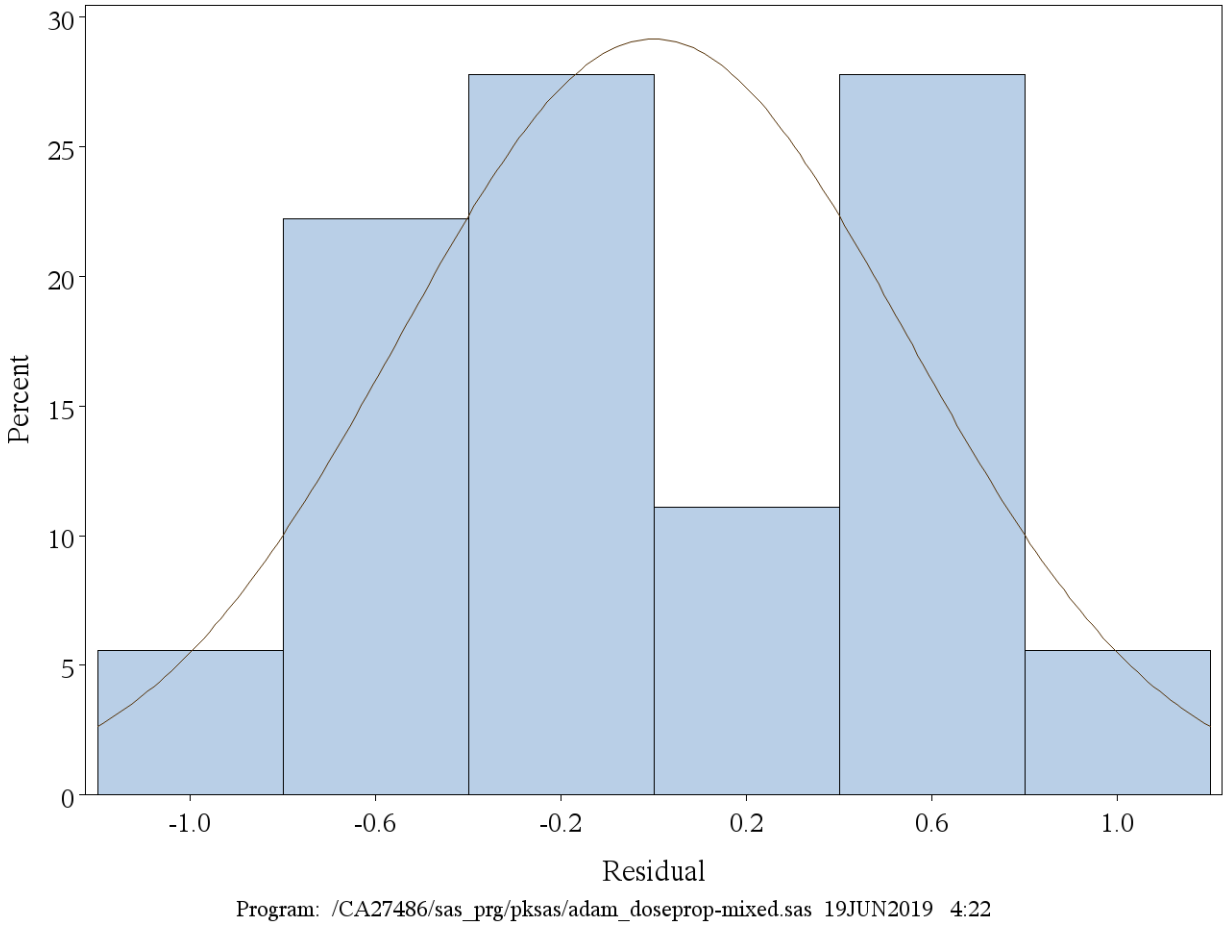
Tests for Normality				
Test	**Statistic**		**p Value**	
Shapiro-Wilk	**W**	0.956817	**Pr < W**	0.5415
Kolmogorov-Smirnov	**D**	0.136012	**Pr > D**	>0.1500
Cramer-von Mises	**W-Sq**	0.058553	**Pr > W-Sq**	>0.2500
Anderson-Darling	**A-Sq**	0.354958	**Pr > A-Sq**	>0.2500

Quantiles (Definition 5)	
Quantile	**Estimate**
100% Max	0.911191
99%	0.911191
95%	0.911191
90%	0.732887
75% Q3	0.418596
50% Median	-0.056869
25% Q1	-0.428560
10%	-0.571557
5%	-1.033276
1%	-1.033276
0% Min	-1.033276

Extreme Observations			
Lowest		**Highest**	
Value	**Obs**	**Value**	**Obs**
-1.033276	4	0.418596	17
-0.571557	5	0.637136	8
-0.538749	13	0.639577	3
-0.502206	11	0.732887	2
-0.428560	12	0.911191	15



