

Statistical Analysis Plan (V4) H8H-CD-LAHN (COL MIG-113)

A Phase I, Multicenter, Open-Label, Parallel-Group Adaptive Pharmacokinetic
Single Dose Study of Oral Lasmiditan in Subjects With Normal and Impaired Renal
Function

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16.1.9 Documentation of Statistical Methods

16.1.9.1 Statistical analysis plan (SAP)

16.1.9.2 Documentation of statistical analysis – SAS[®] output of Lasmiditan

16.1.9.3 Documentation of statistical analysis – SAS[®] output of (S)-M8

16.1.9.4 Documentation of statistical analysis – SAS[®] output of (S,R)-M18

16.1.9.5 Documentation of statistical analysis – SAS[®] output of (S,S)-M18

16.1.9.6 Documentation of statistical analysis – SAS[®] output of M7

16.1.9.7 Documentation of statistical analysis – SAS[®] output of M3

16.1.9.1 Statistical analysis plan (SAP)

[SAP Final v4.0](#)

[Supplementary information record of SAP Final v4.0](#)

[SAP Final v3.2](#)

STATISTICAL ANALYSIS PLAN

For:

CoLucid Pharmaceuticals, Inc.

SPONSOR PROTOCOL No. COL MIG-113

*A Phase I, Multicenter, Open-Label, Parallel-Group Adaptive
Pharmacokinetic Single Dose Study of Oral Lasmiditan in Subjects
with Normal and Impaired Renal Function*

Algorithme Project No. CUD-P4-001

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STATISTICAL ANALYSIS PLAN APPROVAL

We have carefully read this Statistical Analysis Plan and agree it contains the necessary information required to handle the statistical analysis of study data.

PPD

2018/02/16
Date

PPD

2018/02/16
Date

On behalf of the Sponsor

PPD

PPD

2018/02/22

PPD

2018/02/22
Date

VERSION CONTROL

Version Number	Version Date	Author	Description of Significant Changes from Previous Approved Version
DRAFT 0.1	2017/04/28	Sarah Vahey / Josée Michaud	Not Applicable – First Version
DRAFT 0.2	2017/05/15	Sarah Vahey / Josée Michaud	Updated according to client comments
DRAFT 0.3	2017/05/25	Sarah Vahey / Josée Michaud	Updated according to client comments
FINAL 1.0	2017/06/07	Sarah Vahey	Updated version to Final
FINAL 2.0	2017/09/05	Nolwenn Rondet/Jade Huguet	Updated according FDA recommendations from final 1.0 to Final 2.0
FINAL 3.0	2017/09/22	Nolwenn Rondet/Josée Michaud	Updated according FDA recommendations from final 1.0 to Final 2.0
FINAL 3.1	2017/09/22	Nolwenn Rondet	Updated according FDA recommendations from final 1.0 to Final 2.0 and client comments
FINAL 3.2	2017/10/25	Nolwenn Rondet / Josée Michaud	Updated according client comments
FINAL 3.3	2017/10/28	Katia Charland / Josée Michaud	Final Version
FINAL 4.0	2018/02/15	Patrick Guorong Chen	Amendment to include Tmax in statistical analysis and L16.2.2.2 Protocol Deviation

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ABBREVIATIONS

AE	Adverse Event
ANOVA	Analysis of Variance
ATC	Anatomical/Therapeutic/Chemical
AUC	Area Under Curve
BMI	Body Mass Index
CI	Confidence Interval
CLCR	Creatinine Clearance
CNS	Central Nervous System
CRF	Case Report Form
CS	Clinically Significant
C-SSRS	Columbia-Suicide Severity Rating Scale
CSR	Clinical Study Report
eGFR	Estimated Glomerular Filtration Rate
EOS	End of Study
ICF	Informed Consent Form
MedDRA	Medical Dictionary for Regulatory Activities
NCS	Not Clinically Significant
PK	Pharmacokinetic(s)
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SE	Standard Error
SOC	System Organ Class
TEAE	Treatment-Emergent Adverse Event
TFLs	Tables, Figures, and Listings
WHO-DDE	WHO Drug Dictionary Enhanced

1. INTRODUCTION

This statistical analysis plan (SAP) provides a detailed description of the statistical methods and procedures to be implemented for the analyses of data from Protocol No. COL MIG-113. The analyses described in the SAP are based upon the final protocol (Amendment 1) dated 2017/01/06.

2. STUDY OBJECTIVES

Primary Objectives

The primary objective of this study is to evaluate the pharmacokinetic profile of lasmiditan following a single oral 200 mg dose in subjects with impaired renal function relative to matched, healthy controls with normal renal function.

Secondary Objective

The secondary objective of this study is to assess the safety and tolerability of a single oral 200 mg dose of lasmiditan in subjects with normal and impaired renal function.

3. STUDY DESIGN

General Description

This is a multi-center, open-label, non-randomized, parallel-group, adaptive, single dose study.

This study will enroll up to 32 subjects using an adaptive design that can include up to 3 groups of 8 subjects with different degrees of renal impairment and one group of 8 control subjects with normal renal function.

First, approximately 16 subjects will be enrolled with severe renal impairment and matched subjects with normal renal function. There will be 8 subjects in each of the following groups based on renal function at screening:

- Group 1: Healthy subjects with normal renal function ($\text{eGFR} \geq 90 \text{ mL/min/1.73m}^2$)
- Group 2: Severe renal impairment subjects ($\text{eGFR} < 30 \text{ mL/min/1.73m}^2$)

Based on safety and PK results from subjects with severe renal impairment (Group 2), Group 3 (Moderate Renal Impairment) and Group 4 (Mild Renal Impairment) will be enrolled if substantial change in the exposure of lasmiditan is observed in subjects with severe renal impairment. There will be 8 subjects in each of the following groups based on renal function at screening:

- Group 3: Moderate renal impairment subjects ($\text{eGFR } 30\text{-}59 \text{ mL/min/1.73m}^2$)
- Group 4: Mild renal impairment subjects ($\text{eGFR } 60\text{-}89 \text{ mL/min/1.73m}^2$)

All subjects will participate in one treatment period and will receive a single dose of lasmiditan in the fasting state.

The total duration of each subject's participation in the study will be 3 days (Day -1 through the last PK sample taken on Day 2), not including the screening and follow-up phone call. The total duration of the study is expected to be 35 days, including the screening.

The following treatment regimen will be used:

- Experimental treatment: Lasmiditan 200 mg

Study procedures

For complete details on the study assessments to be performed for the study, refer to [Appendix A](#).

Randomization and Unblinding Procedure

No randomization will be performed for this study. Instead subjects will be categorized into either the control group of healthy volunteers with normal renal function, or into one of the three groups of subjects with varying degrees of renal impairment.

Subjects who withdraw from the study may be replaced. Replacement subjects will not be enrolled for subjects who discontinue the study due to treatment-related toxicity.

No unblinding procedure is required, as this is an open-label study.

4. STUDY ENDPOINTS

Pharmacokinetic Endpoints

The following plasma and urine PK parameters of lasmiditan will be calculated: C_{max} , T_{max} , $AUC_{(0-t_{last})}$, $AUC_{(0-\infty)}$, $\%AUC(t_{last}-\infty)$, λ_z , $T_{1/2}$, CL/F , V_z/F , $Ae(0-t)$, fe , CL_r .

For all the metabolites [(S)-M8, (S,R)-M18, M7 and (S,S)-M18], the following PK parameters C_{max} , T_{max} , $AUC_{(0-t_{last})}$, $AUC_{(0-\infty)}$, $\%AUC(t_{last}-\infty)$, λ_z , T_{half} , $Ae(0-t)$, $CL_{r,met}$ and individual metabolic ratio (metabolite AUC/parent AUC) will be calculated, if quantifiable.

Safety Endpoints

Safety endpoints include:

- Adverse Events
- Clinical Laboratory Tests (hematology, chemistry, urinalysis)
- Vital Signs
- Physical examination
- Concomitant medication
- ECGs
- C-SSRS

The details of the safety endpoints' assessment are presented in [Section 10](#).

Sample Size Determination

There is no formal statistical sample size calculation for this study. A sample size of 32; including 8 subjects/patients for each renal function group (8 subjects with normal renal function, 8 patients with mildly impaired renal function, 8 patients with moderately impaired renal function, and 8 with severely impaired renal function) was chosen because it is considered typical for studies evaluating the effect of renal function on the pharmacokinetics of a drug.

5. ANALYSIS POPULATIONS

Safety Population:

All subjects who received a dose of study medication will be included in the safety population. This population will be used for all demography and safety analyses.

Pharmacokinetics (PK) Population:

All subjects who received lasmiditan, had no major protocol deviations, and completed the period with evaluable (sufficient and interpretable) data will be included in the PK population.

If some subjects do not complete the sampling schedule resulting in an inadequately characterized some PK parameters (e.g. AUC, V_z/F , λ_z), samples of these subjects could be included in the statistical pharmacokinetic analysis for only the evaluable parameters.

6. STATISTICAL METHODOLOGY

All analyses will be conducted using the SAS software, version 9.4, or higher. Descriptive statistics of the PK data will be performed by Phoenix® WinNonlin® version 6.3 or higher, Phoenix® Connect™ version 1.3.1 or higher).

Adverse events and medical history will be classified using the standard MedDRA terminology version 19.1.

Prior and concomitant medications will be coded with the WHO-DDE dictionary version March 01, 2016.

In general, all summary tables will be presented for safety population. Summaries will be presented by renal function group.

In general, the data listings will include all enrolled subjects up to the point of study completion or discontinuation; exceptions will be listings pertaining to a subset of subjects only (e.g., subjects with blood sampling time deviations) or a subset of records/events (e.g., abnormal laboratory values).

Categorical variables will be summarized using the PROC FREQ procedure. Continuous variables will be summarized using the PROC UNIVARIATE procedure. For log-transformed endpoints, geometric mean, and coefficient of variation will also be presented.

The following general comments also apply to all statistical analyses and data presentations:

- Duration variables in days will be calculated using the general formula: (end date - start date) +1.
- Individual subject listings of all data represented on the CRFs will be provided to facilitate the investigation of tabulated values and to allow for the clinical review of all efficacy and safety parameters.
- When assessments are repeated for a given timepoint, only the result which is closest to the dosing time will be included in the summary tables.

The analyses described in this plan are considered a priori, that they have been defined prior to database lock. Any analyses performed subsequent to database lock will be considered post hoc and exploratory. Post hoc analyses will be labeled as such in the corresponding statistical output and identified in the CSR.

Analysis Time Points

Unless otherwise specified, the baseline value will be defined as the last non-missing evaluation prior to the first dose of study medication.

Methods for Handling Missing Data

No imputations of values for missing data will be performed. All data recorded on the case report form will be included in the listings that will accompany the clinical study report.

7. STUDY SUBJECTS

Disposition

The subject disposition will be summarized for all subjects enrolled in this study, including:

- The number of subjects enrolled;
- The number of screen failure subjects;
- The number of subjects screened;
- The number and percentage of subjects who completed the study;
- The number and percentage of subjects discontinued from the study by primary reason for discontinuation and overall;
- The number and percentage of subjects included in each of the safety and PK populations.

The percentages will be calculated using the number of subjects randomized as denominator.

A listing of subject's disposition will be provided. A listing of subjects included in each of the analysis populations will also be provided. Screen failure subjects will also be presented in a listing.

Protocol Deviations

All protocol deviations will be presented in a listing. A separate listing will be generate for Inclusion/exclusion criteria violations. All deviations from the scheduled PK sampling time of 2 minutes or more for post dose samples will be taken into consideration for the evaluation of PK parameters.

8. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographic and Background Characteristics

Demographic data and baseline characteristics will be presented in a data listing and summarized by renal function group in a table. Quantitative assessments to be summarized are age, height, body weight and body mass index (BMI) at screening. Subject demographics include sex, age, ethnicity, race and country. Baseline characteristics include height, weight, and BMI.

Lifestyle

Alcohol and smoking intake history will be recorded and presented in separate listings.

Medical/Social history

Any medical history findings will be recorded and presented in a listing. The listing will include the coding terms (e.g., SOC and Preferred Term).

Prior Medication

Any medications taken including prescription, nonprescription, OTC (cold and antacid medications), dietary supplements, vitamins or herbal medications from screening to the first dose of the study drug will be recorded and presented as prior medications in a listing. The listing will include the coding terms (e.g., ATC and Preferred Term).

9. PHARMACOKINETICS AND STATISTICS

Pharmacokinetic Analysis

The PK parameters are presented in [Section 4](#) and [Appendix B](#). All reported sampling time deviations (see [Section 7](#)) will be taken into consideration for evaluation of plasma PK parameters.

Only quantifiable concentrations will be used to calculate PK parameters. An exception to this rule is made for concentrations below the quantification limit (BQL), which will be set to zero when all of the following conditions are met:

- The time points occur before the first quantifiable concentration.

All other BQL concentrations will be treated as missing sample.

The pharmacokinetic parameters will be estimated using a non-compartmental approach with a log-linear terminal phase assumption. The trapezoidal rule will be used to estimate the area under the curve, and the terminal phase will be estimated by maximizing the coefficient of determination estimated from the log-linear regression model. These parameters ($AUC_{(0-\infty)}$, $\%AUC(t_{last-\infty})$, λ_z , $T_{1/2}$, CL/F and V_z/F) will be estimated for individual concentration-time profiles only when the terminal log-linear phase cannot be reliably characterized using the following criteria:

- Phoenix® WinNonlin® Best fit range selection (if adequate):
- R^2 of at least 80%

In the case where less than 3 consecutive measurable plasma concentrations of lasmiditan or its metabolites [(S)-M8, (S,R)-M18, M7 and (S,S)-M18] is observed, the AUC parameters will not be estimated for that particular analyte.

Additional pharmacokinetic parameters may be calculated if deemed appropriate.

Pharmacokinetic analyses and associated descriptive statistics will be generated using Phoenix® WinNonlin® Version 6.3 (or higher).

Statistical Analysis

The natural logarithmic transformation of C_{max} , $AUC_{(0-t_{last})}$, $AUC_{(0-\infty)}$, $Ae(0-t)$, as well as the rank-transformation of T_{max} will be used for all statistical inference for the parent (lasmiditan) and all metabolites [(S)-M8, (S,R)-M18, M7 and (S,S)-M18].

Statistical analyses will be generated using validated SAS® (version 9.4 or higher) using the Reg (and Mixed, if applicable) procedure(s).

The statistical analysis described in this section will be done using both eGFR and Cockcroft-Gault estimate of the creatinine clearance. However, analysis using the eGFR will be considered as the primary analysis and the analysis using the Cockcroft-Gault estimate of the creatinine clearance will be considered as supportive.

Regression Analysis

The eGFR and Cockcroft-Gault estimate of creatinine clearance at baseline will be used as separate measures of renal function for a regression analysis to evaluate the relationships between estimated renal function and the PK parameters.

For each log-transformed PK parameter and the rank-transformation of T_{max} , a regression analysis will be performed, using a model of the form $\alpha + \beta \cdot eGFR + \epsilon$ where the errors (ϵ) will be assumed to be independent and normally distributed with mean zero and variance σ^2 . The parameter β represents the correlation between the relevant PK parameter and eGFR which will be treated as a continuous variable.

The hypothesis of the slope of trend being different from zero will be assumed if the two-sided test of the nullity of the parameter β is statistically significant at the 5% level.

The regression analysis will be repeated for each log-transformed PK parameter and the rank-transformation of T_{\max} with the Cockcroft-Gault estimate of creatinine clearance at baseline.

Analysis of Variance

An analysis of variance (ANOVA) will be performed to assess the difference in the PK parameter among the renal function groups.

The renal function (normal, mild, moderate and severe) will be entered as a fixed effect in the ANOVA model. Pairwise comparisons of renal function groups will be generated using the Tukey-Kramer's procedure of adjustment for multiple comparisons (if more than 2 renal function groups) and statistical significance will be assessed at the two-sided 5% level. The ratio of geometric LS means (of each renal function group being compared), with a corresponding 90% confidence interval (adjusted using Tukey-Kramer's procedure if applicable), will be computed. Heterogeneity of variance among groups will be assumed.

10. SAFETY

Adverse Events

An AE is defined as any untoward medical occurrence in a subject administered a medicinal product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (for example, an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product.

A suspected adverse reaction is any AE for which there is a reasonable possibility that the drug caused the AE. 'Reasonable possibility' means there is evidence to suggest a causal relationship between the drug and the AE. A suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any AE caused by a drug.

AEs occurring after the initiation of the treatment are referred to as treatment emergent adverse events (TEAEs).

As an overall summary of AEs, the following will be presented by renal function group and overall:

- Number of reported AEs;
- Number of reported TEAEs;
- Number and percentage of subjects experiencing TEAEs;
- Number and percentage of subjects experiencing a drug-related TEAE (i.e. those with a relationship classified as reasonable possibility)
- Number and percentage of TEAEs by relationship to study treatment (i.e. reasonable possibility, no reasonable possibility);
- Number and percentage of TEAEs by severity;
- Number of reported SAEs (serious adverse events);
- Number and percentage of subjects experiencing SAEs;
- Number and percentage of subjects experiencing drug-related SAEs;
- Number and percentage of TEAEs leading to withdrawal; and
- SAEs with an outcome of death.

Frequency tables will be presented by renal function group, system organ class and preferred term that summarize all Treatment Emergent Adverse Events (TEAEs) and all drug-related TEAEs.

Subject listings of all Adverse Events (AEs) including severity and relationship to study drug will be provided. AEs leading to withdrawal and SAEs will also be presented in separate listings.

Concomitant Medications

Medications taken after the first dose of study drug until after discharge from the study will be recorded. Concomitant medications will be presented in a listing. The medication name, active ingredient, dose, units, formulation, route, indication or reason taken, code, date and time taken will be presented. The listing will also include the coding terms (e.g., ATC and Preferred Term).

Extent of Exposure

Details of drug dosing (actual treatment received, actual date and time of administration, dose administered, and route of administration) will be listed by subject.

Clinical Laboratory Evaluations

Planned laboratory analyses include:

- General Biochemistry: Sodium, potassium, chloride, glucose, blood urea nitrogen (BUN), creatinine, eGFR, total bilirubin, alkaline phosphatase, AST, ALT and albumin;
- Hematology: White cell count with differential (absolute values of neutrophil, lymphocyte, monocyte, eosinophil, and basophil), red cell count, hemoglobin, hemoglobin A1c, hematocrit, mean corpuscular volume (MCV), and platelets count;
- Urinalysis: Color, appearance, specific gravity, pH, leukocyte, protein, glucose, ketones, bilirubin, blood, nitrite, urobilinogen. Microscopic examination will only be performed if the dipstick test is outside of the reference range for leukocyte, blood, nitrite or protein
- Other: serology urine drug screen and serum pregnancy.

Hematology, chemistry and quantitative urinalysis laboratory test results will be summarized by renal function group, parameter and visit and will also be presented in a listing

Separate listings of for serology, urine drug screen and serum pregnancy will also be provided.

Subject listings of abnormal on-study laboratory values will be provided. Similarly, clinically significant on-study laboratory data will be presented in a second listing.

Vital Signs

Vital signs will include the measurement of blood pressure, heart rate, oral temperature, and orthostatic blood pressure.

For all vital signs, raw values, at each time point will be summarized by renal function group, parameter and visit. Vital signs data will also be presented in a listing.

Subject listing of abnormal on-study vital signs values (Out-of-Range – Not Clinically Significant (NCS) or Clinically Significant (CS)) will be provided. Similarly, CS on-study vital signs values (Out-of-Range – CS) will be presented in a second listing.

Electrocardiogram

A 12-lead ECG will be obtained throughout the study. In some cases, repeat abnormal ECGs may be obtained.

Raw values at each time point will be summarized by renal function group, parameter and visit and will also be presented in a listing. Overall safety assessment will also be presented in the listing.

A subject listing of abnormal on-study ECG assessments (Abnormal – NCS or Abnormal – CS) will be provided. Similarly, CS on-study ECG assessments (Abnormal – CS) will be presented in a second listing.

Physical Examination Findings

A physical examination will be conducted and will be presented in a listing.

Columbia-Suicide Severity Rating Scale (C-SSRS)

The Columbia-Suicide Severity Rating Scale (C-SSRS) is a suicidal ideation rating scale. The scale identifies behaviors and thoughts that are associated with an increased risk of suicidal actions in the future.

Subjects who answer 'Yes' to any of the questions on the C-SSRS questionnaire will be presented in a listing.

11. INTERIM ANALYSES AND DATA SAFETY MONITORING

First, subjects with severe renal impairment and healthy subjects with normal renal function will be enrolled. Samples will be assayed and PK will be performed. If substantial changes in the exposure of lasmiditan are observed in subjects with severe renal impairment compared to subjects with normal renal function, subjects with mild and moderate renal impairment will be enrolled.

Interim analysis of subjects with severe renal impairment and healthy subjects with normal renal function will be performed as described in the regression analysis paragraph of [Section 9](#).

12. CHANGES TO PROTOCOL-SPECIFIED ANALYSES

There is no change from the planned analysis described in the protocol. The analyses described in the protocol was meant to be an overview. The final analyses is per this statistical analysis plan.

13. GENERAL INFORMATION RELATED TO DATA PRESENTATIONS

Safety

All programs used to generate statistical analyses will be validated according to Algorithme Pharma's standard operating procedures.

TFLs will be displayed on letter size paper, 8 ½ inches by 11 inches, using the Courier New font.