Normality Assessment for Plasma LOXO-292 - AUC0-24 for Table 14.2.1.8



Normality Assessment for Plasma LOXO-292 - AUC0-24 for Table 14.2.1.8

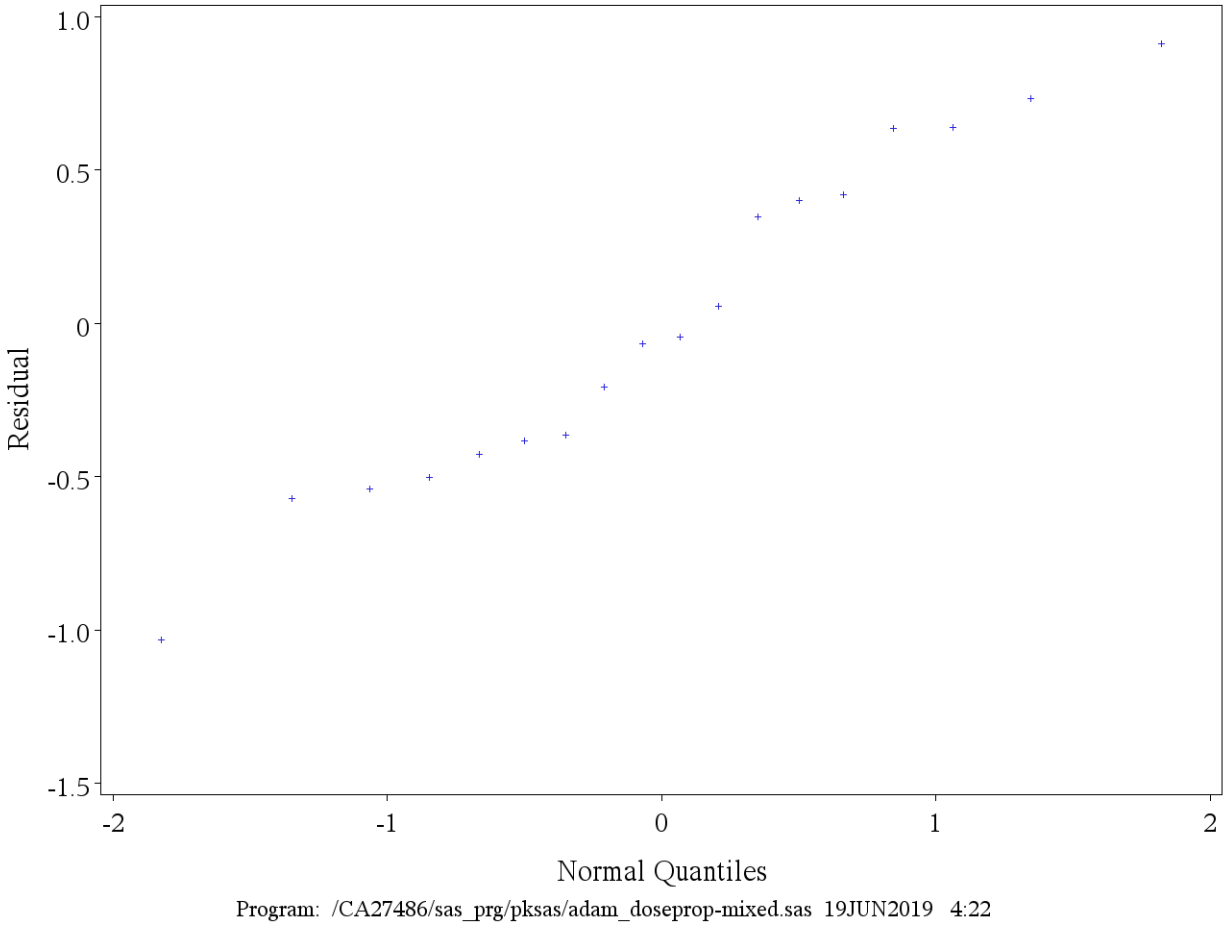
Fitted Normal Distribution for Resid (Residual)

Parameters for Normal Distribution		
Parameter	**Symbol**	**Estimate**
Mean	Mu	0
Std Dev	Sigma	0.54735

Goodness-of-Fit Tests for Normal Distribution				
Test	**Statistic**		**p Value**	
Kolmogorov-Smirnov	**D**	0.13601194	**Pr > D**	>0.150
Cramer-von Mises	**W-Sq**	0.05855315	**Pr > W-Sq**	>0.250
Anderson-Darling	**A-Sq**	0.35495841	**Pr > A-Sq**	>0.250

Quantiles for Normal Distribution		
	Quantile	
Percent	**Observed**	**Estimated**
1.0	-1.03328	-1.27333
5.0	-1.03328	-0.90031
10.0	-0.57156	-0.70146
25.0	-0.42856	-0.36918
50.0	-0.05687	0.00000
75.0	0.41860	0.36918
90.0	0.73289	0.70146
95.0	0.91119	0.90031
99.0	0.91119	1.27333

Normality Assessment for Plasma LOXO-292 - AUC0-24 for Table 14.2.1.8



Normality Assessment for Plasma LOXO-292 - AUC0-t for Table 14.2.1.8

Variable: Resid
(Residual)

Moments			
N	18	**Sum Weights**	18
Mean	0	**Sum Observations**	0
Std Deviation	0.46582814	**Variance**	0.21699586
Skewness	0.02529015	**Kurtosis**	-0.7048472
Uncorrected SS	3.68892959	**Corrected SS**	3.68892959
Coeff Variation	.	**Std Error Mean**	0.10979675

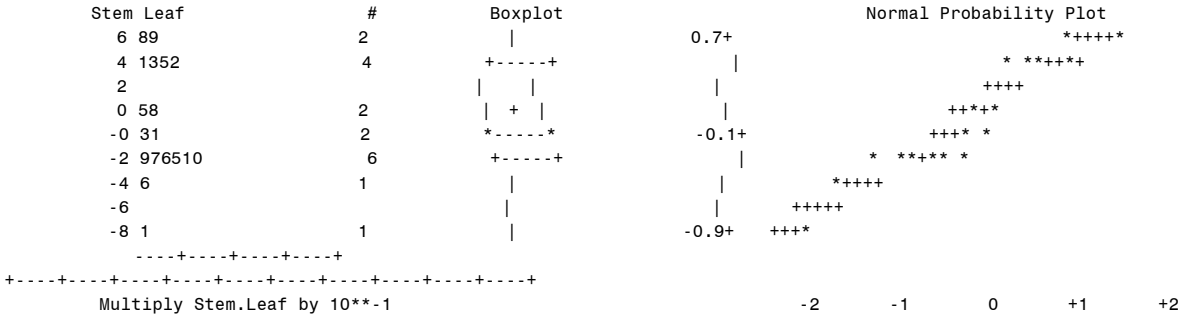
Basic Statistical Measures			
Location		**Variability**	
Mean	0.00000	**Std Deviation**	0.46583
Median	-0.02241	**Variance**	0.21700
Mode	.	**Range**	1.69726
		Interquartile Range	0.79460

Tests for Location: Mu0=0				
Test	**Statistic**		**p Value**	
Student's t	**t**	0	**Pr > |t|**	1.0000
Sign	**M**	-1	**Pr >= |M|**	0.8145
Signed Rank	**S**	4.5	**Pr >= |S|**	0.8650

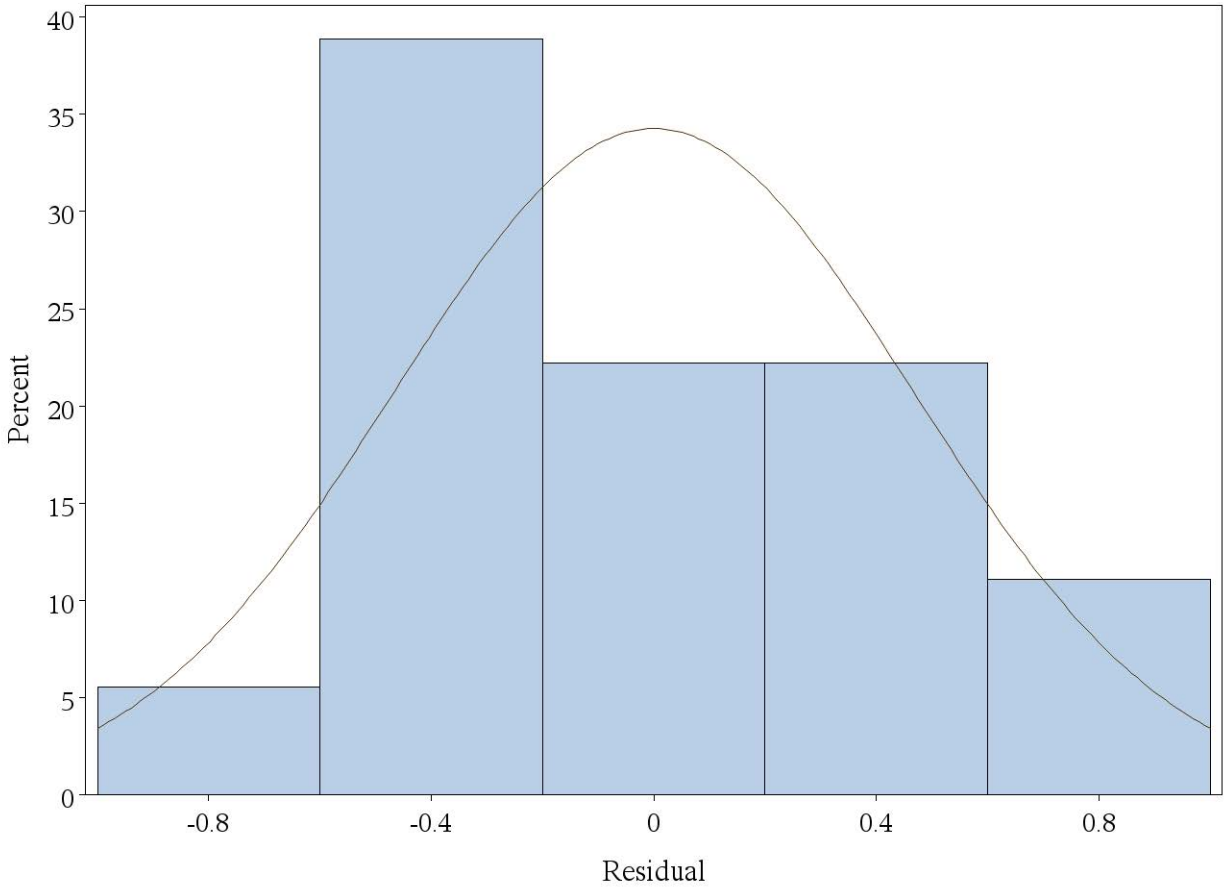
Tests for Normality				
Test	**Statistic**		**p Value**	
Shapiro-Wilk	**W**	0.963641	**Pr < W**	0.6731
Kolmogorov-Smirnov	**D**	0.14155	**Pr > D**	>0.1500
Cramer-von Mises	**W-Sq**	0.05408	**Pr > W-Sq**	>0.2500
Anderson-Darling	**A-Sq**	0.323198	**Pr > A-Sq**	>0.2500