In general, summary statistics for raw variables (i.e., variables measured at the study site or central laboratory) will be displayed as follows: if required minima, maxima, means, quartiles, standard deviations and confidence limits will be displayed to the same number of decimal places as the raw data; if required medians will be displayed to one additional decimal place.

Percentages will be displayed to one decimal place. Percentages between 0 and 0.1 (exclusive) will be displayed as '<0.1'. P-values will be displayed to 3 decimal places. P-values that are less than 0.001 will be displayed as '<0.001'.

The numbers of decimal places for summary statistics of derived variables (i.e., variables that are not measured by the study site but are calculated for analysis based on other measured variables) will be determined on a case by case basis. In general, minima and maxima will be displayed to the commonly used unit of precision for the parameter. Means, medians, quartiles, and confidence limits will be displayed to one additional decimal place and standard deviations will be displayed to two additional decimal places.

The formats and layouts of TFLs are provided in subsequent sections. Actual formats and layouts may be altered slightly from those presented in the templates as necessary to accommodate actual data or statistics. Minor format changes will not require updates to the SAP.

The tables and listings listed below are common data displays. Their numbering and general content follow the ICH E3 guidelines. Some of the tables and listings may not be applicable/appropriate/necessary for a particular study. Additional tables and listings may be included, provided the numbering scheme remains consistent with ICH E3.

PK Data

All programs used to generate statistical analyses will be validated according to Algorithme Pharma's standard operating procedures.

TFLs will be displayed on letter size paper, 8 ½ inches by 11 inches, using Tahoma.

Raw variables (i.e., variables measured at the study site or central laboratory) will be displayed with the same number of decimal places as received as per bioanalytical laboratory. Derived variables (i.e., variables that are not measured by the study site but are calculated for analysis based on other measured variables) will be displayed as follow:

- All calculated pharmacokinetic parameter values should be reported to three significant digits.
- Observed concentration data, e.g. C_{max} , should be reported as received.
- Observed time data, e.g. T_{max} , should be reported as received.
- N and percentage values should be reported as whole numbers, except for the %AUC(tlast-∞).
- Median values should be treated as an observed parameter and reported to the same number of decimal places as minimum and maximum values.

Summary statistics of raw variables: minima, mean, geometric mean, median, maxima, and standard deviation, coefficient of variation will be displayed with the same number of decimal places as the raw data;

- The following summary statistics will be listed for all variables except T_{\max} and $T_{1/2}$, arithmetic mean, SD, and CV; geometric mean and CV; N, minimum, maximum, and median.
- Summary statistics for T_{\max} , and other discrete parameters, will be limited to N, minimum, maximum, and median. Report not calculated (NC) for other statistics
- Summary statistics for $T_{1/2}$ will be limited to geometric mean and CV; N, minimum, maximum, and median. Report not calculated (NC) for other statistics.

Summary statistics of derived variables will be displayed with the same number of decimal places as the derived variable.

PLANNED END-OF-TEXT TABLES

Demographic Data

Table 14.1.1	Subject Disposition – All Subjects
Table 14.1.2.1	Summary of Demographic Characteristics (Safety Population)
Table 14.1.2.2	Summary of Demographic Characteristics (Pharmacokinetic Population)

Pharmacokinetic Data

Section 14.2.1.1	Statistical Analysis – SAS output - Lasmiditan
Section 14.2.1.2	Statistical Analysis – SAS output - (S)-M8
Section 14.2.1.3	Statistical Analysis – SAS output - (S,R)-M18
Section 14.2.1.4	Statistical Analysis – SAS output – M7
Section 14.2.1.5	Statistical Analysis – SAS output - (S,S)-M18

Safety Data

Tables in this section are based on the safety population unless otherwise stated.

Table 14.3.1.1	Summary of Adverse Events
Table 14.3.1.2	Summary of Treatment Emergent Adverse Events by System Organ Class and MedDRA Preferred Term
Table 14.3.1.3	Summary of Drug-Related Treatment Emergent Adverse Events by System Organ Class and MedDRA Preferred Term
Table 14.3.2.1	Listing of Deaths, Other Serious and Significant Adverse Events
Table 14.3.2.2	Listing of Treatment Emergent Adverse Events Leading to Withdrawal
Table 14.3.4.1	Listing of Abnormal On-Study Laboratory Values
Table 14.3.4.2	Listing of Clinically Significant On-Study Laboratory Values
Table 14.3.4.3	Summary of Blood Chemistry
Table 14.3.4.4	Summary of Hematology
Table 14.3.4.5	Summary of Quantitative Urinalysis
Table 14.3.5.1	Listing of Abnormal On-Study Vital Signs Values
Table 14.3.5.2	Listing of Clinically Significant On-Study Vital Signs Values
Table 14.3.5.3	Summary of Vital Signs
Table 14.3.6.1	Listing of Abnormal On-Study ECG Assessments
Table 14.3.6.2	Listing of Clinically Significant On-Study ECG Assessments
Table 14.3.6.3	Summary of ECG Assessments

PLANNED IN-TEXT TABLES

PK Parameters of Lasmiditan
Summary of Statistical Analysis of Lasmiditan
PK Parameters of (S)-M8
Summary of Statistical Analysis of (S)-M8
PK Parameters of (S,R)-M18
Summary of Statistical Analysis of (S,R)-M18
PK Parameters of M7
Summary of Statistical Analysis of M7
PK Parameters of (S,S)-M18
Summary of Statistical Analysis of (S,S)-M18

PLANNED IN-TEXT FIGURES

Linear Profile of the Mean for Lasmiditan
Logarithmic Profile of the Mean for Lasmiditan
Linear Regression of In-Transformed C_{\max} vs eGFR (Lasmiditan)
Linear Regression of In-Transformed $AUC_{(0-\text{last})}$ vs eGFR (Lasmiditan)
Linear Regression of In-Transformed $AUC_{(0-\infty)}$ vs eGFR (Lasmiditan)
Linear Regression of In-Transformed CL/F vs eGFR (Lasmiditan)
Linear Profile of the Mean for (S)-M8
Logarithmic Profile of the Mean for (S)-M8
Linear Profile of the Mean for (S,R)-M18
Logarithmic Profile of the Mean for (S,R)-M18
Linear Profile of the Mean for M7
Logarithmic Profile of the Mean for M7
Linear Profile of the Mean for (S,S)-M18
Logarithmic Profile of the Mean for (S,S)-M18

PLANNED LISTINGS

Listing 16.2.1	Listing of Study Disposition
Listing 16.2.2.1	Listing of PK Blood Sampling Time Deviations
Listing 16.2.2.2	Listing of Protocol Deviations
Listing 16.2.3	Listing of Analysis Populations
Listing 16.2.4.1	Listing of Demographic Characteristics
Listing 16.2.4.2	Listing of Screen Failure Subjects
Listing 16.2.5	Listing of Investigational Product Administration
Listing 16.2.7	Listing of Adverse Events
Listing 16.2.8.1	Listing of Blood Chemistry
Listing 16.2.8.2	Listing of Hematology
Listing 16.2.8.3	Listing of Urinalysis
Listing 16.2.8.4	Listing of Urine Drug Screen
Listing 16.2.8.5	Listing of Pregnancy Test
Listing 16.2.8.6	Listing of Serology
Listing 16.2.9.1	Listing of Alcohol Habits
Listing 16.2.9.2	Listing of Smoking Habits
Listing 16.2.9.3	Listing of Prior Medication
Listing 16.2.9.4	Listing of Concomitant Medication
Listing 16.2.9.5	Listing of Physical Examination
Listing 16.2.9.6	Listing of Vital Signs
Listing 16.2.9.7	Listing of ECG Assessments
Listing 16.2.9.8	Listing of Inclusion/Exclusion Criteria Summary
Listing 16.2.9.9	Listing of Medical History
Listing 16.2.9.10	Listing of Columbia-Suicide Severity Rating Scale (C-SSRS)

Pharmacokinetic Data

Appendix 16.2.6	PK Data
Appendix 16.2.6.1	Lasmiditan
Appendix 16.2.6.1.1	PK Tables – Plasma <ul style="list-style-type: none"> - Table X. Measured Human Plasma Concentrations - Table X. Cumulative Area Under the Curve - Table X. Pharmacokinetic Parameters - Table X. Elimination Parameters - Table X. Actual Sampling Time
Appendix 16.2.6.1.2	PK Tables – Urine <ul style="list-style-type: none"> - Table X. Measured Human Urine Concentrations - Table X. Cumulative Amount by Collection Intervals - Table X. Pharmacokinetic Parameters
Appendix 16.2.6.1.3	PK – Figures – Plasma <ul style="list-style-type: none"> - Figure x: Linear Profile of the Mean - Figure x: Logarithmic Profile of the Mean - Figure x: Individual Linear Profile of Subject x - Figure x: Individual Logarithmic Profile of Subject x - Figure x: Individual Elimination Profiles
Appendix 16.2.6.2	(S)-M8
Appendix 16.2.6.2.1	PK Tables – Plasma <ul style="list-style-type: none"> - Table X. Measured Human Plasma Concentrations

	<ul style="list-style-type: none"> - Table X. Cumulative Area Under the Curve - Table X. Pharmacokinetic Parameters - Table X. Elimination Parameters - Table X. Actual Sampling Time
Appendix 16.2.6.2.2	PK Tables – Urine Table X. Measured Human Urine Concentrations
	<ul style="list-style-type: none"> - Table X. Cumulative Amount by Collection Intervals - Table X. Pharmacokinetic Parameters
Appendix 16.2.6.2.3	PK – Figures – Plasma
	<ul style="list-style-type: none"> - Figure x: Linear Profile of the Mean - Figure x: Logarithmic Profile of the Mean - Figure x: Individual Linear Profile of Subject x - Figure x: Individual Logarithmic Profile of Subject x - Figure x: Individual Elimination Profiles
Appendix 16.2.6.3	(S,R)-M18
Appendix 16.2.6.3.1	PK Tables – Plasma
	<ul style="list-style-type: none"> - Table X. Measured Human Plasma Concentrations - Table X. Cumulative Area Under the Curve - Table X. Pharmacokinetic Parameters - Table X. Elimination Parameters - Table X. Actual Sampling Time
Appendix 16.2.6.3.2	PK Tables – Urine Table X. Measured Human Urine Concentrations
	<ul style="list-style-type: none"> - Table X. Cumulative Amount by Collection Intervals - Table X. Pharmacokinetic Parameters
Appendix 16.2.6.3.3	PK – Figures – Plasma
	<ul style="list-style-type: none"> - Figure x: Linear Profile of the Mean - Figure x: Logarithmic Profile of the Mean - Figure x: Individual Linear Profile of Subject x - Figure x: Individual Logarithmic Profile of Subject x - Figure x: Individual Elimination Profiles
Appendix 16.2.6.4	(S,S)-M18
Appendix 16.2.6.4.1	PK Tables – Plasma
	<ul style="list-style-type: none"> - Table X. Measured Human Plasma Concentrations - Table X. Cumulative Area Under the Curve - Table X. Pharmacokinetic Parameters - Table X. Elimination Parameters - Table X. Actual Sampling Time
Appendix 16.2.6.4.2	PK Tables – Urine Table X. Measured Human Urine Concentrations
	<ul style="list-style-type: none"> - Table X. Cumulative Amount by Collection Intervals - Table X. Pharmacokinetic Parameters
Appendix 16.2.6.4.3	PK – Figures – Plasma
	<ul style="list-style-type: none"> - Figure x: Linear Profile of the Mean - Figure x: Logarithmic Profile of the Mean - Figure x: Individual Linear Profile of Subject x - Figure x: Individual Logarithmic Profile of Subject x - Figure x: Individual Elimination Profiles
Appendix 16.2.6.5	M7
Appendix 16.2.6.5.1	PK Tables – Plasma
	<ul style="list-style-type: none"> - Table X. Measured Human Plasma Concentrations - Table X. Cumulative Area Under the Curve - Table X. Pharmacokinetic Parameters - Table X. Elimination Parameters - Table X. Actual Sampling Time

Appendix 16.2.6.5.2	PK Tables – Urine Table X. Measured Human Urine Concentrations <ul style="list-style-type: none"> - Table X. Cumulative Amount by Collection Intervals Table X. Pharmacokinetic Parameters
Appendix 16.2.6.5.3	PK – Figures – Plasma <ul style="list-style-type: none"> - Figure x: Linear Profile of the Mean - Figure x: Logarithmic Profile of the Mean - Figure x: Individual Linear Profile of Subject x - Figure x: Individual Logarithmic Profile of Subject x - Figure x: Individual Elimination Profiles

APPENDIX A

STUDY SCHEDULES

Examination	Screening	Days			Post-Study Tests or ET ^a	End of Study
	Day 28 to – 1	-1	1	2	2	7 (±3)
Review Inc/Exclusion Criteria & Medical History	X					
Informed Consent	X					
Check-in		X				
Dosing			X			
Clinic Confinement		X	X	X		
Discharge				X		
Demographics	X					
C-SSRS questionnaire	X				X	
Concomitant Medication	X	X	X	X	X	X
Physical Examination	X				X	
Vital Signs	X		X ^b		X	
Height, Weight, and BMI	X					
12-lead ECG	X	X ^c	X ^c		X	
HIV Ag/Ab Combo, HBsAg (B) (Hepatitis B) and HCV (C) Tests	X					
Drug and Alcohol Screen	X	X				
Pregnancy test (females)	X	X			X	
Clinical Laboratory Evaluations	X	X ^d			X	
PK Blood Samples ^e			X	X		
Urine PK Collection ^e			X	X		
Follow-up Call						X
AEs Recording	X	X	X	X	X	

^a Early Termination (ET).

^b Vital signs will be measured prior to dosing and approximately 2 and 4 hours after study drug administration.

- c 12-lead ECG will be performed prior to dosing and approximately 2 hours after study drug administration.
- d Clinical laboratory tests (hematology, biochemistry, and urinalysis) will be performed in the evening prior to drug administration.
- e PK blood and urine samples will be collected according to schedule of PK assessments.

APPENDIX B

Pharmacokinetic Parameters

PK Parameter	Definition
C_{\max}	Maximum observed plasma concentration
T_{\max}	Time of maximum observed plasma concentration; if it occurs at more than one time point, T_{\max} is defined as the first time point with this value
$AUC_{(0-t_{\text{last}})}$	Cumulative area under the plasma concentration time curve calculated from 0 to T_{LQC} using the linear trapezoidal method, where T_{LQC} represents time of last observed quantifiable plasma concentration
$AUC_{(0-\infty)}$	Area under the plasma concentration time curve extrapolated to infinity, calculated as $AUC_{(0-t_{\text{last}})} + \hat{C}_{\text{LQC}}/\lambda_z$, where \hat{C}_{LQC} is the estimated concentration at time T_{LQC}
$\%AUC(t_{\text{last}}-\infty)$	Relative percentage of $AUC_{(0-t_{\text{last}})}$ with respect to $AUC_{(0-\infty)}$ $\% AUC(t_{\text{last}} - \infty) = 100 \times \frac{(AUC(0 - \infty) - AUC(0 - t_{\text{last}}))}{AUC(0 - \infty)}$
λ_z	Apparent elimination rate constant, estimated by linear regression of the terminal linear portion of the log concentration <i>versus</i> time curve
$T_{1/2}$	Terminal elimination half-life, calculated as $\ln(2)/\lambda_z$
CL/F^*	Apparent Total Plasma Clearance, calculated as $\text{dose} / AUC_{(0-\infty)}$
V_z/F^*	Apparent Volume of Distribution, calculated as $\text{dose} / \lambda_z * AUC_{(0-\infty)}$
$A_e(0-t)$	Amount excreted in urine (Total analyte concentration * Volume of Urine)
f_e^*	Fraction of dose excreted in urine (A_e / dose)
CL_r	Renal Clearance ($A_e(0-t)/AUC_{(0-t_{\text{last}})}$)

* Not calculated for metabolites

APPENDIX C

TABLE SHELLS

Table 14.1.1
Subject Disposition
(All Subjects)

	Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Overall (N=XX)
Subjects Enrolled			xx
Screen Fail Subjects			xx
Subjects Screened [N]			xx (xx.x)
Subjects Completed the Study [n(%)]	YES		xx (xx.x)
	NO		xx (xx.x)
If No, Reason of Study Discontinuation [n(%)]	Reason 1		xx (xx.x)
	Reason 2		xx (xx.x)
	Reason 3		xx (xx.x)
	Etc.		xx (xx.x)
Number of Subjects Included in Each Analysis			
Population [n(%)]	Safety Population		xx (xx.x)
	Pharmacokinetic Population		xx (xx.x)

Programming Note: Please add Moderate and Mild Renal Function Groups to the table if enrolled

Note: The percentages are based on the number of subjects screened.

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.1.2.1
Summary of Demographic Characteristics
(Safety Population)

		Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Etc.	Overall (N=XX)
Age (years)	N	xx	xx	xx	xx
	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Gender [n(%)]	MALE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	FEMALE				
Ethnicity [n(%)]	HISPANIC/LATINO	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	NOT HISPANIC/NOT LATINO	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race [n(%)]	RACE1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	RACE2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Weight (kg)	N	xx	xx	xx	xx
	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Height (cm)	N	xx	xx	xx	xx
	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Body Mass Index (kg/m ²)	N	xx	xx	xx	xx
	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Programming Note: Please add Moderate and Mild Renal Function Groups to the table if enrolled					

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Similar Table:

Table 14.1.2.2 Summary of Demographic Characteristics (Pharmacokinetic Population)

Table 14.3.1.1
Summary of Adverse Events
(Safety Population)

	Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Etc.	Overall (N=XX)
Adverse Events (AEs) Reported [n]				XX
Treatment Emergent Adverse Events (TEAEs) Reported [n]	XX	XX	XX	XX
Subjects With At Least One TEAE [n(%)][1]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Subjects With At Least One Drug-Related TEAE [n(%)][1][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
TEAEs Relationship [2]				
Related [n(%)][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Not Related [n(%)][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
TEAEs Severity/Intensity [2]				
Mild [n(%)][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Moderate [n(%)][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Severe [n(%)][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Life-Threatening [n(%)][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Serious Adverse Events (SAEs) Reported [n][2]	XX	XX	XX	XX
Subjects With At Least One SAE [n(%)][1]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Subject With an TEAE Leading to Withdrawal [n(%)][1]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Death [n(%)][1]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Programming Note: Please add Moderate and Mild Renal Function Groups to the table if enrolled				

[1] Percentages are based on the number of subjects in the Safety population in each treatment group.

[2] Percentages are based on the total number of treatment emergent adverse events reported in each treatment group.

[3] TEAE that was reported with a relationship of "reasonable possibility".

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.1.2
Summary of Treatment Emergent Adverse Events by System Organ Class and MedDRA Preferred Term
(Safety Population)

SOC MedDRA Preferred Term	Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Etc.
Subjects With At Least One TEAE [n(%)]		xx (xx.x)	xx (xx.x)
System Organ Class 1 [n(%)]		xx (xx.x)	xx (xx.x)
MedDRA Term 11 [n(%)]		xx (xx.x)	xx (xx.x)
MedDRA Term 12 [n(%)]		xx (xx.x)	xx (xx.x)
MedDRA Term 13 [n(%)]		xx (xx.x)	xx (xx.x)
System Organ Class 2 [n(%)]		xx (xx.x)	xx (xx.x)
MedDRA Term 21 [n(%)]		xx (xx.x)	xx (xx.x)
MedDRA Term 22 [n(%)]		xx (xx.x)	xx (xx.x)
MedDRA Term 23 [n(%)]		xx (xx.x)	xx (xx.x)
Etc.		xx (xx.x)	xx (xx.x)

Programming Note: Please add Moderate and Mild Renal Function Groups to the table if enrolled

Note: Each treatment emergent adverse event is counted only once for each subject within each System Organ Class and MedDRA Preferred Term.

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Similar Table: Table 14.3.1.3 Summary of Drug-Related Treatment Emergent Adverse Events by System Organ Class and MedDRA Preferred Term

Table 14.3.2.1
Listing of Deaths, Other Serious and Significant Adverse Events
(Safety Population)

Subject ID	Day/ Group/ AE #	SOC MedDRA Preferred Term Description of AE	Onset Date Time (Time since Last Dose)	Resolution Date Time (Duration)	I: Maximal Intensity R: Causality Assessment	O: Outcome S: Serious AE D: AE Lead To Discontinuation	Action Taken With Study Treatment / Other Action(s) Taken / Concomitant Given
xxx	xxxxx xxxxx	xxxxxxxxxxxxx xxxxxxxxxxxxx xxxxxxxxxxxxx	YYYY-MM-DD/ HH:MM (DD:HH:MM)	YYYY-MM- DD/ HH:MM (DD:HH:MM)	xxxxxxx	xxxxxx	xxxxxxx

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Similar Tables:

14.3.2.2 Listing of Adverse Events Leading to Withdrawal

Table 14.3.4.1
Listing of Abnormal On-Study Laboratory Values
(Safety Population)

Category/ Parameter (Unit)	Reference Range	Subject ID	Visit	Date / Time	Value	Out-of-Range Flag	Assessment [1]
Lab Category 1							
Lab Test 11	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx
Lab Test 12	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx
Lab Category 2							
Lab Test 21	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx
Lab Test 22	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx
Etc.	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx

[1] NCS: Not Clinically Significant / CS: Clinically Significant / RPT: Repeated / TBC: To Be Controlled.