Quantiles (Definition 5)	
Quantile	**Estimate**
100% Max	0.7897647
99%	0.7897647
95%	0.7897647
90%	0.6790547
75% Q3	0.4344805
50% Median	-0.0224074
25% Q1	-0.3601238
10%	-0.5634883
5%	-0.9074926
1%	-0.9074926
0% Min	-0.9074926

Extreme Observations			
Lowest		**Highest**	
Value	**Obs**	**Value**	**Obs**
-0.907493	4	0.434481	3
-0.563488	11	0.450776	17
-0.388061	14	0.515411	8
-0.373340	13	0.679055	2
-0.360124	12	0.789765	15



Normality Assessment for Plasma LOXO-292 - AUC0-t for Table 14.2.1.8



Normality Assessment for Plasma LOXO-292 - AUC0-t for Table 14.2.1.8

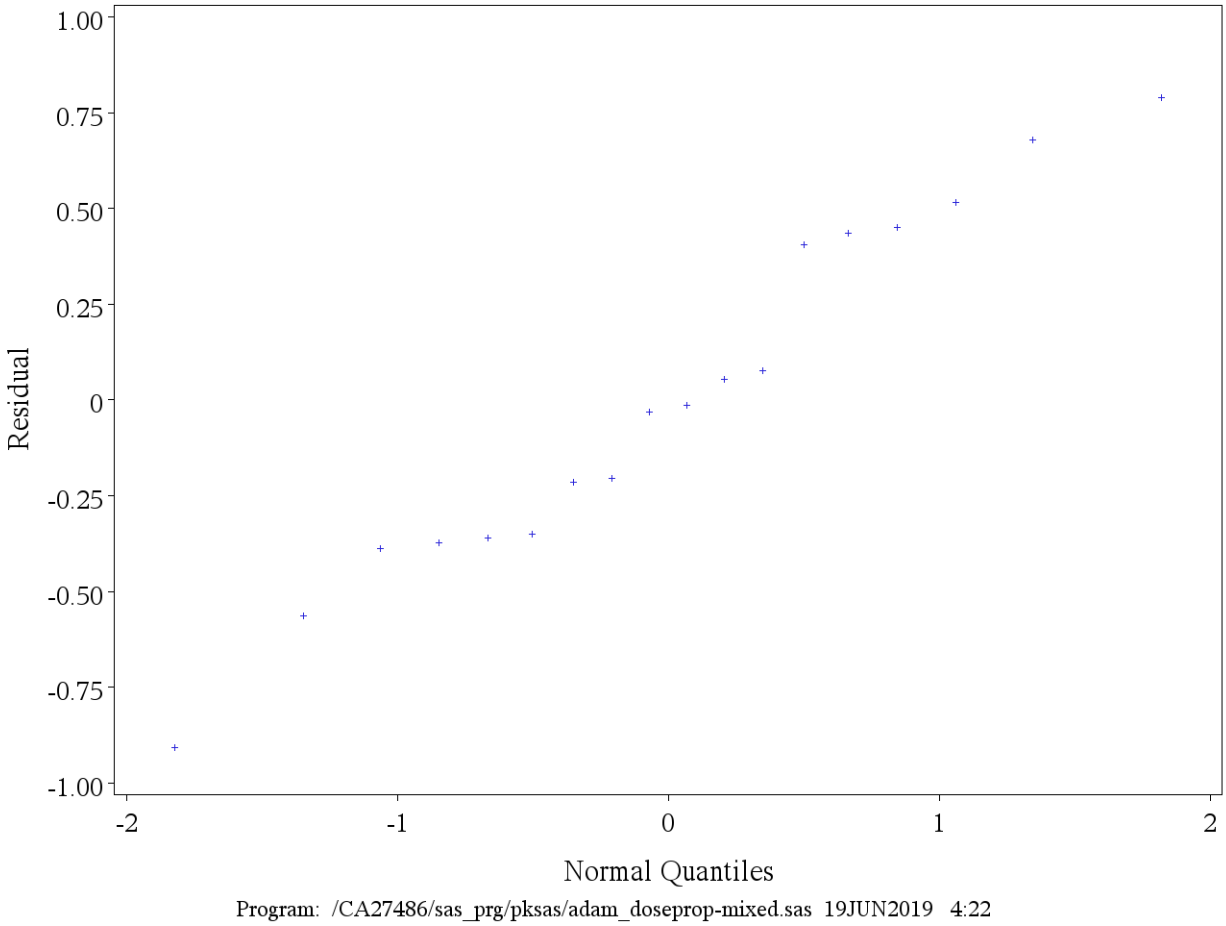
Fitted Normal Distribution for Resid (Residual)

Parameters for Normal Distribution		
Parameter	**Symbol**	**Estimate**
Mean	Mu	0
Std Dev	Sigma	0.465828