Note(s): Abnormal values are determined by applying the reference ranges to the results as reported by the external laboratory analysis.

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.4.2
Listing of Clinically Significant On-Study Laboratory Values
(Safety Population)

Category/ Parameter (Unit)	Reference Range	Subject ID	Visit	Date / Time	Value	Out-of- Range Flag	Assessment [1]
Lab Category 1							
Lab Test 11	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx
Lab Test 12	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx
Lab Category 2							
Lab Test 21	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx
Lab Test 22	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx
Etc.	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx

[1] CS: Clinically Significant / RPT: Repeated / TBC: To Be Controlled

Note(s): Abnormal values are determined by applying the reference ranges to the results as reported by the external laboratory analysis.

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.4.3
Summary of Blood Chemistry
(Safety Population)

Parameter (unit)		Statistic		Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Etc. (N=XX)	
Visit Name							
xxx (xxx)	Screening	Value	N	xx	xx	xx	xx
			Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
			Median	xx.x	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Day -1	Value	N	xx	xx	xx	xx
			Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
			Median	xx.x	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Etc.		N	xx	xx	xx	xx
			Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
			Median	xx.x	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx	xx, xx

Programming Note: Please add Moderate and Mild Renal Function Groups to the table if enrolled

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Similar Tables:

14.3.4.4 Summary of Hematology

14.3.4.5 Summary of Quantitative Urinalysis

Table 14.3.5.1
Listing of Abnormal On-Study Vital Signs Values
(Safety Population)

Assessment (Units)	Subject ID	Visit	Elapsed Time	Position	Date / Time	Value	Safety Review
Vital Sign Test 1	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
Vital Sign Test 2	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
Etc.	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx

Date: VERSION - YYYY-MM-DD Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.5.2
Listing of Clinically Significant On-Study Vital Signs Values
(Safety Population)

Assessment (Units)	Subject ID	Visit	Elapsed Time	Position	Date / Time	Value	Safety Review
Vital Sign Test 1	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
Vital Sign Test 2	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
Etc.	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx

Date: VERSION - YYYY-MM-DD Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.5.3
Summary of Vital Signs
(Safety Population)

Parameter (unit)	Visit	Timepoint	Statistic	Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Etc. (N=XX)
Vital Sign Test 1	Screening	Value	N Mean (SD) Median Min, Max			xx xx (xx.x) xx.x xx, xx
	Day 1	2 Hours	Value	N Mean (SD) Median Min, Max	xx xx (xx.x) xx.x xx, xx	xx xx (xx.x) xx.x xx, xx
	Day 1	4 Hours	Value	N Mean (SD) Median Min, Max	xx xx (xx.x) xx.x xx, xx	xx xx (xx.x) xx.x xx, xx
Etc.	Etc.					

PROGRAMMING NOTE: All visits outlined in Appendix A will be included. **Please add Moderate and Mild Renal Function Groups to the table if enrolled**

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.6.1
Listing of Abnormal On-Study ECG Assessments
(Safety Population)

Subject ID	Visit	Time Point	Date / Time	Position	Safety Review	Parameter (Unit)	Value
xxxxxx	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
xxxxxx	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
xxxxxx	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.6.2
Listing of Clinically On-Study ECG Assessments
(Safety Population)

Subject ID	Visit	Time Point	Date / Time	Position	Safety Review	Parameter (Unit)	Value
xxxxxx	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
xxxxxx	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
xxxxxx	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
xxxxxx	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
xxxxxx	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.6.3
Summary of ECG Assessments
(Safety Population)

Parameter (unit)	Visit	Timepoint	Statistic	Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Etc. (N=XX)
ECG Assessment Test 1	Screening	Value	N			xx
			Mean (SD)			xx (xx.x)
			Median			xx.x
			Min, Max			xx, xx
	Day -1	Value	N	xx	xx	xx
			Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
			Median	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx
	Day 1	Pre-dose	N	xx	xx	xx
			Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
			Median	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx
Etc.	Etc.					

PROGRAMMING NOTE: All visits outlined in Appendix A will be included. **Please add Moderate and Mild Renal Function Groups to the table if enrolled**

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

APPENDIX D

PHARMACOKINETIC OUTPUTS SHELLS

Measured Human Plasma Concentrations of Lasmiditan, Normal Renal Function, CUD-P4-001

		Time (h)									
		0.00	0.25	0.50	1.00	36.00
Renal Function	Subject	Concentration (ng/mL)									
Normal	101										
	...										
	...										
	...										
	...										
	...										
	...										
	108										
N											
Mean											
SD											
Min											
Median											
Max											
CV%											
Geometric Mean											
Geometric CV%											
BLQ : Below Limit of Quantitation											
NC: Not Calculated											

Similar tables will be presented for all renal groups, for urine concentrations and for all analytes.

Cumulative Area Under the Curve of Lasmiditan, Normal Renal Function, CUD-P4-001

		Time (h)									
		0.00	0.25	0.50	1.00	36.00
Renal Function	Subject	Cumulative AUC (ng*h/mL)									
Normal	101										
	...										
	...										
	...										
	...										
	...										
	...										
	108										
N											
Mean											
SD											
Min											
Median											
Max											
CV%											
Geometric Mean											
Geometric CV%											
NC: Not Calculated											

Similar tables will be presented for all renal groups, for urine data by intervals and for all analytes.

Pharmacokinetic Parameters of Lasmiditan, Normal Renal Function, CUD-P4-001

Renal Function	Subject	C _{max} (ng/mL)	T _{max} (h)	AUC _(0-tlast) (ng*h/mL)	AUC _(0-∞) (ng*h/mL)	%AUC _(0-tlast/∞) (%)	T _{1/2} (h)	CL/F (L/h)	V _Z /F (L)
Normal	101								
	...								
	...								
	...								
	...								
	...								
	...								
	108								
N									
Mean			NC				NC		
SD			NC				NC		
Min									
Median									
Max									
CV%			NC				NC		
Geometric Mean			NC						
Geometric CV%			NC						

Similar tables will be presented for all renal groups, for urine parameters and for all analytes.

Elimination Parameters of Lasmiditan, Normal Renal Function, CUD-P4-001

Renal Function	Subject	T_{LIN} (h)	T_{LQC} (h)	Number of Points	R^2	λ_z (1/h)
Normal	101					
	...					
	...					
	...					
	...					
	...					
	...					
	108					
N Mean SD Min Median Max CV% Geometric Mean Geometric CV%						

A similar table will be presented for all renal groups and for all analytes.

Actual Sampling Time of Lasmiditan, Normal Renal Function, CUD-P4-001

		Time (h)													
		0.00	0.25	0.50	1.00	36.00
Renal Function	Subject	Actual Time (h)													
Normal	101														
	...														
	...														
	...														
	...														
	...														
	...														
	108														
N															
Mean															
SD															
Min															
Median															
Max															
CV%															
Geometric Mean															
Geometric CV%															
NC: Not Calculated															

A similar table will be presented for all renal groups and for all analytes.

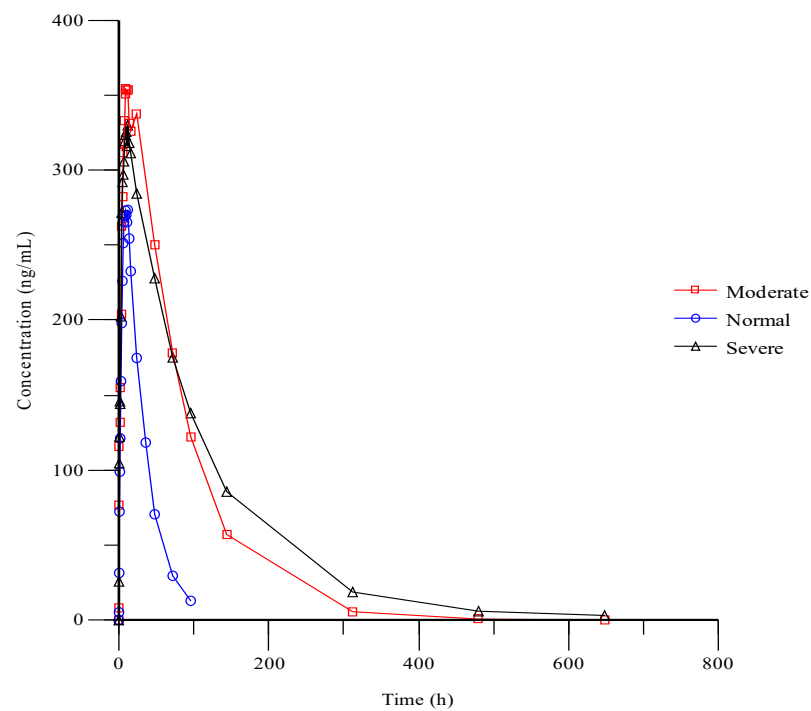
Pairwise Comparisons of Lasmiditan, CUD-P4-001

Parameters	Geometric LSmeans ^a		Comparison	Adjusted p-value	Ratio (%)	90% Confidence Limits (%)	
	Group					Lower	Upper
C _{max}	Mild (n=x)		Mild vs Normal				
	Moderate (n=x)		Moderate vs Normal				
	Severe (n=x)		Severe vs Normal				
	Normal (n=x)		Mild vs Moderate				
	NA	NA	Mild vs Severe				
	NA	NA	Moderate vs Severe				
AUC _(0-tlast)	Mild (n=x)		Mild vs Normal				
	Moderate (n=x)		Moderate vs Normal				
	Severe (n=x)		Severe vs Normal				
	Normal (n=x)		Mild vs Moderate				
	NA	NA	Mild vs Severe				
	NA	NA	Moderate vs Severe				
AUC _(0-∞)	Mild (n=x)		Mild vs Normal				
	Moderate (n=x)		Moderate vs Normal				
	Severe (n=x)		Severe vs Normal				
	Normal (n=x)		Mild vs Moderate				
	NA	NA	Mild vs Severe				
	NA	NA	Moderate vs Severe				

^a C_{max} is presented in ng/mL, AUC_(0-tlast) and AUC_(0-∞) are presented in ng*h/mL

PHARMACOKINETIC FIGURES SHELLS

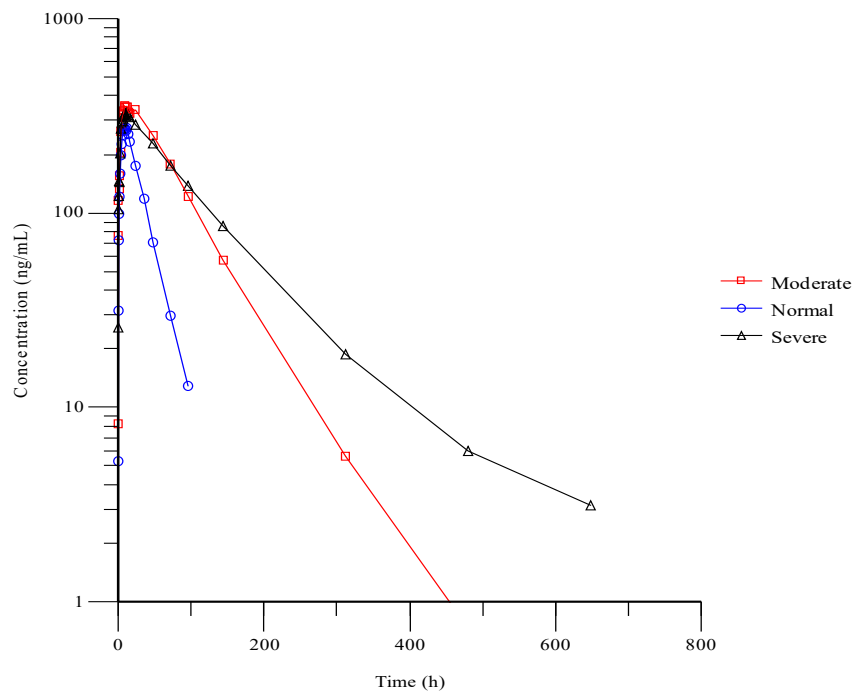
Figure 1: Linear Profile of the Mean of Lasmiditan in Plasma



The figure does not reflect the actual data of the study

Figures will be presented for all analytes.

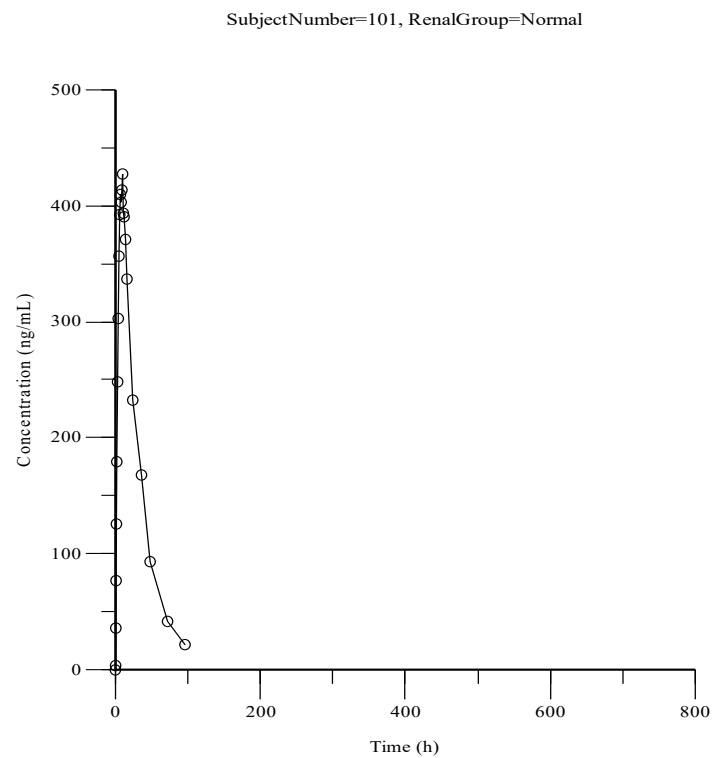
Figure 2: Logarithmic Profile of the Mean of Lasmiditan in Plasma



The figure does not reflect the actual data of the study.

Figures will be presented for all analytes.

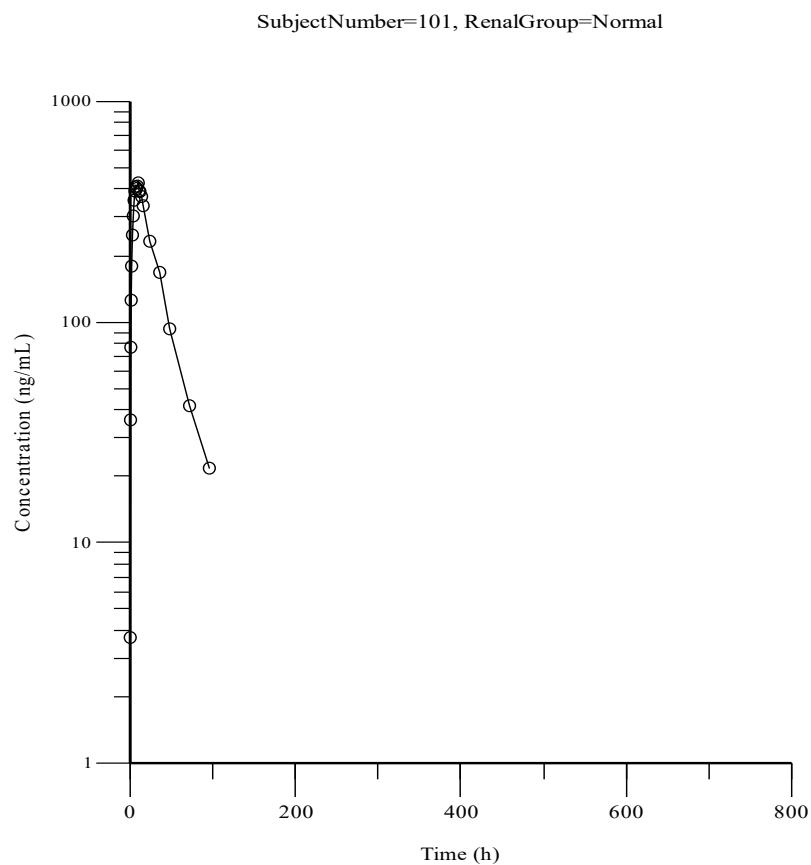
Figures 2+1 to (2+1)+N: Individual Linear Profile of Lasmiditan in Plasma



The figure does not reflect the actual data of the study

Figures will be presented for all analytes.

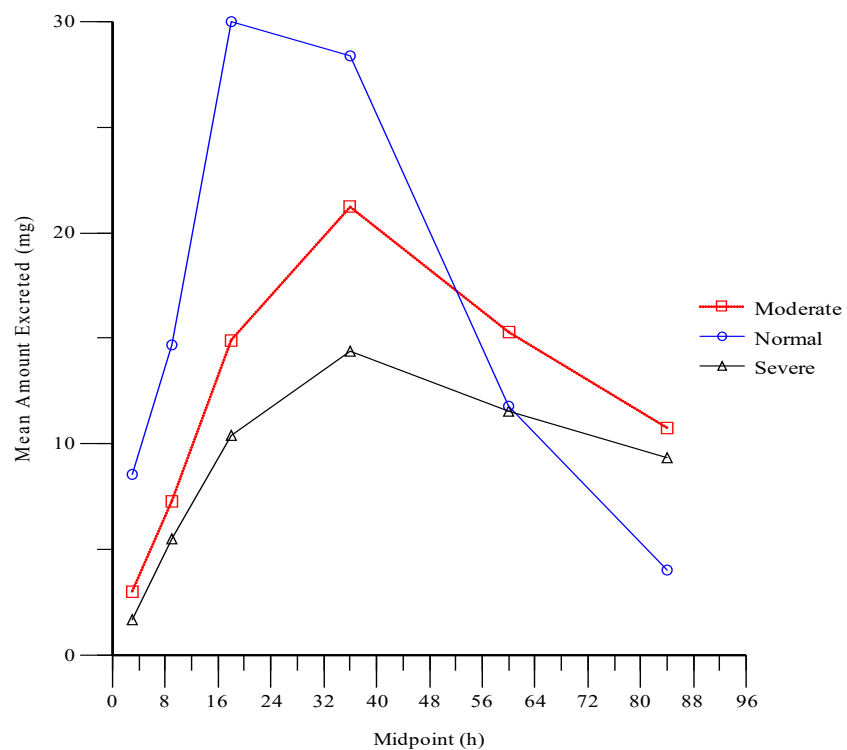
Figure X: Individual Logarithmic Profile of Lasmiditan in Plasma



The figure does not reflect the actual data of the study.

Figures will be presented for all analytes.

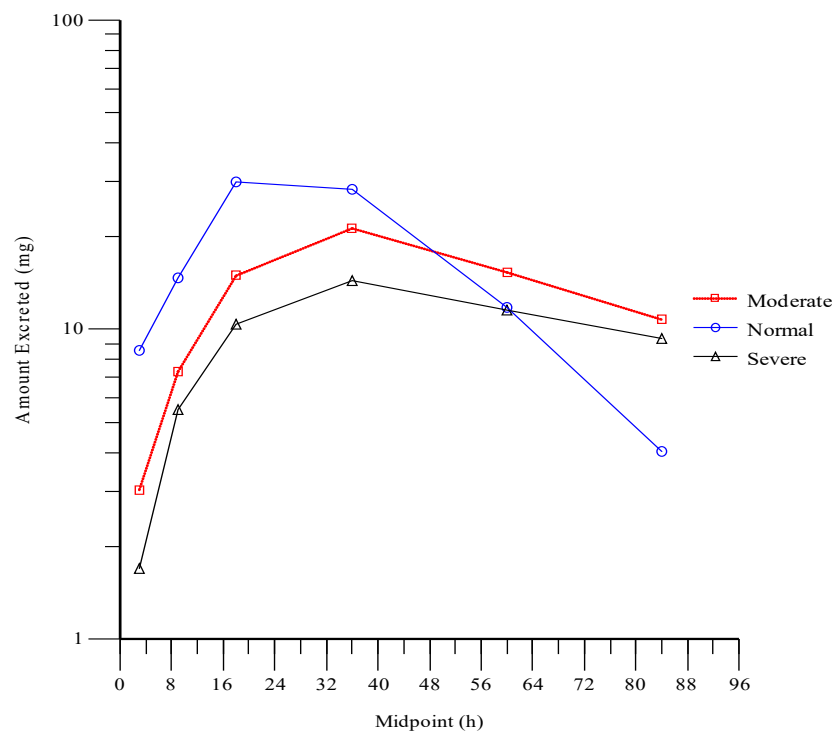
Figure 1: Linear Profile of the Mean of Lasmiditan in Urine



The figure does not reflect the actual data of the study.

Figures will be presented for all analytes.

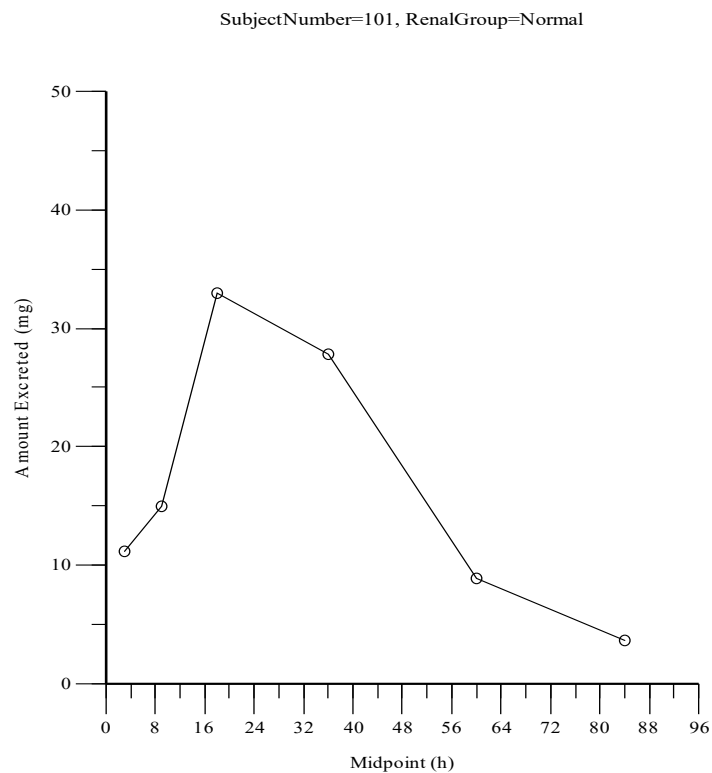
Figure 2: Logarithmic Profile of the Mean of Lasmiditan in Urine



The figure does not reflect the actual data of the study.

Figures will be presented for all analytes.

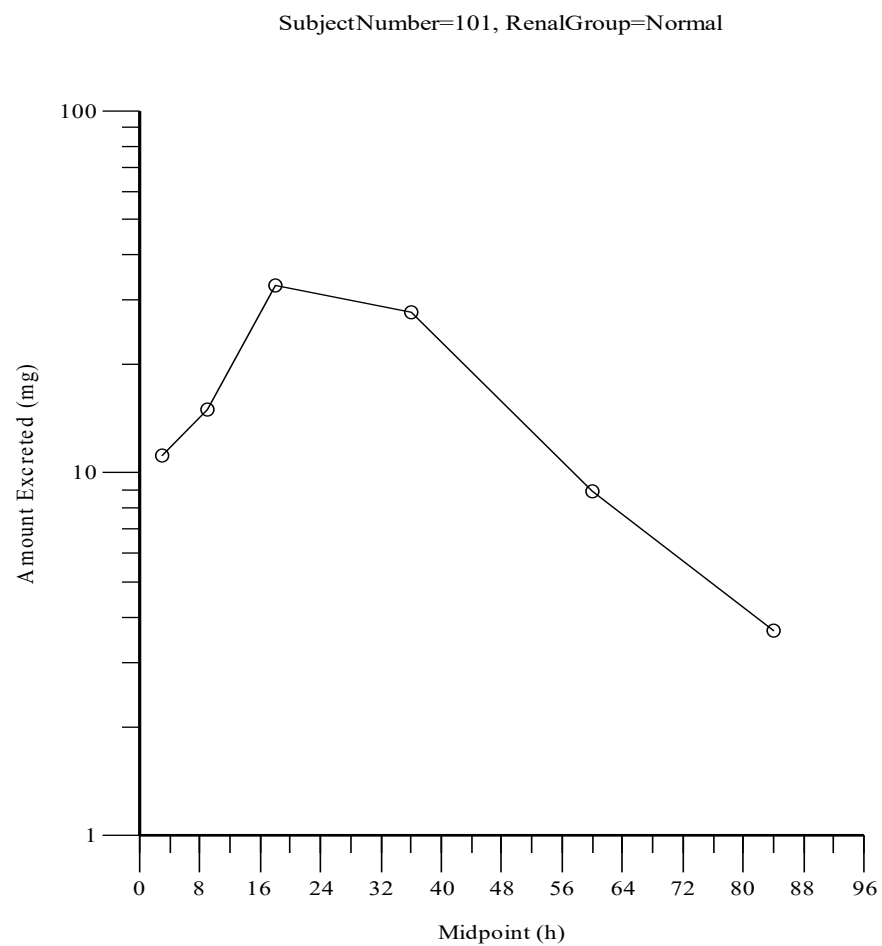
Figures 2+1 to (2+1)+N: Individual Linear Profile of the Mean of Lasmiditan in Urine



The figure does not reflect the actual data of the study

Figures will be presented for all analytes.

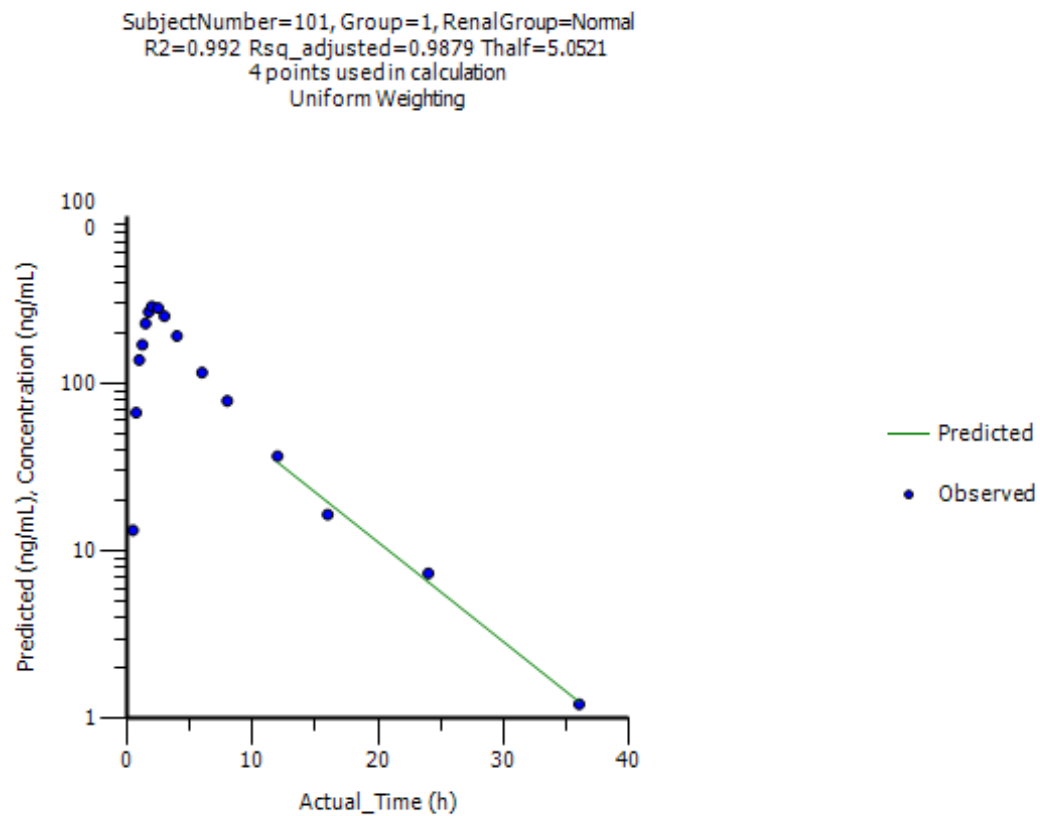
Figure N: Individual Logarithmic Profile of the Mean of Lasmiditan in Urine



The figure does not reflect the actual data of the study

Figures will be presented for all analytes.

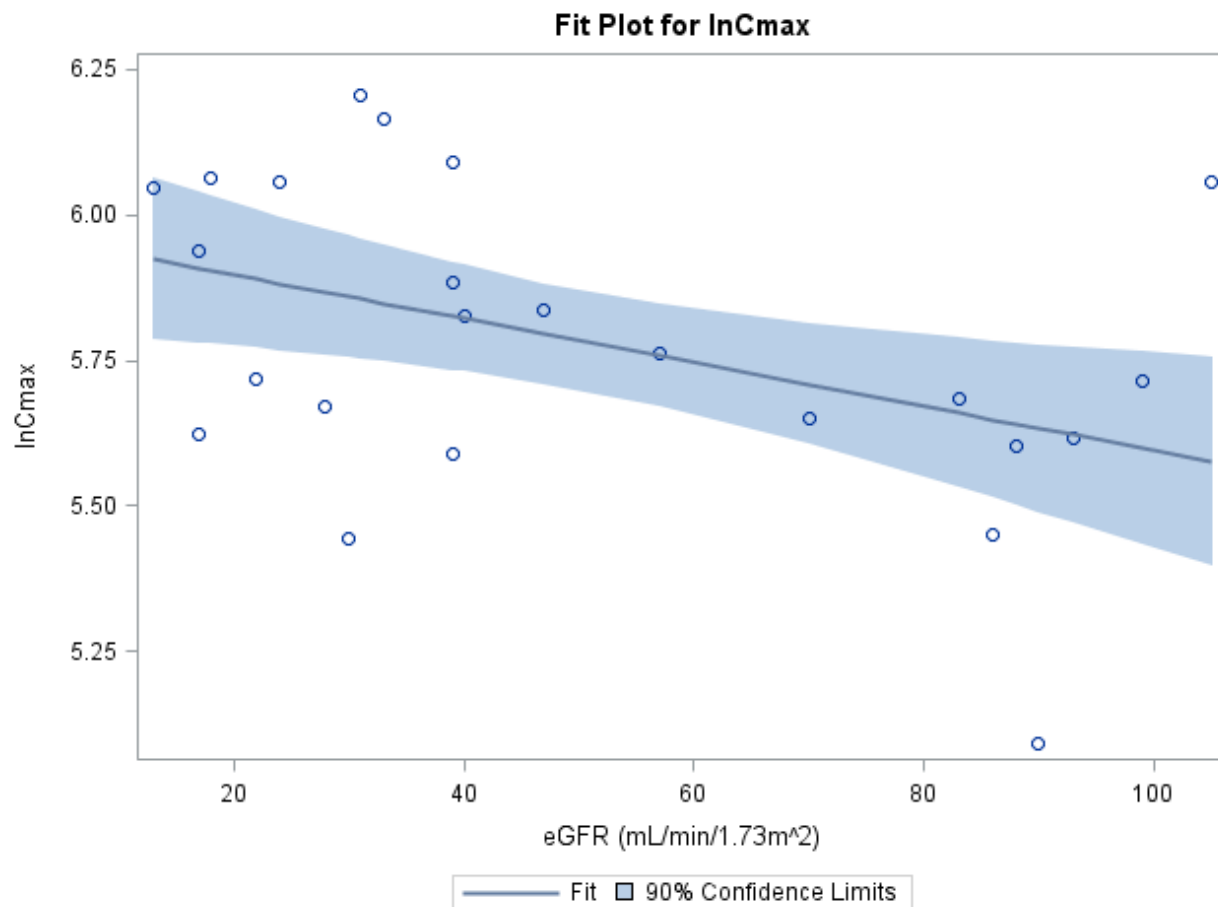
Figure N: Individual Elimination Profiles



The figure does not reflect the actual data of the study.

In Text Figure:

Figure 1: Linear Regression of In-Transformed C_{max} vs eGFR (Lasmiditan)



The figure does not reflect the actual data of the study. Same graph will be presented for $AUC_{(0-last)}$, $AUC_{(0-\infty)}$ and CL/F.

APPENDIX E

LISTING SHELLS

Listing 16.2.1
Listing of Study Disposition

Subject ID	Date of Completion or Discontinuation	Subject Status	Specify	AE #	Date of Death
------------	--	----------------	---------	------	---------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.2.1
Listing of PK Blood Sampling Time Deviations

Group	Elapsed Time (h)	Subject ID	Scheduled Date/Time	Actual Date/Time	Deviation (min)
-------	---------------------	------------	------------------------	---------------------	-----------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.2.2
Listing of Protocol Deviations

Group	Subject ID	Protocol Deviation Term	Start Date
-------	------------	-------------------------	------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.3
Listing of Analysis Populations

Subject ID	Safety Population	PK Population	Reason if Excluded from one Population
------------	----------------------	---------------	--

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

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Project # COL MIG-113/CUD-P4-001

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Listing 16.2.4.1
Listing of Demographic Characteristics

Subject ID	Age	Date of Birth	Gender	Ethnicity	Race	Other Race	Weight (kg)	Height (cm)	BMI (kg/m ²)
------------	-----	---------------	--------	-----------	------	------------	-------------	-------------	--------------------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.4.2
Listing of Screen Failures

Subject ID	Date	Specify Primary Reason
------------	------	------------------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.5
Listing of Investigational Product Administration

Subject ID	Visit	Start Date/Time	Treatment	Dose Administered (mg)	Route	If Any Dosing Issues, Specify
------------	-------	--------------------	-----------	---------------------------	-------	----------------------------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.7
Listing of Adverse Events

Subject ID	Visit/ Group/ AE #	SOC MedDRA Preferred Term Description of AE	Onset Date Time (Time since Last Dose)	Resolution Date Time (Duration)	I: Maximal Severity R: Causality Assessment	O: Outcome S: Serious AE D: AE Leading To Discontinuation	Action Taken With Study Treatment / Other Action(s) Taken / Concomitant Given
xxx	xxxxx xxxxx	xxxxxxxxxxxxx xxxxxxxxxxxxx xxxxxxxxxxxxx	YYYY-MM-DD/ HH:MM (DD:HH:MM)	YYYY-MM-DD/ HH:MM (DD:HH:MM)	xxxxxxx	xxxxxx	xxxxxxx

Listing 16.2.8.1
Listing of Blood Chemistry

Subject ID	Lab Test Name (Units)	Reference Range	Visit	Date / Time	Value	Out-of-Range Flag	Assessment [1]
------------	-----------------------	-----------------	-------	-------------	-------	-------------------	----------------

[1] NCS: Not Clinically Significant / CS: Clinically Significant / RPT: Repeated / TBC: To Be Controlled.

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Similar listing(s) :

L16.2.8.2	Listing of Hematology
L16.2.8.3	Listing of Urinalysis
L16.2.8.4	Listing of Urine Drug Screen
L16.2.8.5	Listing of Pregnancy Test
L16.2.8.5	Listing of Serology

Listing 16.2.9.1
Listing of Alcohol Habits

Subject ID	Intake Status	Quantity	Frequency	Start Date	End Date
------------	---------------	----------	-----------	------------	----------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.9.2
Listing of Smoking Habits

Subject ID	Intake Status	Quantity	Frequency	Start Date	End Date
------------	---------------	----------	-----------	------------	----------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

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Project # COL MIG-113/CUD-P4-001

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Listing 16.2.9.3
Listing of Prior Medication

Subject ID	#CM	Related to AE#/MH#	ATC / PT / Medication Name	Indication	Dose (unit)	Frequency	Formulation	Total Daily Dose	Route	Start Date/ Time	End Date/ Time
------------	-----	-----------------------	-------------------------------------	------------	----------------	-----------	-------------	------------------------	-------	------------------------	----------------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Similar Listing:

Listing 16.2.9.4 Listing of Concomitant Medication

Listing 16.2.9.5
Listing of Physical Examination

Subject ID	Visit	Date / Time	Body System Examined	Result (Abnormal Findings)
------------	-------	-------------	----------------------	----------------------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.9.6
Listing of Vital Signs

Subject ID	Visit	Elapsed Time	Position	Date / Time	Assessment (Units)	Value	Safety Review
------------	-------	--------------	----------	-------------	-----------------------	-------	------------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.9.7
Listing of ECG Assessments

Subject ID	Visit	Time Point	Date / Time	Position	Safety Review	Parameter (Unit)	Value
xxxxxx	xxxxxxx		YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		
			YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		
			YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		
xxxxxx	xxxxxxx		YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		
xxxxxx	xxxxxxx		YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.9.8
Listing of Inclusion/Exclusion Criteria Summary

Subject ID	Has the participant met all screening eligibility criteria?	Inclusion/Exclusion	Failed Criterion Number
------------	---	---------------------	-------------------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

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Project # COL MIG-113/CUD-P4-001

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Listing 16.2.9.9
Listing of Medical History

Subject ID	MH #	System Organ Class	MedDRA Preferred Term	Description of Medical History	Start Date	End Date

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

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Listing 16.2.9.10
Listing of Columbia-Suicide Severity Rating Scale (C-SSRS)

Subject ID	Visit	Category	Question	Answer
------------	-------	----------	----------	--------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas



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United States

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SUPPLEMENTARY INFORMATION RECORD

SPONSOR PROJECT N°: COL MIG-113					
ALTASCIENCES PROJECT N°: CUD-P4-001					
Date 2018/04/05					
CATEGORY					
Requested by: SRA Team, Algorithme Pharma					
Documents:					
Protocol	()	SOP N°:	()	Regulatory documents	()
Other (<input checked="" type="checkbox"/>), specify : SAP					

DESCRIPTION
<p>Description:</p> <p>This serves to clarify an error of date in SAP version Final 4.0 dated 2018/02/15. On the cover page(1st page) of SAP, the date reads 2017/02/15. In fact it should be 2018/02/15, as the footnote indicates.</p> <p>The clarifications described herein are judged to have no impact on the conduct of the study or on subjects' safety.</p>

Completed By:

PPD

Date: 2018/04/06

Date: 2018/04/06

STATISTICAL ANALYSIS PLAN

For:

CoLucid Pharmaceuticals, Inc.

SPONSOR PROTOCOL No. COL MIG-113

*A Phase I, Multicenter, Open-Label, Parallel-Group Adaptive
Pharmacokinetic Single Dose Study of Oral Lasmiditan in Subjects
with Normal and Impaired Renal Function*

Algorithm Project No. CUD-P4-001

Prepared by:

Algorithm Pharma
575 Armand-Frappier
Laval, Quebec
Canada, H7V 4B3

Version: Final 3.2

Date: 2017/10/25

STATISTICAL ANALYSIS PLAN APPROVAL

We have carefully read this Statistical Analysis Plan and agree it contains the necessary information required to handle the statistical analysis of study data.

PPD

30-01-2017
Date

PPD

2017/10/31
Date

On behalf of the Sponsor:

PPD

Date

VERSION CONTROL

Version Number	Version Date	Author	Description of Significant Changes from Previous Approved Version
DRAFT 0.1	2017/04/28	Sarah Vahey / Josée Michaud	Not Applicable – First Version
DRAFT 0.2	2017/05/15	Sarah Vahey / Josée Michaud	Updated according to client comments
DRAFT 0.3	2017/05/25	Sarah Vahey / Josée Michaud	Updated according to client comments
FINAL 1.0	2017/06/07	Sarah Vahey	Updated version to Final
FINAL 2.0	2017/09/05	Nolwenn Rondet/Jade Huguet	Updated according FDA recommendations from final 1.0 to Final 2.0
FINAL 3.0	2017/09/22	Nolwenn Rondet/Josée Michaud	Updated according FDA recommendations from final 1.0 to Final 2.0
FINAL 3.1	2017/09/22	Nolwenn Rondet	Updated according FDA recommendations from final 1.0 to Final 2.0 and client comments
FINAL 3.2	2017/10/25	Nolwenn Rondet / Josée Michaud	Updated according client comments
FINAL 3.3	2017/10/28	Katia Charland / Josée Michaud	Final Version

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ABBREVIATIONS

AE	Adverse Event
ANOVA	Analysis of Variance
ATC	Anatomical/Therapeutic/Chemical
AUC	Area Under Curve
BMI	Body Mass Index
CI	Confidence Interval
CLCR	Creatinine Clearance
CNS	Central Nervous System
CRF	Case Report Form
CS	Clinically Significant
C-SSRS	Columbia-Suicide Severity Rating Scale
CSR	Clinical Study Report
eGFR	Estimated Glomerular Filtration Rate
EOS	End of Study
ICF	Informed Consent Form
MedDRA	Medical Dictionary for Regulatory Activities
NCS	Not Clinically Significant
PK	Pharmacokinetic(s)
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SE	Standard Error
SOC	System Organ Class
TEAE	Treatment-Emergent Adverse Event
TFLs	Tables, Figures, and Listings
WHO-DDE	WHO Drug Dictionary Enhanced

1. INTRODUCTION

This statistical analysis plan (SAP) provides a detailed description of the statistical methods and procedures to be implemented for the analyses of data from Protocol No. COL MIG-113. The analyses described in the SAP are based upon the final protocol (Amendment 1) dated 2017/01/06.

2. STUDY OBJECTIVES

Primary Objectives

The primary objective of this study is to evaluate the pharmacokinetic profile of lasmiditan following a single oral 200 mg dose in subjects with impaired renal function relative to matched, healthy controls with normal renal function.

Secondary Objective

The secondary objective of this study is to assess the safety and tolerability of a single oral 200 mg dose of lasmiditan in subjects with normal and impaired renal function.

3. STUDY DESIGN

General Description

This is a multi-center, open-label, non-randomized, parallel-group, adaptive, single dose study.

This study will enroll up to 32 subjects using an adaptive design that can include up to 3 groups of 8 subjects with different degrees of renal impairment and one group of 8 control subjects with normal renal function.

First, approximately 16 subjects will be enrolled with severe renal impairment and matched subjects with normal renal function. There will be 8 subjects in each of the following groups based on renal function at screening:

- Group 1: Healthy subjects with normal renal function (eGFR ≥ 90 mL/min/1.73m²)
- Group 2: Severe renal impairment subjects (eGFR < 30 mL/min/1.73m²)

Based on safety and PK results from subjects with severe renal impairment (Group 2), Group 3 (Moderate Renal Impairment) and Group 4 (Mild Renal Impairment) will be enrolled if substantial change in the exposure of lasmiditan is observed in subjects with severe renal impairment. There will be 8 subjects in each of the following groups based on renal function at screening:

- Group 3: Moderate renal impairment subjects (eGFR 30-59 mL/min/1.73m²)
- Group 4: Mild renal impairment subjects (eGFR 60-89 mL/min/1.73m²)

All subjects will participate in one treatment period and will receive a single dose of lasmiditan in the fasting state.