Goodness-of-Fit Tests for Normal Distribution				
Test	**Statistic**		**p Value**	
Kolmogorov-Smirnov	**D**	0.14154968	**Pr > D**	>0.150
Cramer-von Mises	**W-Sq**	0.05408010	**Pr > W-Sq**	>0.250
Anderson-Darling	**A-Sq**	0.32319805	**Pr > A-Sq**	>0.250

Quantiles for Normal Distribution		
	Quantile	
Percent	**Observed**	**Estimated**
1.0	-0.90749	-1.08368
5.0	-0.90749	-0.76622
10.0	-0.56349	-0.59698
25.0	-0.36012	-0.31420
50.0	-0.02241	0.00000
75.0	0.43448	0.31420
90.0	0.67905	0.59698
95.0	0.78976	0.76622
99.0	0.78976	1.08368

Normality Assessment for Plasma LOXO-292 - AUC0-t for Table 14.2.1.8



Normality Assessment for Plasma LOXO-292 - AUC0-inf for Table 14.2.1.8

Variable: Resid
(Residual)

Moments			
N	18	**Sum Weights**	18
Mean	0	**Sum Observations**	0
Std Deviation	0.46645909	**Variance**	0.21758408
Skewness	0.02449645	**Kurtosis**	-0.7030042
Uncorrected SS	3.69892938	**Corrected SS**	3.69892938
Coeff Variation	.	**Std Error Mean**	0.10994546

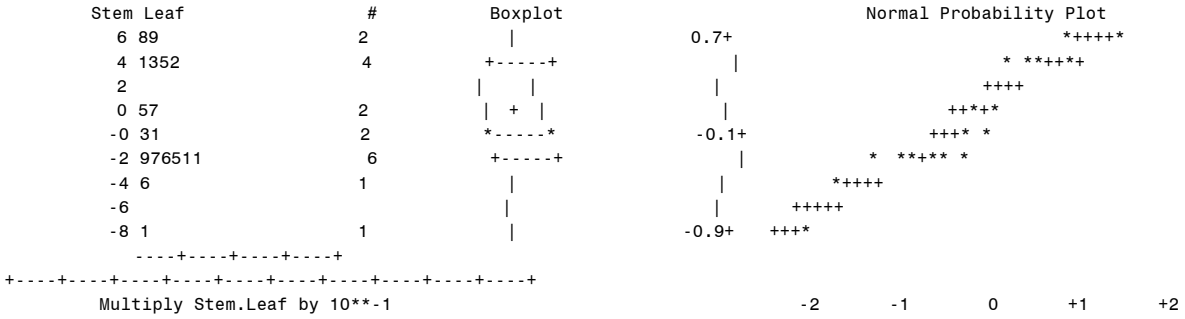
Basic Statistical Measures			
Location		**Variability**	
Mean	0.00000	**Std Deviation**	0.46646
Median	-0.02399	**Variance**	0.21758
Mode	.	**Range**	1.69857
		Interquartile Range	0.79328

Tests for Location: Mu0=0				
Test	**Statistic**		**p Value**	
Student's t	**t**	0	**Pr > |t|**	1.0000
Sign	**M**	-1	**Pr >= |M|**	0.8145
Signed Rank	**S**	4.5	**Pr >= |S|**	0.8650

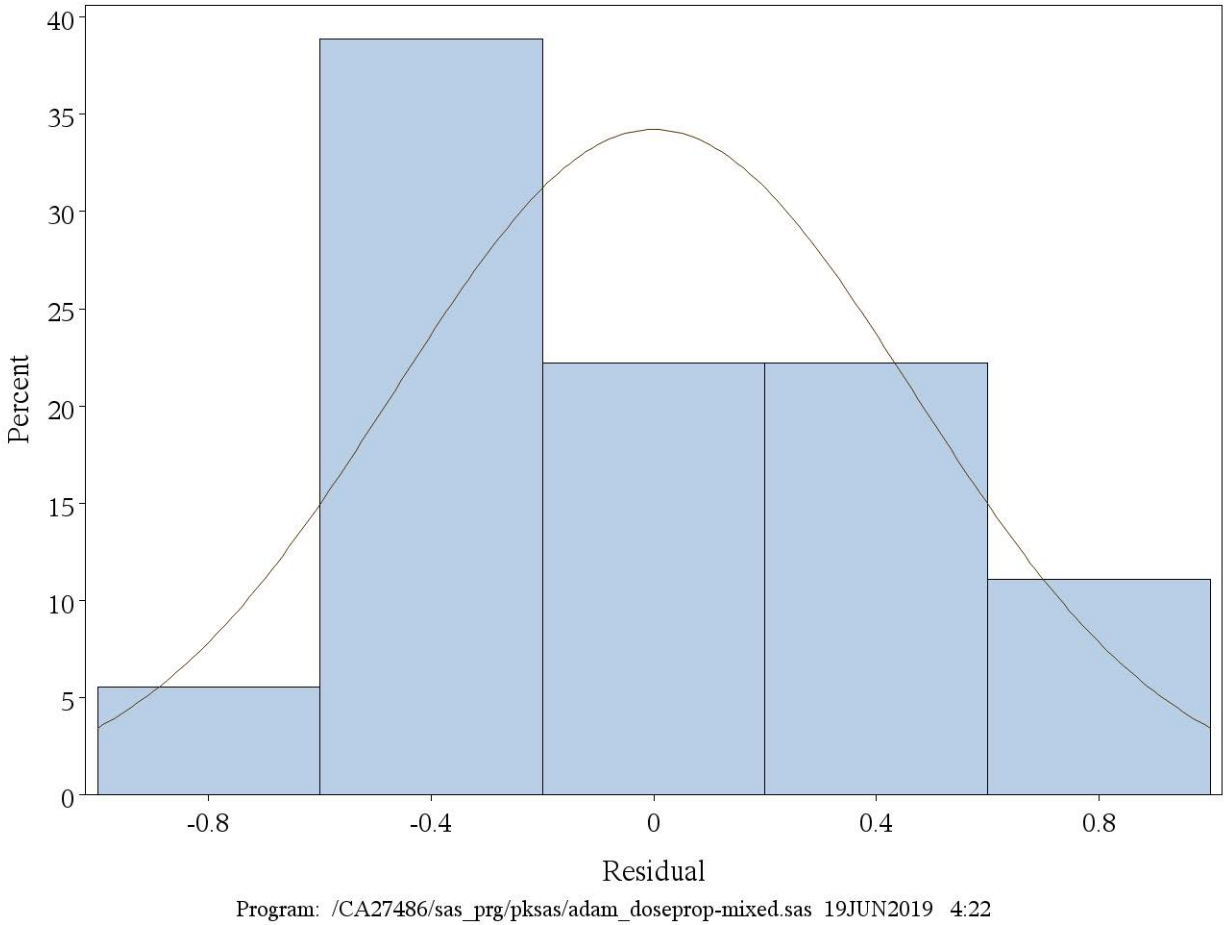
Tests for Normality				
Test	**Statistic**		**p Value**	
Shapiro-Wilk	**W**	0.963429	**Pr < W**	0.6689
Kolmogorov-Smirnov	**D**	0.143674	**Pr > D**	>0.1500
Cramer-von Mises	**W-Sq**	0.054387	**Pr > W-Sq**	>0.2500
Anderson-Darling	**A-Sq**	0.324758	**Pr > A-Sq**	>0.2500