The total duration of each subject's participation in the study will be 3 days (Day -1 through the last PK sample taken on Day 2), not including the screening and follow-up phone call. The total duration of the study is expected to be 35 days, including the screening.

The following treatment regimen will be used:

- Experimental treatment: Lasmiditan 200 mg

Study procedures

For complete details on the study assessments to be performed for the study, refer to [Appendix A](#).

Randomization and Unblinding Procedure

No randomization will be performed for this study. Instead subjects will be categorized into either the control group of healthy volunteers with normal renal function, or into one of the three groups of subjects with varying degrees of renal impairment.

Subjects who withdraw from the study may be replaced. Replacement subjects will not be enrolled for subjects who discontinue the study due to treatment-related toxicity.

No unblinding procedure is required, as this is an open-label study.

4. STUDY ENDPOINTS

Pharmacokinetic Endpoints

The following plasma and urine PK parameters of lasmiditan will be calculated: C_{max} , T_{max} , $AUC_{(0-t_{last})}$, $AUC_{(0-\infty)}$, $\%AUC(t_{last}-\infty)$, λ_z , $T_{1/2}$, CL/F , V_z/F , $Ae(0-t)$, fe , CL_r .

For all the metabolites [(S)-M8, (S,R)-M18, M7 and (S,S)-M18], the following PK parameters C_{max} , T_{max} , $AUC_{(0-t_{last})}$, $AUC_{(0-\infty)}$, $\%AUC(t_{last}-\infty)$, λ_z , T_{half} , $Ae(0-t)$, $CL_{r,met}$ and individual metabolic ratio (metabolite AUC/parent AUC) will be calculated, if quantifiable.

Safety Endpoints

Safety endpoints include:

- Adverse Events
- Clinical Laboratory Tests (hematology, chemistry, urinalysis)
- Vital Signs
- Physical examination
- Concomitant medication
- ECGs
- C-SSRS

The details of the safety endpoints' assessment are presented in [Section 10](#).

Sample Size Determination

There is no formal statistical sample size calculation for this study. A sample size of 32; including 8 subjects/patients for each renal function group (8 subjects with normal renal function, 8 patients with mildly impaired renal function, 8 patients with moderately impaired renal function, and 8 with severely impaired renal function) was chosen because it is considered typical for studies evaluating the effect of renal function on the pharmacokinetics of a drug.

5. ANALYSIS POPULATIONS

Safety Population:

All subjects who received a dose of study medication will be included in the safety population. This population will be used for all demography and safety analyses.

Pharmacokinetics (PK) Population:

All subjects who received lasmiditan, had no major protocol deviations, and completed the period with evaluable (sufficient and interpretable) data will be included in the PK population.

If some subjects do not complete the sampling schedule resulting in an inadequately characterized some PK parameters (e.g. AUC, V_z/F , λ_z), samples of these subjects could be included in the statistical pharmacokinetic analysis for only the evaluable parameters.

6. STATISTICAL METHODOLOGY

All analyses will be conducted using the SAS software, version 9.4, or higher. Descriptive statistics of the PK data will be performed by Phoenix® WinNonlin® version 6.3 or higher, Phoenix® Connect™ version 1.3.1 or higher).

Adverse events and medical history will be classified using the standard MedDRA terminology version 19.1.

Prior and concomitant medications will be coded with the WHO-DDE dictionary version March 01, 2016.

In general, all summary tables will be presented for safety population. Summaries will be presented by renal function group.

In general, the data listings will include all enrolled subjects up to the point of study completion or discontinuation; exceptions will be listings pertaining to a subset of subjects only (e.g., subjects with blood sampling time deviations) or a subset of records/events (e.g., abnormal laboratory values).

Categorical variables will be summarized using the PROC FREQ procedure. Continuous variables will be summarized using the PROC UNIVARIATE procedure. For log-transformed endpoints, geometric mean, and coefficient of variation will also be presented.

The following general comments also apply to all statistical analyses and data presentations:

- Duration variables in days will be calculated using the general formula: (end date - start date) +1.
- Individual subject listings of all data represented on the CRFs will be provided to facilitate the investigation of tabulated values and to allow for the clinical review of all efficacy and safety parameters.
- When assessments are repeated for a given timepoint, only the result which is closest to the dosing time will be included in the summary tables.

The analyses described in this plan are considered a priori, that they have been defined prior to database lock. Any analyses performed subsequent to database lock will be considered post hoc and exploratory. Post hoc analyses will be labeled as such in the corresponding statistical output and identified in the CSR.

Analysis Time Points

Unless otherwise specified, the baseline value will be defined as the last non-missing evaluation prior to the first dose of study medication.

Methods for Handling Missing Data

No imputations of values for missing data will be performed. All data recorded on the case report form will be included in the listings that will accompany the clinical study report.

7. STUDY SUBJECTS

Disposition

The subject disposition will be summarized for all subjects enrolled in this study, including:

- The number of subjects enrolled;
- The number of screen failure subjects;
- The number of subjects screened;
- The number and percentage of subjects who completed the study;
- The number and percentage of subjects discontinued from the study by primary reason for discontinuation and overall;
- The number and percentage of subjects included in each of the safety and PK populations.

The percentages will be calculated using the number of subjects randomized as denominator.

A listing of subject's disposition will be provided. A listing of subjects included in each of the analysis populations will also be provided. Screen failure subjects will also be presented in a listing.

Protocol Deviations

Inclusion/exclusion criteria violations will be presented in a listing.

All deviations from the scheduled PK sampling time of 2 minutes or more for post dose samples will be taken into consideration for the evaluation of PK parameters.

8. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographic and Background Characteristics

Demographic data and baseline characteristics will be presented in a data listing and summarized by renal function group in a table. Quantitative assessments to be summarized are age, height, body weight and body mass index (BMI) at screening. Subject demographics include sex, age, ethnicity, race and country. Baseline characteristics include height, weight, and BMI.

Lifestyle

Alcohol and smoking intake history will be recorded and presented in separate listings.

Medical/Social history

Any medical history findings will be recorded and presented in a listing. The listing will include the coding terms (e.g., SOC and Preferred Term).

Prior Medication

Any medications taken including prescription, nonprescription, OTC (cold and antacid medications), dietary supplements, vitamins or herbal medications from screening to the first dose of the study drug will be recorded and presented as prior medications in a listing. The listing will include the coding terms (e.g., ATC and Preferred Term).

9. PHARMACOKINETICS AND STATISTICS

Pharmacokinetic Analysis

The PK parameters are presented in [Section 4](#) and [Appendix B](#). All reported sampling time deviations (see [Section 7](#)) will be taken into consideration for evaluation of plasma PK parameters.

Only quantifiable concentrations will be used to calculate PK parameters. An exception to this rule is made for concentrations below the quantification limit (BQL), which will be set to zero when all of the following conditions are met:

- The time points occur before the first quantifiable concentration.

All other BQL concentrations will be treated as missing sample.

The pharmacokinetic parameters will be estimated using a non-compartmental approach with a log-linear terminal phase assumption. The trapezoidal rule will be used to estimate the area under the curve, and the terminal phase will be estimated by maximizing the coefficient of determination estimated from the log-linear regression model. These parameters ($AUC_{(0-\infty)}$, $\%AUC_{(t_{last}-\infty)}$, λ_z , $T_{1/2}$, CL/F and V_z/F) will be estimated for individual concentration-time profiles only when the terminal log-linear phase cannot be reliably characterized using the following criteria:

- Phoenix® WinNonlin® Best fit range selection (if adequate):
- R^2 of at least 80%

In the case where less than 3 consecutive measurable plasma concentrations of lasmiditan or its metabolites [(S)-M8, (S,R)-M18, M7 and (S,S)-M18] is observed, the AUC parameters will not be estimated for that particular analyte.

Additional pharmacokinetic parameters may be calculated if deemed appropriate.

Pharmacokinetic analyses and associated descriptive statistics will be generated using Phoenix® WinNonlin® Version 6.3 (or higher).

Statistical Analysis

The natural logarithmic transformation of C_{max} , $AUC_{(0-t_{last})}$, $AUC_{(0-\infty)}$, $Ae(0-t)$, as well as the rank-transformation of T_{max} will be used for all statistical inference for the parent (lasmiditan) and all metabolites [(S)-M8, (S,R)-M18, M7 and (S,S)-M18].

Statistical analyses will be generated using validated SAS® (version 9.4 or higher) using the Reg (and Mixed, if applicable) procedure(s).

The statistical analysis described in this section will be done using both eGFR and Cockcroft-Gault estimate of the creatinine clearance. However, analysis using the eGFR will be considered as the primary analysis and the analysis using the Cockcroft-Gault estimate of the creatinine clearance will be considered as supportive.

Regression Analysis

The eGFR and Cockcroft-Gault estimate of creatinine clearance at baseline will be used as separate measures of renal function for a regression analysis to evaluate the relationships between estimated renal function and the PK parameters.

For each log-transformed PK parameter, a regression analysis will be performed, using a model of the form $\alpha + \beta \cdot eGFR + \epsilon$ where the errors (ϵ) will be assumed to be independent and normally distributed with mean zero and variance σ^2 . The parameter β represents the correlation between the relevant PK parameter and eGFR which will be treated as a continuous variable.

The hypothesis of the slope of trend being different from zero will be assumed if the two-sided test of the nullity of the parameter β is statistically significant at the 5% level.

The regression analysis will be repeated for each log-transformed PK parameter with the Cockcroft-Gault estimate of creatinine clearance at baseline.

Analysis of Variance

An analysis of variance (ANOVA) will be performed to assess the difference in the PK parameter among the renal function groups.

The renal function (normal, mild, moderate and severe) will be entered as a fixed effect in the ANOVA model. Pairwise comparisons of renal function groups will be generated using the Tukey-Kramer's procedure of adjustment for multiple comparisons (if more than 2 renal function groups) and statistical significance will be assessed at the two-sided 5% level. The ratio of geometric LS means (of each renal function group being compared), with a corresponding 90% confidence interval (adjusted using Tukey-Kramer's procedure if applicable), will be computed. Heterogeneity of variance among groups will be assumed.

10. SAFETY

Adverse Events

An AE is defined as any untoward medical occurrence in a subject administered a medicinal product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (for example, an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product.

A suspected adverse reaction is any AE for which there is a reasonable possibility that the drug caused the AE. 'Reasonable possibility' means there is evidence to suggest a causal relationship between the drug and the AE. A suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any AE caused by a drug.

AEs occurring after the initiation of the treatment are referred to as treatment emergent adverse events (TEAEs).

As an overall summary of AEs, the following will be presented by renal function group and overall:

- Number of reported AEs;
- Number of reported TEAEs;
- Number and percentage of subjects experiencing TEAEs;
- Number and percentage of subjects experiencing a drug-related TEAE (i.e. those with a relationship classified as reasonable possibility)
- Number and percentage of TEAEs by relationship to study treatment (i.e. reasonable possibility, no reasonable possibility);
- Number and percentage of TEAEs by severity;
- Number of reported SAEs (serious adverse events);
- Number and percentage of subjects experiencing SAEs;
- Number and percentage of subjects experiencing drug-related SAEs;
- Number and percentage of TEAEs leading to withdrawal; and
- SAEs with an outcome of death.

Frequency tables will be presented by renal function group, system organ class and preferred term that summarize all Treatment Emergent Adverse Events (TEAEs) and all drug-related TEAEs.

Subject listings of all Adverse Events (AEs) including severity and relationship to study drug will be provided. AEs leading to withdrawal and SAEs will also be presented in separate listings.

Concomitant Medications

Medications taken after the first dose of study drug until after discharge from the study will be recorded. Concomitant medications will be presented in a listing. The medication name, active ingredient, dose, units, formulation, route, indication or reason taken, code, date and time taken will be presented. The listing will also include the coding terms (e.g., ATC and Preferred Term).

Extent of Exposure

Details of drug dosing (actual treatment received, actual date and time of administration, dose administered, and route of administration) will be listed by subject.

Clinical Laboratory Evaluations

Planned laboratory analyses include:

- General Biochemistry: Sodium, potassium, chloride, glucose, blood urea nitrogen (BUN), creatinine, eGFR, total bilirubin, alkaline phosphatase, AST, ALT and albumin;
- Hematology: White cell count with differential (absolute values of neutrophil, lymphocyte, monocyte, eosinophil, and basophil), red cell count, hemoglobin, hemoglobin A1c, hematocrit, mean corpuscular volume (MCV), and platelets count;
- Urinalysis: Color, appearance, specific gravity, pH, leukocyte, protein, glucose, ketones, bilirubin, blood, nitrite, urobilinogen. Microscopic examination will only be performed if the dipstick test is outside of the reference range for leukocyte, blood, nitrite or protein
- Other: serology urine drug screen and serum pregnancy.

Hematology, chemistry and quantitative urinalysis laboratory test results will be summarized by renal function group, parameter and visit and will also be presented in a listing

Separate listings of for serology, urine drug screen and serum pregnancy will also be provided.

Subject listings of abnormal on-study laboratory values will be provided. Similarly, clinically significant on-study laboratory data will be presented in a second listing.

Vital Signs

Vital signs will include the measurement of blood pressure, heart rate, oral temperature, and orthostatic blood pressure.

For all vital signs, raw values, at each time point will be summarized by renal function group, parameter and visit. Vital signs data will also be presented in a listing.

Subject listing of abnormal on-study vital signs values (Out-of-Range – Not Clinically Significant (NCS) or Clinically Significant (CS)) will be provided. Similarly, CS on-study vital signs values (Out-of-Range – CS) will be presented in a second listing.

Electrocardiogram

A 12-lead ECG will be obtained throughout the study. In some cases, repeat abnormal ECGs may be obtained.

Raw values at each time point will be summarized by renal function group, parameter and visit and will also be presented in a listing. Overall safety assessment will also be presented in the listing.

A subject listing of abnormal on-study ECG assessments (Abnormal – NCS or Abnormal – CS) will be provided. Similarly, CS on-study ECG assessments (Abnormal – CS) will be presented in a second listing.

Physical Examination Findings

A physical examination will be conducted and will be presented in a listing.

Columbia-Suicide Severity Rating Scale (C-SSRS)

The Columbia-Suicide Severity Rating Scale (C-SSRS) is a suicidal ideation rating scale. The scale identifies behaviors and thoughts that are associated with an increased risk of suicidal actions in the future.

Subjects who answer 'Yes' to any of the questions on the C-SSRS questionnaire will be presented in a listing.

11. INTERIM ANALYSES AND DATA SAFETY MONITORING

First, subjects with severe renal impairment and healthy subjects with normal renal function will be enrolled. Samples will be assayed and PK will be performed. If substantial changes in the exposure of lasmiditan are observed in subjects with severe renal impairment compared to subjects with normal renal function, subjects with mild and moderate renal impairment will be enrolled.

Interim analysis of subjects with severe renal impairment and healthy subjects with normal renal function will be performed as described in the regression analysis paragraph of [Section 9](#).

12. CHANGES TO PROTOCOL-SPECIFIED ANALYSES

There is no change from the planned analysis described in the protocol. The analyses described in the protocol was meant to be an overview. The final analyses is per this statistical analysis plan.

13. GENERAL INFORMATION RELATED TO DATA PRESENTATIONS

Safety

All programs used to generate statistical analyses will be validated according to Algorithme Pharma's standard operating procedures.

TFLs will be displayed on letter size paper, 8 ½ inches by 11 inches, using the Courier New font.

In general, summary statistics for raw variables (i.e., variables measured at the study site or central laboratory) will be displayed as follows: if required minima, maxima, means, quartiles, standard deviations and confidence limits will be displayed to the same number of decimal places as the raw data; if required medians will be displayed to one additional decimal place.

Percentages will be displayed to one decimal place. Percentages between 0 and 0.1 (exclusive) will be displayed as '<0.1'. P-values will be displayed to 3 decimal places. P-values that are less than 0.001 will be displayed as '<0.001'.

The numbers of decimal places for summary statistics of derived variables (i.e., variables that are not measured by the study site but are calculated for analysis based on other measured variables) will be determined on a case by case basis. In general, minima and maxima will be displayed to the commonly used unit of precision for the parameter. Means, medians, quartiles, and confidence limits will be displayed to one additional decimal place and standard deviations will be displayed to two additional decimal places.

The formats and layouts of TFLs are provided in subsequent sections. Actual formats and layouts may be altered slightly from those presented in the templates as necessary to accommodate actual data or statistics. Minor format changes will not require updates to the SAP.

The tables and listings listed below are common data displays. Their numbering and general content follow the ICH E3 guidelines. Some of the tables and listings may not be applicable/appropriate/necessary for a particular study. Additional tables and listings may be included, provided the numbering scheme remains consistent with ICH E3.

PK Data

All programs used to generate statistical analyses will be validated according to Algorithme Pharma's standard operating procedures.

TFLs will be displayed on letter size paper, 8 ½ inches by 11 inches, using Tahoma.

Raw variables (i.e., variables measured at the study site or central laboratory) will be displayed with the same number of decimal places as received as per bioanalytical laboratory. Derived variables (i.e., variables that are not measured by the study site but are calculated for analysis based on other measured variables) will be displayed as follow:

- All calculated pharmacokinetic parameter values should be reported to three significant digits.
- Observed concentration data, e.g. C_{max} , should be reported as received.
- Observed time data, e.g. T_{max} , should be reported as received.
- N and percentage values should be reported as whole numbers, except for the %AUC(tlast-∞).
- Median values should be treated as an observed parameter and reported to the same number of decimal places as minimum and maximum values.

Summary statistics of raw variables: minima, mean, geometric mean, median, maxima, and standard deviation, coefficient of variation will be displayed with the same number of decimal places as the raw data;

- The following summary statistics will be listed for all variables except T_{\max} and $T_{1/2}$, arithmetic mean, SD, and CV; geometric mean and CV; N, minimum, maximum, and median.
- Summary statistics for T_{\max} , and other discrete parameters, will be limited to N, minimum, maximum, and median. Report not calculated (NC) for other statistics
- Summary statistics for $T_{1/2}$ will be limited to geometric mean and CV; N, minimum, maximum, and median. Report not calculated (NC) for other statistics.

Summary statistics of derived variables will be displayed with the same number of decimal places as the derived variable.

PLANNED END-OF-TEXT TABLES

Demographic Data

Table 14.1.1	Subject Disposition – All Subjects
Table 14.1.2.1	Summary of Demographic Characteristics (Safety Population)
Table 14.1.2.2	Summary of Demographic Characteristics (Pharmacokinetic Population)

Pharmacokinetic Data

Section 14.2.1.1	Statistical Analysis – SAS output - Lasmiditan
Section 14.2.1.2	Statistical Analysis – SAS output - (S)-M8
Section 14.2.1.3	Statistical Analysis – SAS output - (S,R)-M18
Section 14.2.1.4	Statistical Analysis – SAS output – M7
Section 14.2.1.5	Statistical Analysis – SAS output - (S,S)-M18

Safety Data

Tables in this section are based on the safety population unless otherwise stated.

Table 14.3.1.1	Summary of Adverse Events
Table 14.3.1.2	Summary of Treatment Emergent Adverse Events by System Organ Class and MedDRA Preferred Term
Table 14.3.1.3	Summary of Drug-Related Treatment Emergent Adverse Events by System Organ Class and MedDRA Preferred Term
Table 14.3.2.1	Listing of Deaths, Other Serious and Significant Adverse Events
Table 14.3.2.2	Listing of Treatment Emergent Adverse Events Leading to Withdrawal
Table 14.3.4.1	Listing of Abnormal On-Study Laboratory Values
Table 14.3.4.2	Listing of Clinically Significant On-Study Laboratory Values
Table 14.3.4.3	Summary of Blood Chemistry
Table 14.3.4.4	Summary of Hematology
Table 14.3.4.5	Summary of Quantitative Urinalysis
Table 14.3.5.1	Listing of Abnormal On-Study Vital Signs Values
Table 14.3.5.2	Listing of Clinically Significant On-Study Vital Signs Values
Table 14.3.5.3	Summary of Vital Signs
Table 14.3.6.1	Listing of Abnormal On-Study ECG Assessments
Table 14.3.6.2	Listing of Clinically Significant On-Study ECG Assessments
Table 14.3.6.3	Summary of ECG Assessments

PLANNED IN-TEXT TABLES

PK Parameters of Lasmiditan
Summary of Statistical Analysis of Lasmiditan
PK Parameters of (S)-M8
Summary of Statistical Analysis of (S)-M8
PK Parameters of (S,R)-M18
Summary of Statistical Analysis of (S,R)-M18
PK Parameters of M7
Summary of Statistical Analysis of M7
PK Parameters of (S,S)-M18
Summary of Statistical Analysis of (S,S)-M18

PLANNED IN-TEXT FIGURES

Linear Profile of the Mean for Lasmiditan
Logarithmic Profile of the Mean for Lasmiditan
Linear Regression of In-Transformed C_{\max} vs eGFR (Lasmiditan)
Linear Regression of In-Transformed $AUC_{(0-\text{last})}$ vs eGFR (Lasmiditan)
Linear Regression of In-Transformed $AUC_{(0-\infty)}$ vs eGFR (Lasmiditan)
Linear Regression of In-Transformed CL/F vs eGFR (Lasmiditan)
Linear Profile of the Mean for (S)-M8
Logarithmic Profile of the Mean for (S)-M8
Linear Profile of the Mean for (S,R)-M18
Logarithmic Profile of the Mean for (S,R)-M18
Linear Profile of the Mean for M7
Logarithmic Profile of the Mean for M7
Linear Profile of the Mean for (S,S)-M18
Logarithmic Profile of the Mean for (S,S)-M18

PLANNED LISTINGS

Listing 16.2.1	Listing of Study Disposition
Listing 16.2.2.1	Listing of PK Blood Sampling Time Deviations
Listing 16.2.2.2	Listing of PK Urine Sampling Time Deviations
Listing 16.2.3	Listing of Analysis Populations
Listing 16.2.4.1	Listing of Demographic Characteristics
Listing 16.2.4.2	Listing of Screen Failure Subjects
Listing 16.2.5	Listing of Investigational Product Administration
Listing 16.2.7	Listing of Adverse Events
Listing 16.2.8.1	Listing of Blood Chemistry
Listing 16.2.8.2	Listing of Hematology
Listing 16.2.8.3	Listing of Urinalysis
Listing 16.2.8.4	Listing of Urine Drug Screen
Listing 16.2.8.5	Listing of Pregnancy Test
Listing 16.2.8.6	Listing of Serology
Listing 16.2.9.1	Listing of Alcohol Habits
Listing 16.2.9.2	Listing of Smoking Habits
Listing 16.2.9.3	Listing of Prior Medication
Listing 16.2.9.4	Listing of Concomitant Medication
Listing 16.2.9.5	Listing of Physical Examination
Listing 16.2.9.6	Listing of Vital Signs
Listing 16.2.9.7	Listing of ECG Assessments
Listing 16.2.9.8	Listing of Inclusion/Exclusion Criteria Summary
Listing 16.2.9.9	Listing of Medical History
Listing 16.2.9.10	Listing of Columbia-Suicide Severity Rating Scale (C-SSRS)

Pharmacokinetic Data

Appendix 16.2.6	PK Data
Appendix 16.2.6.1	Lasmiditan
Appendix 16.2.6.1.1	PK Tables – Plasma <ul style="list-style-type: none"> - Table X. Measured Human Plasma Concentrations - Table X. Cumulative Area Under the Curve - Table X. Pharmacokinetic Parameters - Table X. Elimination Parameters - Table X. Actual Sampling Time
Appendix 16.2.6.1.2	PK Tables – Urine <ul style="list-style-type: none"> - Table X. Measured Human Urine Concentrations - Table X. Cumulative Amount by Collection Intervals - Table X. Pharmacokinetic Parameters
Appendix 16.2.6.1.3	PK – Figures – Plasma <ul style="list-style-type: none"> - Figure x: Linear Profile of the Mean - Figure x: Logarithmic Profile of the Mean - Figure x: Individual Linear Profile of Subject x - Figure x: Individual Logarithmic Profile of Subject x - Figure x: Individual Elimination Profiles
Appendix 16.2.6.2	(S)-M8
Appendix 16.2.6.2.1	PK Tables – Plasma <ul style="list-style-type: none"> - Table X. Measured Human Plasma Concentrations

	<ul style="list-style-type: none"> - Table X. Cumulative Area Under the Curve - Table X. Pharmacokinetic Parameters - Table X. Elimination Parameters - Table X. Actual Sampling Time
Appendix 16.2.6.2.2	PK Tables – Urine Table X. Measured Human Urine Concentrations
	<ul style="list-style-type: none"> - Table X. Cumulative Amount by Collection Intervals - Table X. Pharmacokinetic Parameters
Appendix 16.2.6.2.3	PK – Figures – Plasma
	<ul style="list-style-type: none"> - Figure x: Linear Profile of the Mean - Figure x: Logarithmic Profile of the Mean - Figure x: Individual Linear Profile of Subject x - Figure x: Individual Logarithmic Profile of Subject x - Figure x: Individual Elimination Profiles
Appendix 16.2.6.3	(S,R)-M18
Appendix 16.2.6.3.1	PK Tables – Plasma
	<ul style="list-style-type: none"> - Table X. Measured Human Plasma Concentrations - Table X. Cumulative Area Under the Curve - Table X. Pharmacokinetic Parameters - Table X. Elimination Parameters - Table X. Actual Sampling Time
Appendix 16.2.6.3.2	PK Tables – Urine Table X. Measured Human Urine Concentrations
	<ul style="list-style-type: none"> - Table X. Cumulative Amount by Collection Intervals - Table X. Pharmacokinetic Parameters
Appendix 16.2.6.3.3	PK – Figures – Plasma
	<ul style="list-style-type: none"> - Figure x: Linear Profile of the Mean - Figure x: Logarithmic Profile of the Mean - Figure x: Individual Linear Profile of Subject x - Figure x: Individual Logarithmic Profile of Subject x - Figure x: Individual Elimination Profiles
Appendix 16.2.6.4	(S,S)-M18
Appendix 16.2.6.4.1	PK Tables – Plasma
	<ul style="list-style-type: none"> - Table X. Measured Human Plasma Concentrations - Table X. Cumulative Area Under the Curve - Table X. Pharmacokinetic Parameters - Table X. Elimination Parameters - Table X. Actual Sampling Time
Appendix 16.2.6.4.2	PK Tables – Urine Table X. Measured Human Urine Concentrations
	<ul style="list-style-type: none"> - Table X. Cumulative Amount by Collection Intervals - Table X. Pharmacokinetic Parameters
Appendix 16.2.6.4.3	PK – Figures – Plasma
	<ul style="list-style-type: none"> - Figure x: Linear Profile of the Mean - Figure x: Logarithmic Profile of the Mean - Figure x: Individual Linear Profile of Subject x - Figure x: Individual Logarithmic Profile of Subject x - Figure x: Individual Elimination Profiles
Appendix 16.2.6.5	M7
Appendix 16.2.6.5.1	PK Tables – Plasma
	<ul style="list-style-type: none"> - Table X. Measured Human Plasma Concentrations - Table X. Cumulative Area Under the Curve - Table X. Pharmacokinetic Parameters - Table X. Elimination Parameters - Table X. Actual Sampling Time

Appendix 16.2.6.5.2	PK Tables – Urine Table X. Measured Human Urine Concentrations
	- Table X. Cumulative Amount by Collection Intervals
	Table X. Pharmacokinetic Parameters
Appendix 16.2.6.5.3	PK – Figures – Plasma
	<ul style="list-style-type: none"> - Figure x: Linear Profile of the Mean - Figure x: Logarithmic Profile of the Mean - Figure x: Individual Linear Profile of Subject x - Figure x: Individual Logarithmic Profile of Subject x - Figure x: Individual Elimination Profiles

APPENDIX A

STUDY SCHEDULES

Examination	Screening	Days			Post-Study Tests or ET ^a	End of Study
	Day 28 to – 1	-1	1	2	2	7 (±3)
Review Inc/Exclusion Criteria & Medical History	X					
Informed Consent	X					
Check-in		X				
Dosing			X			
Clinic Confinement		X	X	X		
Discharge				X		
Demographics	X					
C-SSRS questionnaire	X				X	
Concomitant Medication	X	X	X	X	X	X
Physical Examination	X				X	
Vital Signs	X		X ^b		X	
Height, Weight, and BMI	X					
12-lead ECG	X	X ^c	X ^c		X	
HIV Ag/Ab Combo, HBsAg (B) (Hepatitis B) and HCV (C) Tests	X					
Drug and Alcohol Screen	X	X				
Pregnancy test (females)	X	X			X	
Clinical Laboratory Evaluations	X	X ^d			X	
PK Blood Samples ^e			X	X		
Urine PK Collection ^e			X	X		
Follow-up Call						X
AEs Recording	X	X	X	X	X	

^a Early Termination (ET).

^b Vital signs will be measured prior to dosing and approximately 2 and 4 hours after study drug administration.

- c 12-lead ECG will be performed prior to dosing and approximately 2 hours after study drug administration.
- d Clinical laboratory tests (hematology, biochemistry, and urinalysis) will be performed in the evening prior to drug administration.
- e PK blood and urine samples will be collected according to schedule of PK assessments.

APPENDIX B

Pharmacokinetic Parameters

PK Parameter	Definition
C_{\max}	Maximum observed plasma concentration
T_{\max}	Time of maximum observed plasma concentration; if it occurs at more than one time point, T_{\max} is defined as the first time point with this value
$AUC_{(0-t_{\text{last}})}$	Cumulative area under the plasma concentration time curve calculated from 0 to T_{LQC} using the linear trapezoidal method, where T_{LQC} represents time of last observed quantifiable plasma concentration
$AUC_{(0-\infty)}$	Area under the plasma concentration time curve extrapolated to infinity, calculated as $AUC_{(0-t_{\text{last}})} + \hat{C}_{LQC}/\lambda_z$, where \hat{C}_{LQC} is the estimated concentration at time T_{LQC}
$\%AUC(t_{\text{last}}-\infty)$	Relative percentage of $AUC_{(0-t_{\text{last}})}$ with respect to $AUC_{(0-\infty)}$ $\%AUC(t_{\text{last}} - \infty) = 100 \times \frac{(AUC(0 - \infty) - AUC(0 - t_{\text{last}}))}{AUC(0 - \infty)}$
λ_z	Apparent elimination rate constant, estimated by linear regression of the terminal linear portion of the log concentration <i>versus</i> time curve
$T_{1/2}$	Terminal elimination half-life, calculated as $\ln(2)/\lambda_z$
CL/F^*	Apparent Total Plasma Clearance, calculated as $\text{dose} / AUC_{(0-\infty)}$
V_z/F^*	Apparent Volume of Distribution, calculated as $\text{dose} / \lambda_z * AUC_{(0-\infty)}$
$A_e(0-t)$	Amount excreted in urine (Total analyte concentration * Volume of Urine)
f_e^*	Fraction of dose excreted in urine (A_e / dose)
CL_r	Renal Clearance ($A_e(0-t)/AUC_{(0-t_{\text{last}})}$)

* Not calculated for metabolites

APPENDIX C

TABLE SHELLS

Table 14.1.1
Subject Disposition
(All Subjects)

		Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Overall (N=XX)
Subjects Enrolled				xx
Screen Fail Subjects				xx
Subjects Screened [N]				xx (xx.x)
Subjects Completed the Study [n(%)]	YES			xx (xx.x)
	NO			xx (xx.x)
If No, Reason of Study Discontinuation [n(%)]	Reason 1			xx (xx.x)
	Reason 2			xx (xx.x)
	Reason 3			xx (xx.x)
	Etc.			xx (xx.x)
Number of Subjects Included in Each Analysis Population [n(%)]	Safety Population			xx (xx.x)
	Pharmacokinetic Population			xx (xx.x)

Programming Note: Please add Moderate and Mild Renal Function Groups to the table if enrolled

Note: The percentages are based on the number of subjects screened.

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.1.2.1
Summary of Demographic Characteristics
(Safety Population)

		Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Etc.	Overall (N=XX)
Age (years)	N	xx	xx	xx	xx
	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Gender [n(%)]	MALE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	FEMALE				
Ethnicity [n(%)]	HISPANIC/LATINO	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	NOT HISPANIC/NOT LATINO	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race [n(%)]	RACE1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	RACE2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Weight (kg)	N	xx	xx	xx	xx
	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Height (cm)	N	xx	xx	xx	xx
	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Body Mass Index (kg/m ²)	N	xx	xx	xx	xx
	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Programming Note: Please add Moderate and Mild Renal Function Groups to the table if enrolled					

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Similar Table:

Table 14.1.2.2 Summary of Demographic Characteristics (Pharmacokinetic Population)

Table 14.3.1.1
Summary of Adverse Events
(Safety Population)

	Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Etc.	Overall (N=XX)
Adverse Events (AEs) Reported [n]				XX
Treatment Emergent Adverse Events (TEAEs) Reported [n]	XX	XX	XX	XX
Subjects With At Least One TEAE [n(%)][1]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Subjects With At Least One Drug-Related TEAE [n(%)][1][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
TEAEs Relationship [2]				
Related [n(%)][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Not Related [n(%)][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
TEAEs Severity/Intensity [2]				
Mild [n(%)][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Moderate [n(%)][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Severe [n(%)][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Life-Threatening [n(%)][3]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Serious Adverse Events (SAEs) Reported [n][2]	XX	XX	XX	XX
Subjects With At Least One SAE [n(%)][1]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Subject With an TEAE Leading to Withdrawal [n(%)][1]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Death [n(%)][1]	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Programming Note: Please add Moderate and Mild Renal Function Groups to the table if enrolled				

[1] Percentages are based on the number of subjects in the Safety population in each treatment group.

[2] Percentages are based on the total number of treatment emergent adverse events reported in each treatment group.

[3] TEAE that was reported with a relationship of "reasonable possibility".

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.1.2
Summary of Treatment Emergent Adverse Events by System Organ Class and MedDRA Preferred Term
(Safety Population)

SOC MedDRA Preferred Term	Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Etc.
Subjects With At Least One TEAE [n(%)]		xx (xx.x)	xx (xx.x)
System Organ Class 1 [n(%)]		xx (xx.x)	xx (xx.x)
MedDRA Term 11 [n(%)]		xx (xx.x)	xx (xx.x)
MedDRA Term 12 [n(%)]		xx (xx.x)	xx (xx.x)
MedDRA Term 13 [n(%)]		xx (xx.x)	xx (xx.x)
System Organ Class 2 [n(%)]		xx (xx.x)	xx (xx.x)
MedDRA Term 21 [n(%)]		xx (xx.x)	xx (xx.x)
MedDRA Term 22 [n(%)]		xx (xx.x)	xx (xx.x)
MedDRA Term 23 [n(%)]		xx (xx.x)	xx (xx.x)
Etc.		xx (xx.x)	xx (xx.x)

Programming Note: Please add Moderate and Mild Renal Function Groups to the table if enrolled

Note: Each treatment emergent adverse event is counted only once for each subject within each System Organ Class and MedDRA Preferred Term.

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Similar Table: Table 14.3.1.3 Summary of Drug-Related Treatment Emergent Adverse Events by System Organ Class and MedDRA Preferred Term

Table 14.3.2.1
Listing of Deaths, Other Serious and Significant Adverse Events
(Safety Population)

Subject ID	Day/ Group/ AE #	SOC MedDRA Preferred Term Description of AE	Onset Date Time (Time since Last Dose)	Resolution Date Time (Duration)	I: Maximal Intensity R: Causality Assessment	O: Outcome S: Serious AE D: AE Lead To Discontinuation	Action Taken With Study Treatment / Other Action(s) Taken / Concomitant Given
xxx	xxxxx xxxxx	xxxxxxxxxxxxx xxxxxxxxxxxxx xxxxxxxxxxxxx	YYYY-MM-DD/ HH:MM (DD:HH:MM)	YYYY-MM- DD/ HH:MM (DD:HH:MM)	xxxxxxx	xxxxxx	xxxxxxx

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Similar Tables:

14.3.2.2 Listing of Adverse Events Leading to Withdrawal

Table 14.3.4.1
Listing of Abnormal On-Study Laboratory Values
(Safety Population)

Category/ Parameter (Unit)	Reference Range	Subject ID	Visit	Date / Time	Value	Out-of-Range Flag	Assessment [1]
Lab Category 1							
Lab Test 11	xxx-xxx	xxx	xxxxxxx	xxxxxxx	xxx	xxx	xxx
Lab Test 12	xxx-xxx	xxx	xxxxxxx	xxxxxxx	xxx	xxx	xxx
Lab Category 2							
Lab Test 21	xxx-xxx	xxx	xxxxxxx	xxxxxxx	xxx	xxx	xxx
Lab Test 22	xxx-xxx	xxx	xxxxxxx	xxxxxxx	xxx	xxx	xxx
Etc.	xxx-xxx	xxx	xxxxxxx	xxxxxxx	xxx	xxx	xxx

[1] NCS: Not Clinically Significant / CS: Clinically Significant / RPT: Repeated / TBC: To Be Controlled.

Note(s): Abnormal values are determined by applying the reference ranges to the results as reported by the external laboratory analysis.

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.4.2
Listing of Clinically Significant On-Study Laboratory Values
(Safety Population)

Category/ Parameter (Unit)	Reference Range	Subject ID	Visit	Date / Time	Value	Out-of- Range Flag	Assessment [1]
Lab Category 1							
Lab Test 11	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx
Lab Test 12	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx
Lab Category 2							
Lab Test 21	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx
Lab Test 22	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx
Etc.	xxx-xxx	xxx	xxxxxx	xxxxxx	xxx	xxx	xxx

[1] CS: Clinically Significant / RPT: Repeated / TBC: To Be Controlled

Note(s): Abnormal values are determined by applying the reference ranges to the results as reported by the external laboratory analysis.

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.4.3
Summary of Blood Chemistry
(Safety Population)

Parameter (unit)	Statistic	Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Etc. (N=XX)
Visit Name				
xxx (xxx)	Screening Value	N Mean (SD) Median Min, Max	xx xx.x (xx.xx) xx.x xx, xx	xx xx.x (xx.xx) xx.x xx, xx
	Day -1 Value	N Mean (SD) Median Min, Max	xx xx.x (xx.xx) xx.x xx, xx	xx xx.x (xx.xx) xx.x xx, xx
	Etc.	N Mean (SD) Median Min, Max	xx xx.x (xx.xx) xx.x xx, xx	xx xx.x (xx.xx) xx.x xx, xx

Programming Note: Please add Moderate and Mild Renal Function Groups to the table if enrolled

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Similar Tables:

14.3.4.4 Summary of Hematology

14.3.4.5 Summary of Quantitative Urinalysis

Table 14.3.5.1
Listing of Abnormal On-Study Vital Signs Values
(Safety Population)

Assessment (Units)	Subject ID	Visit	Elapsed Time	Position	Date / Time	Value	Safety Review
Vital Sign Test 1	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
Vital Sign Test 2	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
Etc.	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx

Date: VERSION - YYYY-MM-DD Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.5.2
Listing of Clinically Significant On-Study Vital Signs Values
(Safety Population)

Assessment (Units)	Subject ID	Visit	Elapsed Time	Position	Date / Time	Value	Safety Review
Vital Sign Test 1	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
Vital Sign Test 2	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx
Etc.	xxx	xxxxxx	xxxxxx	xxxxxx	YYYY-MM-DD:XX:XX	xxx	xxx

Date: VERSION - YYYY-MM-DD Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.5.3
Summary of Vital Signs
(Safety Population)

Parameter (unit)	Visit	Timepoint	Statistic	Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Etc. (N=XX)
Vital Sign Test 1	Screening	Value	N			xx
			Mean (SD)			xx (xx.x)
			Median			xx.x
			Min, Max			xx, xx
	Day 1	2 Hours	N	xx	xx	xx
			Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
			Median	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx
	Day 1	4 Hours	N	xx	xx	xx
			Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
			Median	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx
Etc.	Etc.					

PROGRAMMING NOTE: All visits outlined in Appendix A will be included. **Please add Moderate and Mild Renal Function Groups to the table if enrolled**

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.6.1
Listing of Abnormal On-Study ECG Assessments
(Safety Population)

Subject ID	Visit	Time Point	Date / Time	Position	Safety Review	Parameter (Unit)	Value
xxxxx	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
xxxxx	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		
xxxxx	xxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxx	xxxxxx		

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.6.2
Listing of Clinically On-Study ECG Assessments
(Safety Population)

Subject ID	Visit	Time Point	Date / Time	Position	Safety Review	Parameter (Unit)	Value
xxxxxx	xxxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		
xxxxxx	xxxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		
xxxxxx	xxxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		
xxxxxx	xxxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		
xxxxxx	xxxxxxx	xxx	YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Table 14.3.6.3
Summary of ECG Assessments
(Safety Population)

Parameter (unit)	Visit	Timepoint	Statistic	Healthy Renal Function (N=XX)	Severe Renal Function (N=XX)	Etc. (N=XX)
ECG Assessment Test 1	Screening	Value	N			xx
			Mean (SD)			xx (xx.x)
			Median			xx.x
			Min, Max			xx, xx
	Day -1	Value	N	xx	xx	xx
			Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
			Median	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx
	Day 1	Pre-dose	N	xx	xx	xx
			Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
			Median	xx.x	xx.x	xx.x
			Min, Max	xx, xx	xx, xx	xx, xx
Etc.	Etc.					

PROGRAMMING NOTE: All visits outlined in Appendix A will be included. **Please add Moderate and Mild Renal Function Groups to the table if enrolled**

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

APPENDIX D

PHARMACOKINETIC OUTPUTS SHELLS

Measured Human Plasma Concentrations of Lasmiditan, Normal Renal Function, CUD-P4-001

		Time (h)									
		0.00	0.25	0.50	1.00	36.00
Renal Function	Subject	Concentration (ng/mL)									
Normal	101										
	...										
	...										
	...										
	...										
	...										
	...										
	108										
N											
Mean											
SD											
Min											
Median											
Max											
CV%											
Geometric Mean											
Geometric CV%											
BLQ : Below Limit of Quantitation											
NC: Not Calculated											

Similar tables will be presented for all renal groups, for urine concentrations and for all analytes.

Cumulative Area Under the Curve of Lasmiditan, Normal Renal Function, CUD-P4-001

		Time (h)									
		0.00	0.25	0.50	1.00	36.00
Renal Function	Subject	Cumulative AUC (ng*h/mL)									
Normal	101										
	...										
	...										
	...										
	...										
	...										
	...										
	108										
N											
Mean											
SD											
Min											
Median											
Max											
CV%											
Geometric Mean											
Geometric CV%											
NC: Not Calculated											

Similar tables will be presented for all renal groups, for urine data by intervals and for all analytes.