Quantiles (Definition 5)	
Quantile	**Estimate**
100% Max	0.7893745
99%	0.7893745
95%	0.7893745
90%	0.6807874
75% Q3	0.4301697
50% Median	-0.0239911
25% Q1	-0.3631091
10%	-0.5645001
5%	-0.9091996
1%	-0.9091996
0% Min	-0.9091996

Extreme Observations			
Lowest		**Highest**	
Value	**Obs**	**Value**	**Obs**
-0.909200	4	0.430170	3
-0.564500	11	0.453220	17
-0.392096	14	0.517990	8
-0.368800	13	0.680787	2
-0.363109	12	0.789374	15



Normality Assessment for Plasma LOXO-292 - AUC0-inf for Table 14.2.1.8



Normality Assessment for Plasma LOXO-292 - AUC0-inf for Table 14.2.1.8

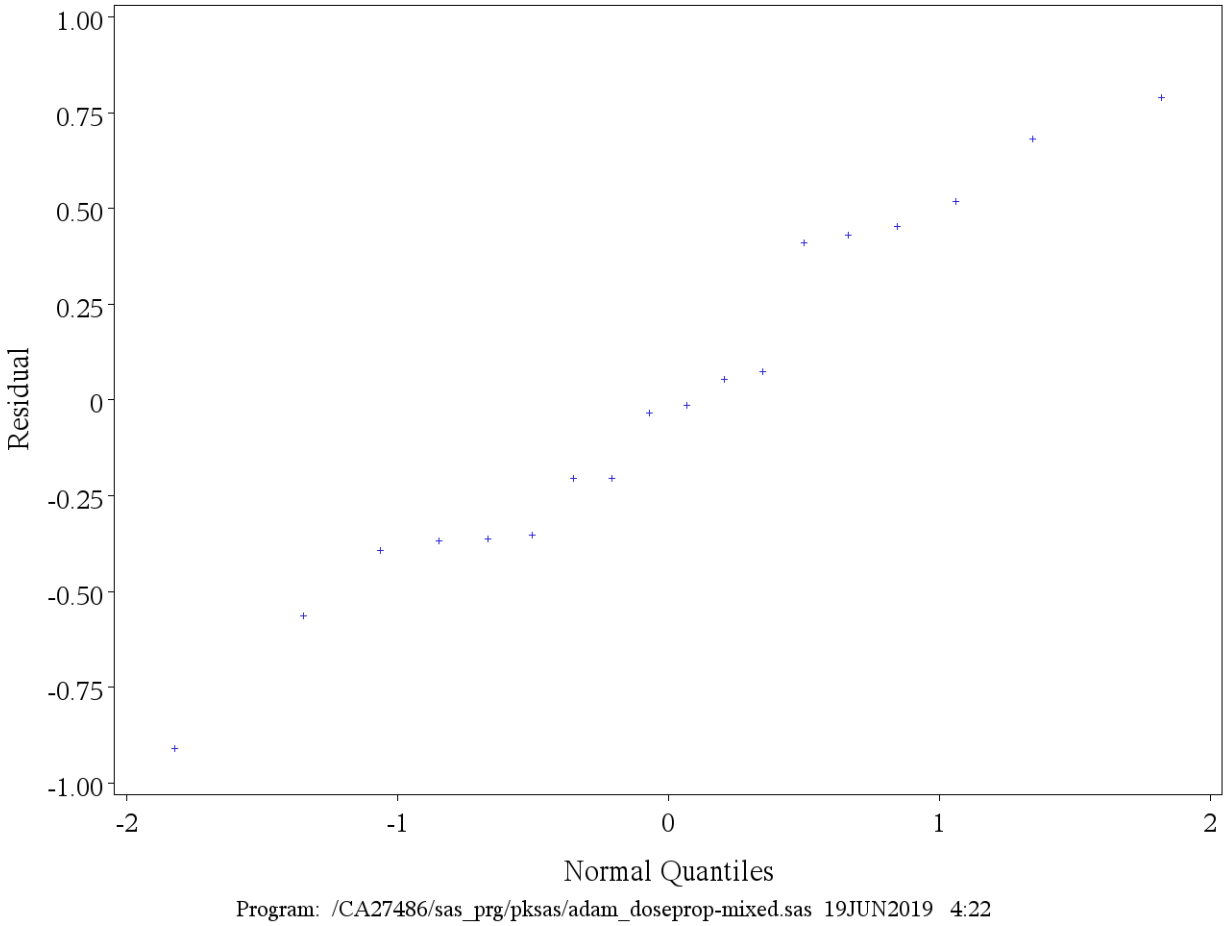
Fitted Normal Distribution for Resid (Residual)

Parameters for Normal Distribution		
Parameter	**Symbol**	**Estimate**
Mean	Mu	0
Std Dev	Sigma	0.466459

Goodness-of-Fit Tests for Normal Distribution				
Test	**Statistic**		**p Value**	
Kolmogorov-Smirnov	**D**	0.14367408	**Pr > D**	>0.150
Cramer-von Mises	**W-Sq**	0.05438651	**Pr > W-Sq**	>0.250
Anderson-Darling	**A-Sq**	0.32475804	**Pr > A-Sq**	>0.250

Quantiles for Normal Distribution		
	Quantile	
Percent	**Observed**	**Estimated**
1.0	-0.90920	-1.08515
5.0	-0.90920	-0.76726
10.0	-0.56450	-0.59779
25.0	-0.36311	-0.31462
50.0	-0.02399	0.00000
75.0	0.43017	0.31462
90.0	0.68079	0.59779
95.0	0.78937	0.76726
99.0	0.78937	1.08515

Normality Assessment for Plasma LOXO-292 - AUC0-inf for Table 14.2.1.8



Normality Assessment for Plasma LOXO-292 - Cmax for Table 14.2.1.8

Variable: Resid
(Residual)

Moments			
N	18	**Sum Weights**	18
Mean	0	**Sum Observations**	0
Std Deviation	0.57456894	**Variance**	0.33012946
Skewness	0.23968228	**Kurtosis**	-0.950472
Uncorrected SS	5.61220085	**Corrected SS**	5.61220085
Coeff Variation	.	**Std Error Mean**	0.1354272

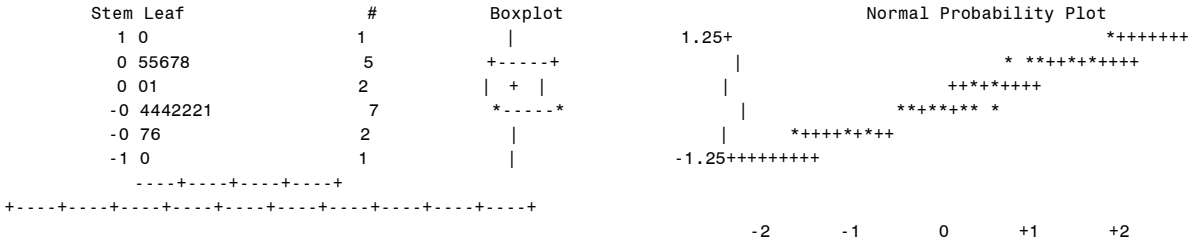
Basic Statistical Measures			
Location		**Variability**	
Mean	0.00000	**Std Deviation**	0.57457
Median	-0.16680	**Variance**	0.33013
Mode	.	**Range**	2.01438
		Interquartile Range	0.93976

Tests for Location: Mu0=0				
Test	**Statistic**		**p Value**	
Student's t	**t**	0	**Pr > |t|**	1.0000
Sign	**M**	-1	**Pr >= |M|**	0.8145
Signed Rank	**S**	-0.5	**Pr >= |S|**	1.0000