Pharmacokinetic Parameters of Lasmiditan, Normal Renal Function, CUD-P4-001

Renal Function	Subject	C _{max} (ng/mL)	T _{max} (h)	AUC _(0-tlast) (ng*h/mL)	AUC _(0-∞) (ng*h/mL)	%AUC _(0-tlast/∞) (%)	T _{1/2} (h)	CL/F (L/h)	V _Z /F (L)
Normal	101								
	...								
	...								
	...								
	...								
	...								
	...								
	108								
N									
Mean			NC				NC		
SD			NC				NC		
Min									
Median									
Max									
CV%			NC				NC		
Geometric Mean			NC						
Geometric CV%			NC						

Similar tables will be presented for all renal groups, for urine parameters and for all analytes.

Elimination Parameters of Lasmiditan, Normal Renal Function, CUD-P4-001

Renal Function	Subject	T_{LIN} (h)	T_{LQC} (h)	Number of Points	R^2	λ_z (1/h)
Normal	101					
	...					
	...					
	...					
	...					
	...					
	...					
	108					
N Mean SD Min Median Max CV% Geometric Mean Geometric CV%						

A similar table will be presented for all renal groups and for all analytes.

Actual Sampling Time of Lasmiditan, Normal Renal Function, CUD-P4-001

		Time (h)													
		0.00	0.25	0.50	1.00	36.00
Renal Function	Subject	Actual Time (h)													
Normal	101														
	...														
	...														
	...														
	...														
	...														
	...														
	108														
N															
Mean															
SD															
Min															
Median															
Max															
CV%															
Geometric Mean															
Geometric CV%															
NC: Not Calculated															

A similar table will be presented for all renal groups and for all analytes.

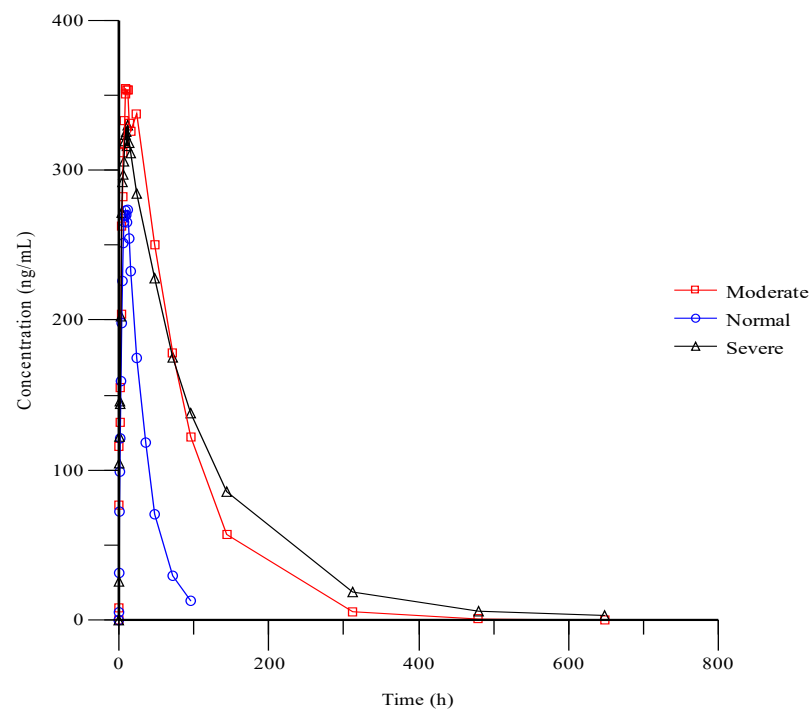
Pairwise Comparisons of Lasmiditan, CUD-P4-001

Parameters	Geometric LSmeans ^a		Comparison	Adjusted p-value	Ratio (%)	90% Confidence Limits (%)	
	Group					Lower	Upper
C _{max}	Mild (n=x)		Mild vs Normal				
	Moderate (n=x)		Moderate vs Normal				
	Severe (n=x)		Severe vs Normal				
	Normal (n=x)		Mild vs Moderate				
	NA	NA	Mild vs Severe				
	NA	NA	Moderate vs Severe				
AUC _(0-tlast)	Mild (n=x)		Mild vs Normal				
	Moderate (n=x)		Moderate vs Normal				
	Severe (n=x)		Severe vs Normal				
	Normal (n=x)		Mild vs Moderate				
	NA	NA	Mild vs Severe				
	NA	NA	Moderate vs Severe				
AUC _(0-∞)	Mild (n=x)		Mild vs Normal				
	Moderate (n=x)		Moderate vs Normal				
	Severe (n=x)		Severe vs Normal				
	Normal (n=x)		Mild vs Moderate				
	NA	NA	Mild vs Severe				
	NA	NA	Moderate vs Severe				

^a C_{max} is presented in ng/mL, AUC_(0-tlast) and AUC_(0-∞) are presented in ng*h/mL

PHARMACOKINETIC FIGURES SHELLS

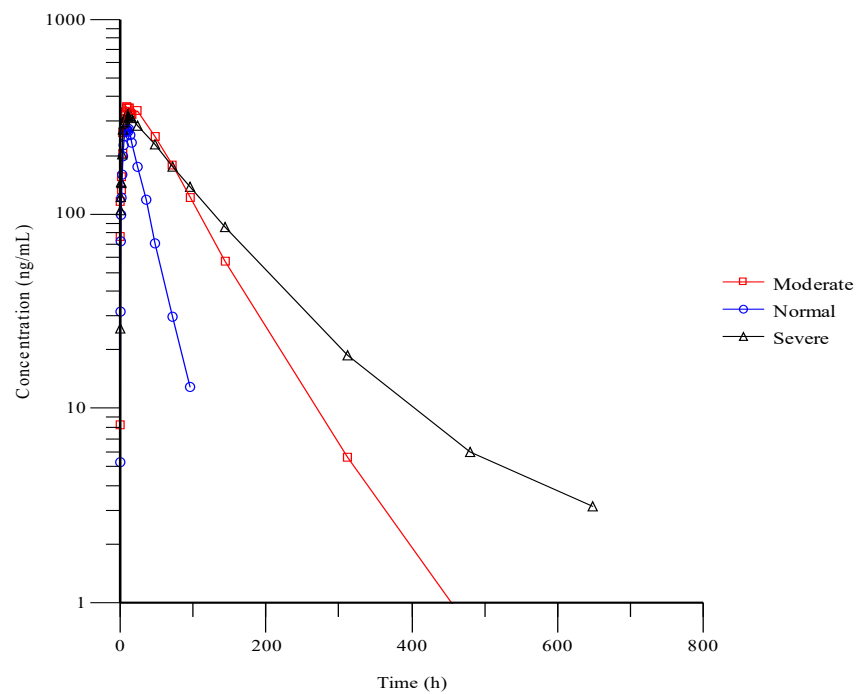
Figure 1: Linear Profile of the Mean of Lasmiditan in Plasma



The figure does not reflect the actual data of the study

Figures will be presented for all analytes.

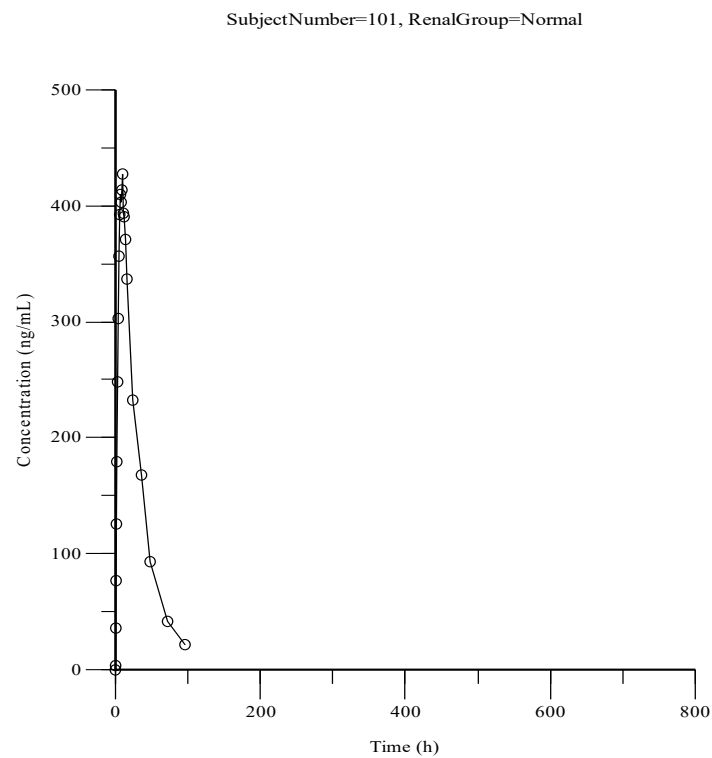
Figure 2: Logarithmic Profile of the Mean of Lasmiditan in Plasma



The figure does not reflect the actual data of the study.

Figures will be presented for all analytes.

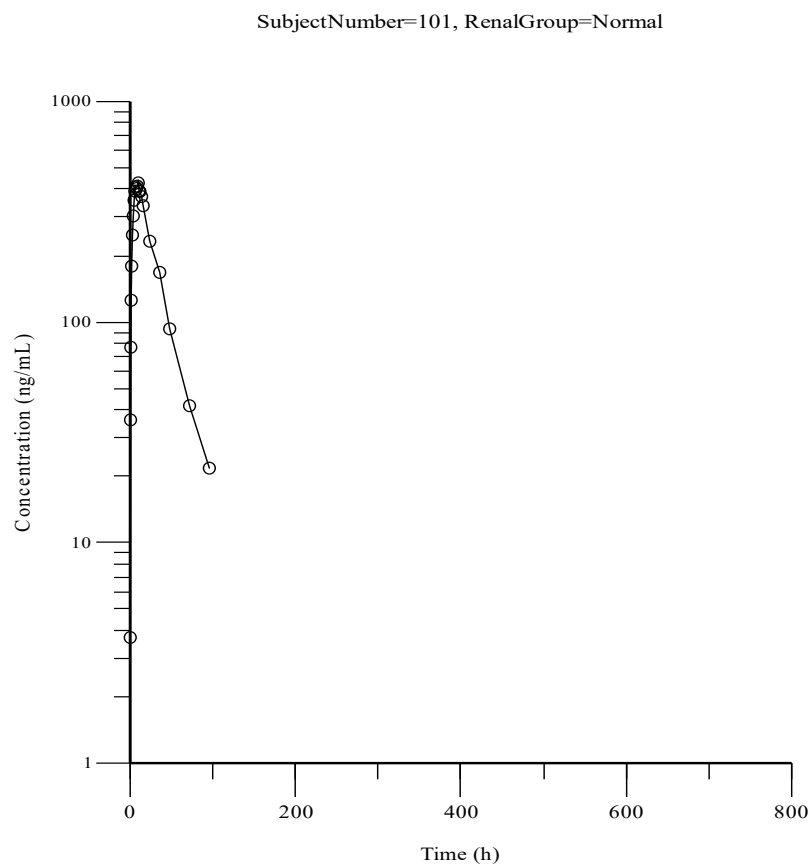
Figures 2+1 to (2+1)+N: Individual Linear Profile of Lasmiditan in Plasma



The figure does not reflect the actual data of the study

Figures will be presented for all analytes.

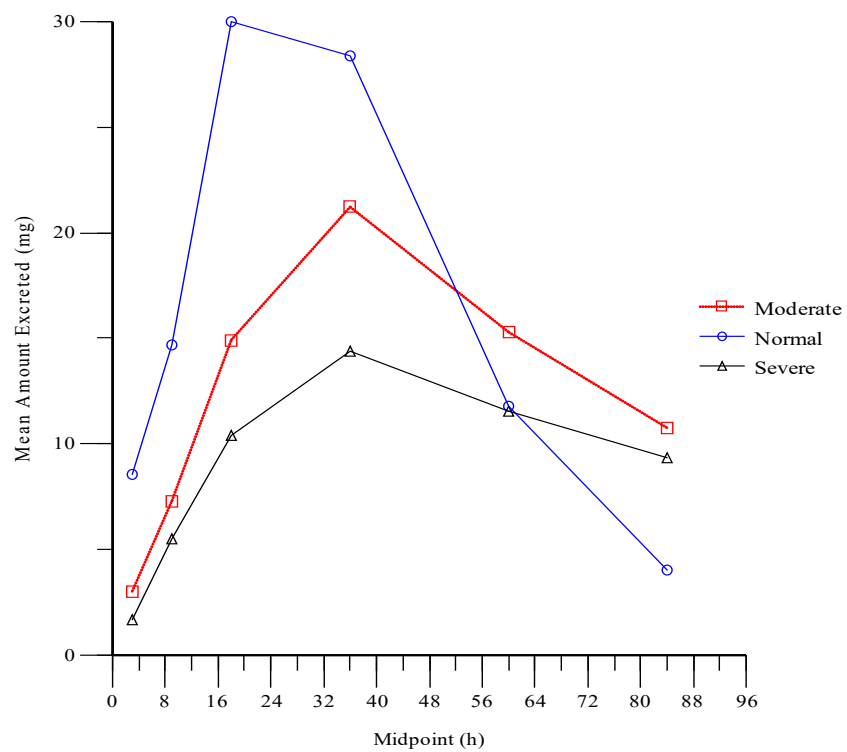
Figure X: Individual Logarithmic Profile of Lasmiditan in Plasma



The figure does not reflect the actual data of the study.

Figures will be presented for all analytes.

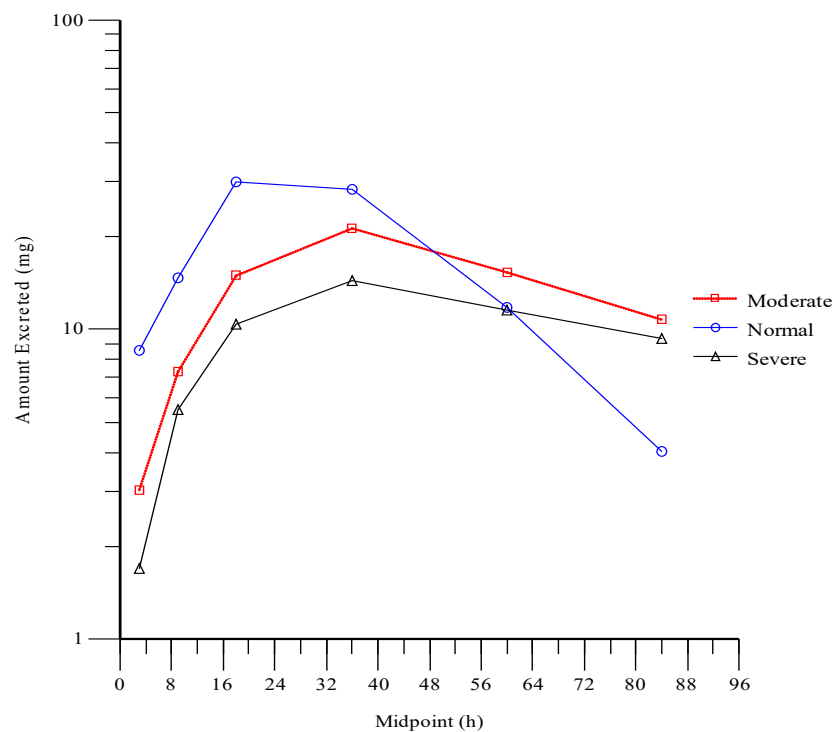
Figure 1: Linear Profile of the Mean of Lasmiditan in Urine



The figure does not reflect the actual data of the study.

Figures will be presented for all analytes.

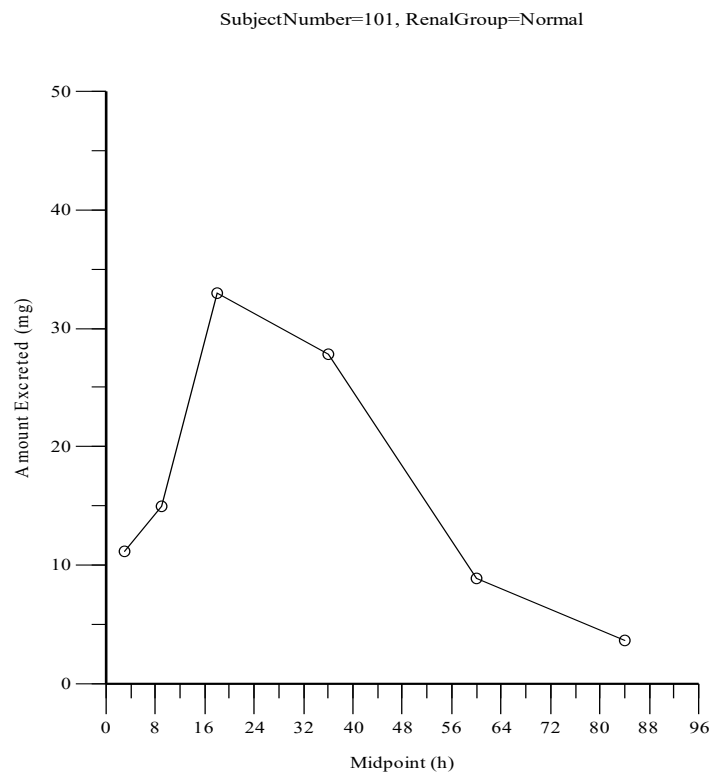
Figure 2: Logarithmic Profile of the Mean of Lasmiditan in Urine



The figure does not reflect the actual data of the study.

Figures will be presented for all analytes.

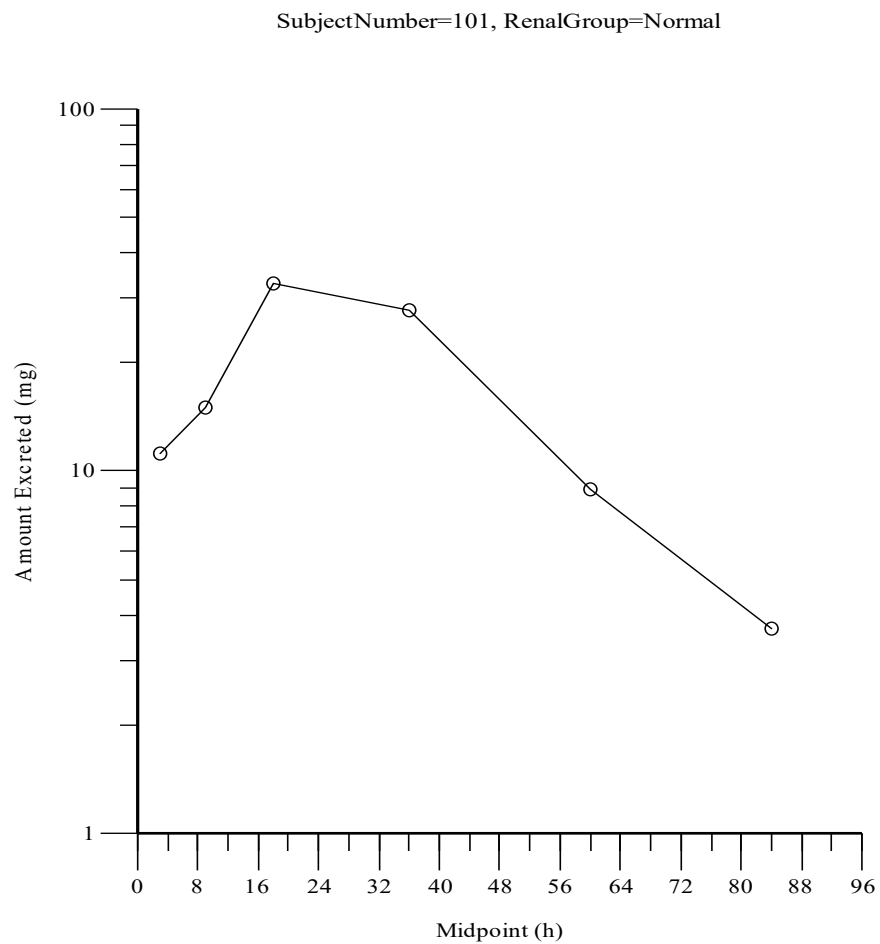
Figures 2+1 to (2+1)+N: Individual Linear Profile of the Mean of Lasmiditan in Urine



The figure does not reflect the actual data of the study

Figures will be presented for all analytes.