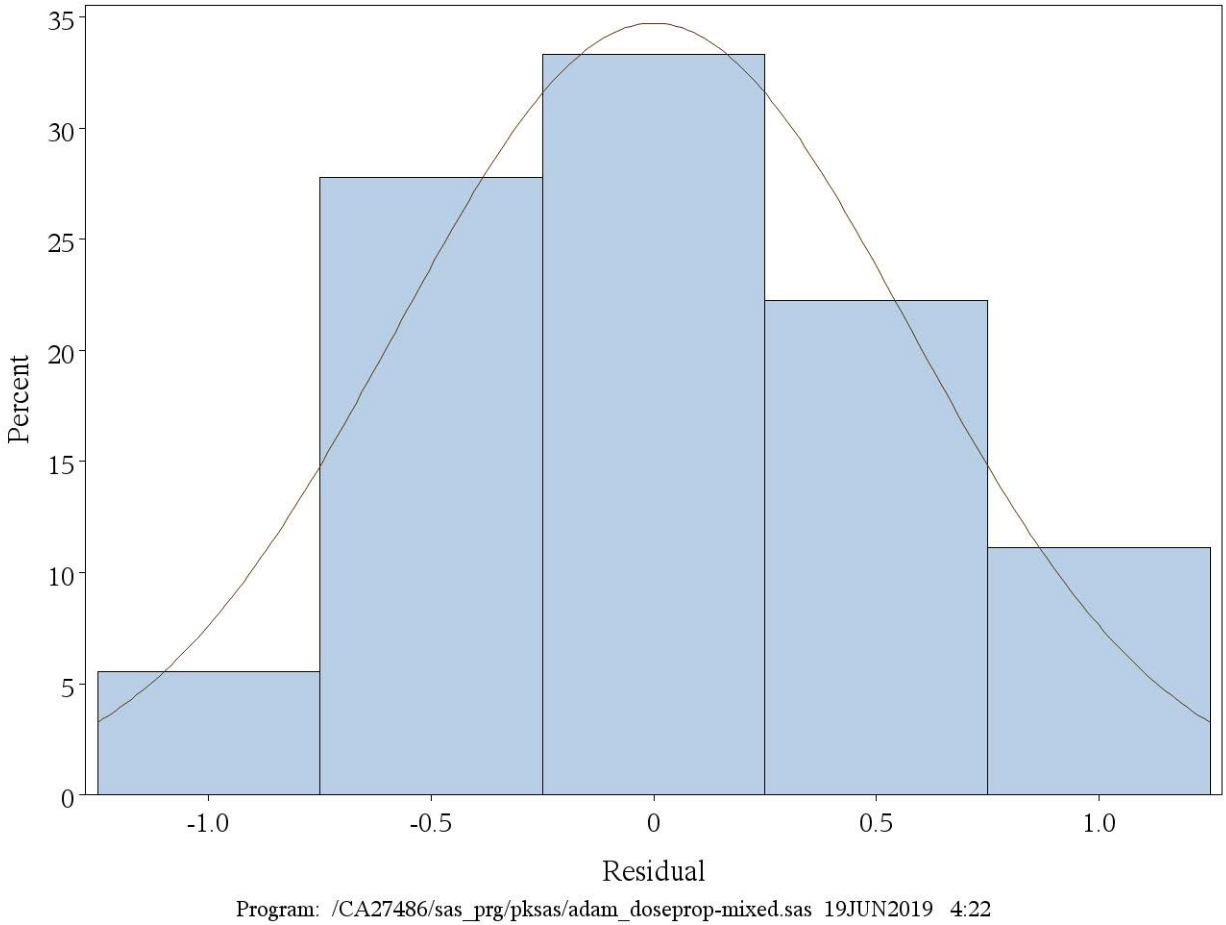
Tests for Normality				
Test	**Statistic**		**p Value**	
Shapiro-Wilk	**W**	0.950454	**Pr < W**	0.4322
Kolmogorov-Smirnov	**D**	0.156434	**Pr > D**	>0.1500
Cramer-von Mises	**W-Sq**	0.078884	**Pr > W-Sq**	0.2084
Anderson-Darling	**A-Sq**	0.433324	**Pr > A-Sq**	>0.2500

Quantiles (Definition 5)	
Quantile	**Estimate**
100% Max	1.026269
99%	1.026269
95%	1.026269
90%	0.751894
75% Q3	0.547859
50% Median	-0.166802
25% Q1	-0.391901
10%	-0.684769
5%	-0.988116
1%	-0.988116
0% Min	-0.988116

Extreme Observations			
Lowest		**Highest**	
Value	**Obs**	**Value**	**Obs**
-0.988116	4	0.547859	10
-0.684769	12	0.615043	8
-0.638559	5	0.747736	2
-0.416163	11	0.751894	3
-0.391901	13	1.026269	15



Normality Assessment for Plasma LOXO-292 - Cmax for Table 14.2.1.8



Normality Assessment for Plasma LOXO-292 - Cmax for Table 14.2.1.8

Fitted Normal Distribution for Resid (Residual)

Parameters for Normal Distribution		
Parameter	**Symbol**	**Estimate**
Mean	Mu	0
Std Dev	Sigma	0.574569

Goodness-of-Fit Tests for Normal Distribution				
Test	**Statistic**		**p Value**	
Kolmogorov-Smirnov	**D**	0.15643424	**Pr > D**	>0.150
Cramer-von Mises	**W-Sq**	0.07888421	**Pr > W-Sq**	0.208
Anderson-Darling	**A-Sq**	0.43332377	**Pr > A-Sq**	>0.250

Quantiles for Normal Distribution		
	Quantile	
Percent	**Observed**	**Estimated**
1.0	-0.98812	-1.33665
5.0	-0.98812	-0.94508
10.0	-0.68477	-0.73634
25.0	-0.39190	-0.38754
50.0	-0.16680	0.00000
75.0	0.54786	0.38754
90.0	0.75189	0.73634
95.0	1.02627	0.94508
99.0	1.02627	1.33665

Normality Assessment for Plasma LOXO-292 - Cmax for Table 14.2.1.8