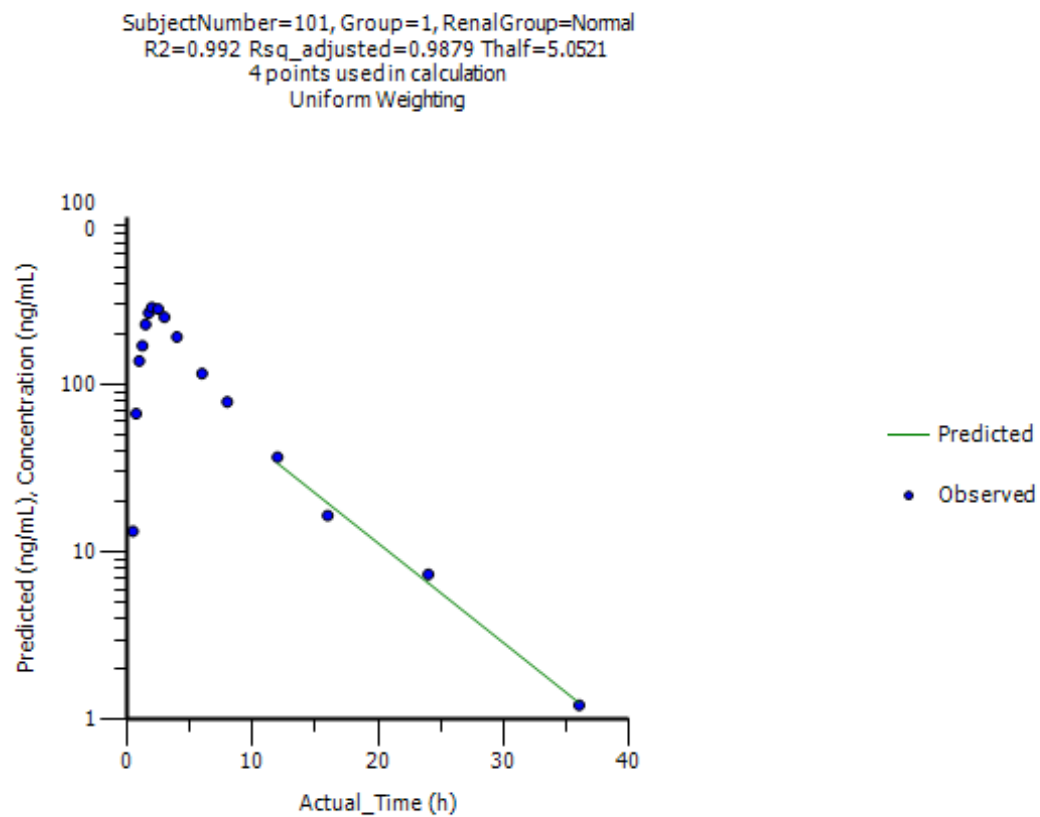
Figure N: Individual Logarithmic Profile of the Mean of Lasmiditan in Urine



The figure does not reflect the actual data of the study

Figures will be presented for all analytes.

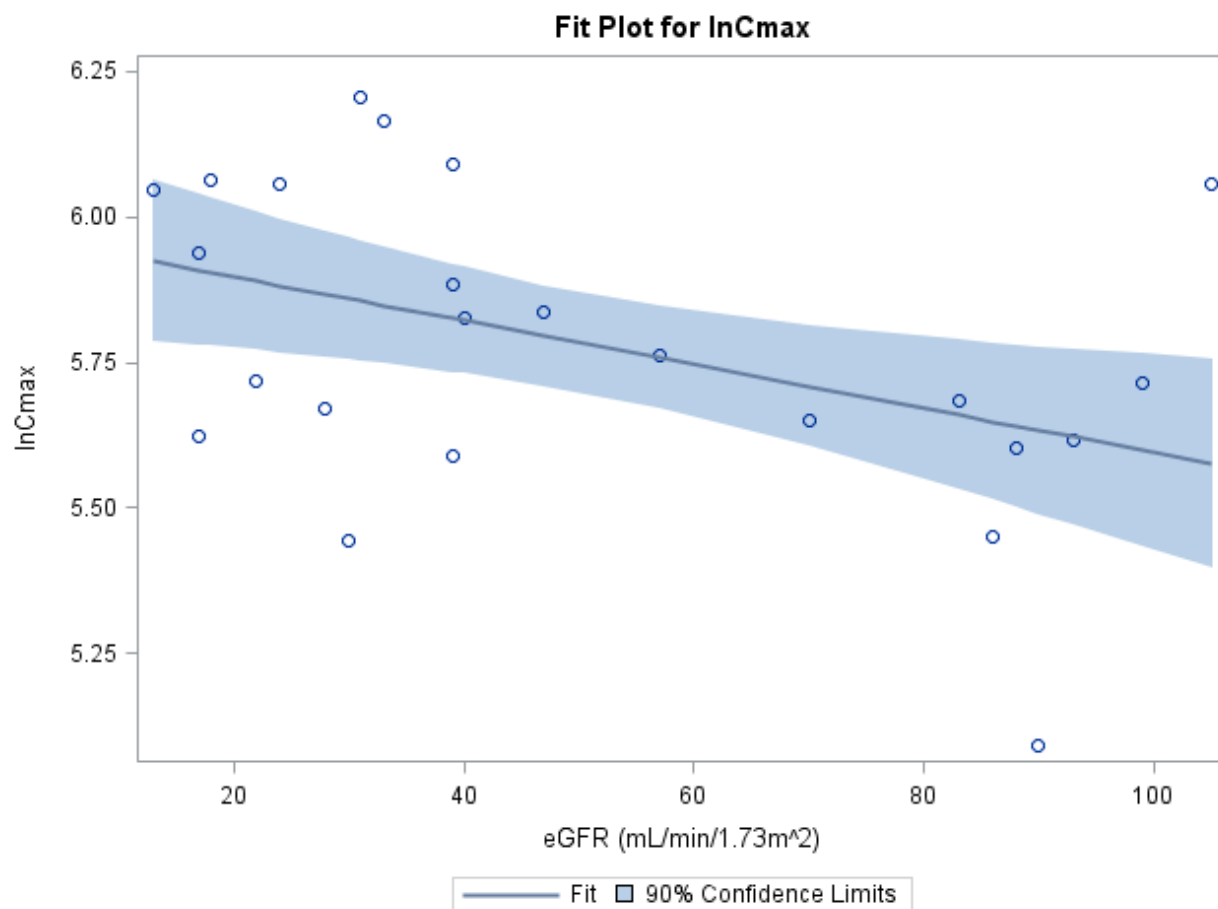
Figure N: Individual Elimination Profiles



The figure does not reflect the actual data of the study.

In Text Figure:

Figure 1: Linear Regression of In-Transformed C_{max} vs eGFR (Lasmiditan)



The figure does not reflect the actual data of the study. Same graph will be presented for $AUC_{(0-last)}$, $AUC_{(0-\infty)}$ and CL/F.

APPENDIX E

LISTING SHELLS

Listing 16.2.1
Listing of Study Disposition

Subject ID	Date of Completion or Discontinuation	Subject Status	Specify	AE #	Date of Death
------------	--	----------------	---------	------	---------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.2.1
Listing of PK Blood Sampling Time Deviations

Group	Elapsed Time (h)	Subject ID	Scheduled Date/Time	Actual Date/Time	Deviation (min)
-------	---------------------	------------	------------------------	---------------------	-----------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Similar Listing: Listing 16.2.2.2 Listing of PK Urine Sampling Time Deviations

Listing 16.2.3
Listing of Analysis Populations

Subject ID	Safety Population	PK Population	Reason if Excluded from one Population
------------	----------------------	---------------	--

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

CoLucid Pharmaceuticals, Inc.
Project # COL MIG-113/CUD-P4-001

Algorithme Pharma
Page 1 of x

Listing 16.2.4.1
Listing of Demographic Characteristics

Subject ID	Age	Date of Birth	Gender	Ethnicity	Race	Other Race	Weight (kg)	Height (cm)	BMI (kg/m ²)
------------	-----	---------------	--------	-----------	------	------------	-------------	-------------	--------------------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.4.2
Listing of Screen Failures

Subject ID	Date	Specify Primary Reason
------------	------	------------------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

CoLucid Pharmaceuticals, Inc.
Project # COL MIG-113/CUD-P4-001

Algorithme Pharma
Page 1 of x

Listing 16.2.5
Listing of Investigational Product Administration

Subject ID	Visit	Start Date/Time	Treatment	Dose Administered (mg)	Route	If Any Dosing Issues, Specify
------------	-------	--------------------	-----------	---------------------------	-------	----------------------------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.7
Listing of Adverse Events

Subject ID	Visit/ Group/ AE #	SOC MedDRA Preferred Term Description of AE	Onset Date Time (Time since Last Dose)	Resolution Date Time (Duration)	I: Maximal Severity R: Causality Assessment	O: Outcome S: Serious AE D: AE Leading To Discontinuation	Action Taken With Study Treatment / Other Action(s) Taken / Concomitant Given
xxx	xxxxx xxxxx	xxxxxxxxxxxxx xxxxxxxxxxxxx xxxxxxxxxxxxx	YYYY-MM-DD/ HH:MM (DD:HH:MM)	YYYY-MM-DD/ HH:MM (DD:HH:MM)	xxxxxxx	xxxxxx	xxxxxxx

Listing 16.2.8.1
Listing of Blood Chemistry

Subject ID	Lab Test Name (Units)	Reference Range	Visit	Date / Time	Value	Out-of-Range Flag	Assessment [1]
------------	-----------------------	-----------------	-------	-------------	-------	-------------------	----------------

[1] NCS: Not Clinically Significant / CS: Clinically Significant / RPT: Repeated / TBC: To Be Controlled.

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Similar listing(s) :

L16.2.8.2	Listing of Hematology
L16.2.8.3	Listing of Urinalysis
L16.2.8.4	Listing of Urine Drug Screen
L16.2.8.5	Listing of Pregnancy Test
L16.2.8.5	Listing of Serology

Listing 16.2.9.1
Listing of Alcohol Habits

Subject ID	Intake Status	Quantity	Frequency	Start Date	End Date
------------	---------------	----------	-----------	------------	----------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.9.2
Listing of Smoking Habits

Subject ID	Intake Status	Quantity	Frequency	Start Date	End Date
------------	---------------	----------	-----------	------------	----------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

CoLucid Pharmaceuticals, Inc.
Project # COL MIG-113/CUD-P4-001

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Listing 16.2.9.3
Listing of Prior Medication

Subject ID	#CM	Related to AE#/MH#	ATC / PT /	Indication	Dose (unit)	Frequency	Formulation	Total Daily Dose	Route	Start Date/ Time	End Date/ Time
			Medication Name								

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Similar Listing:

Listing 16.2.9.4 Listing of Concomitant Medication

Listing 16.2.9.5
Listing of Physical Examination

Subject ID	Visit	Date / Time	Body System Examined	Result (Abnormal Findings)
------------	-------	-------------	----------------------	----------------------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.9.6
Listing of Vital Signs

Subject ID	Visit	Elapsed Time	Position	Date / Time	Assessment (Units)	Value	Safety Review
------------	-------	--------------	----------	-------------	-----------------------	-------	------------------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.9.7
Listing of ECG Assessments

Subject ID	Visit	Time Point	Date / Time	Position	Safety Review	Parameter (Unit)	Value
xxxxxx	xxxxxxx		YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		
			YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		
			YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		
xxxxxx	xxxxxxx		YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		
xxxxxx	xxxxxxx		YYYY-MM-DD: HH:MM	xxxxxxx	xxxxxxx		

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

Listing 16.2.9.8
Listing of Inclusion/Exclusion Criteria Summary

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

CoLucid Pharmaceuticals, Inc.
Project # COL MIG-113/CUD-P4-001

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Listing 16.2.9.9
Listing of Medical History

Subject ID	MH #	System Organ Class	MedDRA Preferred Term	Description of Medical History	Start Date	End Date

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas

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Project # COL MIG-113/CUD-P4-001

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Listing 16.2.9.10
Listing of Columbia-Suicide Severity Rating Scale (C-SSRS)

Subject ID	Visit	Category	Question	Answer
------------	-------	----------	----------	--------

Date: VERSION - YYYY-MM-DD

Data Source: XXXX

Program Source: XXXXX.sas



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Overland Park, KS 66212

United States

913 696-1601

vinceandassociates.com



4837 Amber Valley Parkway

Fargo, ND 58104

United States

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algopharm.com

16.1.9.2 Documentation of statistical analysis – SAS® output of Lasmiditan

Legend:

- AUCinf= $AUC_{(0-\infty)}$
- AUCT= $AUC_{(0-tlast)}$
- V_{Z_F}= V_Z/F
- CL_F= CL/F
- LambdaZ = λ_Z
- lCmax= $\ln(C_{max})$
- lAUCT= $\ln(AUC_{(0-tlast)})$
- lAUCinf= $\ln(AUC_{(0-\infty)})$
- lCLF= $\ln(CL/F)$
- lLambdaZ = $\ln(\lambda_Z)$
- lV_{Z_F}= $\ln(V_Z/F)$
- RkTmax= Rank of T_{max}

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Normal

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	fe	CLr	Vz F	Cl F	AUCinf	Res Area
1	101	288.00000	2.00000	1742.02000	5.05210	4.46677	2.23338	2564.12957	832.41956	114.20774	1751.19483	0.52392
2	102	303.00000	3.00000	2269.41500	5.89140	6.98788	3.49394	3079.15256	741.32912	87.22046	2293.04005	1.03029
3	103	514.00000	1.25000	2253.80500	3.57464	7.23717	3.61858	3211.08792	455.15651	88.25795	2266.08474	0.54189
4	104	326.00000	2.50000	1829.20892	3.54085	3.12512	1.56256	1708.45439	552.42749	108.14168	1849.42566	1.09314
5	105	126.00000	1.00000	618.34750	3.51372	2.74783	1.37392	4443.82811	1623.58102	320.28197	624.44976	0.97722
6	106	276.00000	2.50000	1514.40000	3.02245	4.12476	2.06238	2723.68991	572.82872	131.36837	1522.43647	0.52787
7	107	173.00000	3.00000	1327.93883	4.05010	4.73839	2.36919	3568.22610	863.25825	147.74065	1353.72355	1.90473
8	108	232.00000	2.50000	1955.87600	5.89271	5.64905	2.82453	2888.24547	859.21551	101.06779	1978.86981	1.16197

Obs	Lambda z	lnCmax	lnAUCT	lnAUCinf	lnAe	lnCLr	lnLambda z	lnCl F	lnfe	lnVz F	RkTmax	eGFR	CrCL
1	0.13720	5.66296	7.46280	7.46805	1.49666	7.84937	-1.98632	4.73802	0.80352	6.72434	8.0	115.00000	163.85000
2	0.11765	5.71373	7.72728	7.73763	1.94418	8.03241	-2.14001	4.46844	1.25103	6.60844	14.5	102.00000	152.84000
3	0.19391	6.24222	7.72038	7.72581	1.97923	8.07437	-1.64038	4.48026	1.28608	6.12064	5.0	94.00000	100.45000
4	0.19576	5.78690	7.51164	7.52263	1.13947	7.44334	-1.63088	4.68344	0.44633	6.31432	10.0	109.00000	124.34000
5	0.19727	4.83628	6.42705	6.43687	1.01081	8.39927	-1.62319	5.76920	0.31766	7.39239	3.5	102.00000	155.18000
6	0.22933	5.62040	7.32277	7.32807	1.41701	7.90974	-1.47258	4.87801	0.72386	6.35059	10.0	116.00000	120.18000
7	0.17114	5.15329	7.19138	7.21061	1.55570	8.17982	-1.76526	4.99546	0.86255	6.76071	14.5	98.00000	116.39000
8	0.11763	5.44674	7.57859	7.59028	1.73149	7.96840	-2.14023	4.61579	1.03834	6.75602	10.0	118.00000	147.36000

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Severe

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	fe	CLr	Vz_F	Cl_F	AUCinf	Res Area
9	201	341.00000	0.75000	2224.39000	6.29100	1.96752	0.98376	884.51935	806.25652	88.83396	2251.39127	1.19932
10	202	163.00000	3.00000	1103.70000	3.41530	1.47176	0.73588	1333.47377	884.24501	179.46073	1114.44994	0.96460
11	203	235.00000	3.00000	2075.78225	6.68086	3.55816	1.77908	1714.12729	910.20931	94.43528	2117.85268	1.98647
12	204	294.00000	1.81667	1762.09667	3.32045	0.99397	0.49698	564.08143	539.37588	112.59515	1776.27542	0.79823
13	205	424.00000	1.75000	3325.83000	6.47006	2.65410	1.32705	798.02636	553.25258	59.27081	3374.34231	1.43768
14	206	470.00000	0.75000	1825.62167	3.16277	1.13428	0.56714	621.31329	497.02008	108.92594	1836.10995	0.57122
15	207	263.00000	1.00000	1555.42500	4.26959	2.25069	1.12534	1446.99037	777.65537	126.24861	1584.17584	1.81488
16	208	269.00000	2.56667	1728.08917	3.55680	1.98568	0.99284	1149.06108	587.07806	114.40937	1748.10852	1.14520

Obs	Lambda_z	lnCmax	lnAUCT	lnAUCinf	lnAe	lnCLr	lnLambda_z	lnCl_F	lnfe	lnVz_F	RkTmax	eGFR	CrCL
9	0.11018	5.83188	7.70724	7.71930	0.67677	6.78504	-2.20563	4.48677	-0.01638	6.69240	1.5	26.00000	40.09000
10	0.20295	5.09375	7.00642	7.01612	0.38646	7.19554	-1.59478	5.18996	-0.30669	6.78473	14.5	23.00000	29.51000
11	0.10375	5.45959	7.63809	7.65816	1.26924	7.44666	-2.26576	4.54791	0.57609	6.81367	14.5	26.00000	43.68000
12	0.20875	5.68358	7.47426	7.48227	-0.00605	6.33520	-1.56661	4.72380	-0.69920	6.29041	7.0	19.00000	30.22000
13	0.10713	6.04973	8.10947	8.12396	0.97611	6.68214	-2.23370	4.08212	0.28296	6.31581	6.0	27.00000	26.90000
14	0.21916	6.15273	7.50968	7.51540	0.12600	6.43184	-1.51796	4.69067	-0.56715	6.20863	1.5	16.00000	20.27000
15	0.16235	5.57215	7.34950	7.36782	0.81123	7.27724	-1.81803	4.83825	0.11809	6.65628	3.5	21.00000	30.33000
16	0.19488	5.59471	7.45477	7.46629	0.68596	7.04670	-1.63537	4.73978	-0.00719	6.37516	12.0	28.00000	65.77000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 DESCRIPTIVE RESULTS (OVERALL)
 ----- SUMMARY REPORT -----

Parameter	Renal Function Group	n	Min	Mean	Geometric Mean	Median	Max	Standard Deviation	Coefficient of Variation
Cmax	Normal	8	126.00000	279.75000	259.25593	282.00000	514.00000	116.46551	41.632
Cmax	Severe	8	163.00000	307.37500	292.88094	281.50000	470.00000	100.62794	32.738
Tmax	Normal	8	1.00000	2.21875	2.08090	2.50000	3.00000	0.74926	33.769
Tmax	Severe	8	0.75000	1.82917	1.59223	1.78333	3.00000	0.94934	51.900
AUCT	Normal	8	618.34750	1688.87641	1584.04463	1785.61446	2269.41500	542.04977	32.095
AUCT	Severe	8	1103.70000	1950.11684	1865.30538	1793.85917	3325.83000	649.83012	33.323
Thalf	Normal	8	3.02245	4.31725	4.19268	3.81237	5.89271	1.13690	26.334
Thalf	Severe	8	3.16277	4.64585	4.42920	3.91320	6.68086	1.55718	33.518
Ae	Normal	8	2.74783	4.88462	4.63816	4.60258	7.23717	1.64654	33.709
Ae	Severe	8	0.99397	2.00202	1.85098	1.97660	3.55816	0.84180	42.048
fe	Normal	8	1.37392	2.44231	2.31908	2.30129	3.61858	0.82327	33.709
fe	Severe	8	0.49698	1.00101	0.92549	0.98830	1.77908	0.42090	42.048
CLr	Normal	8	1708.45439	3023.35175	2928.05019	2983.69901	4443.82811	792.90521	26.226
CLr	Severe	8	564.08143	1063.94912	992.31982	1016.79021	1714.12729	413.70175	38.884
Vz_F	Normal	8	455.15651	812.52702	756.29525	786.87434	1623.58102	362.69776	44.638
Vz_F	Severe	8	497.02008	694.38660	676.63956	682.36672	910.20931	167.54105	24.128
Cl_F	Normal	8	87.22046	137.28583	125.03299	111.17471	320.28197	76.75183	55.907
Cl_F	Severe	8	59.27081	110.52248	105.89071	110.76055	179.46073	34.59494	31.301
AUCinf	Normal	8	624.44976	1704.90311	1599.57784	1800.31024	2293.04005	545.49033	31.995
AUCinf	Severe	8	1114.44994	1975.33824	1888.73988	1806.19268	3374.34231	661.00665	33.463
Res_Area	Normal	8	0.52392	0.97013	0.88165	1.00376	1.90473	0.46401	47.830
Res_Area	Severe	8	0.57122	1.23970	1.15335	1.17226	1.98647	0.48634	39.230
Lambda_z	Normal	8	0.11763	0.16999	0.16532	0.18252	0.22933	0.04151	24.417
Lambda_z	Severe	8	0.10375	0.16364	0.15649	0.17861	0.21916	0.04968	30.360
lnCmax	Normal	8	4.83628	5.55782		5.64168	6.24222	0.42372	7.624
lnCmax	Severe	8	5.09375	5.67977		5.63915	6.15273	0.33688	5.931
lnAUCT	Normal	8	6.42705	7.36774		7.48722	7.72728	0.42187	5.726
lnAUCT	Severe	8	7.00642	7.53118		7.49197	8.10947	0.31504	4.183
lnAUCinf	Normal	8	6.43687	7.37750		7.49534	7.73763	0.42099	5.706
lnAUCinf	Severe	8	7.01612	7.54367		7.49884	8.12396	0.31634	4.193
lnAe	Normal	8	1.01081	1.53432		1.52618	1.97923	0.34855	22.717
lnAe	Severe	8	-0.00605	0.61571		0.68137	1.26924	0.42809	69.528
lnCLr	Normal	8	7.44334	7.98209		8.00041	8.39927	0.27709	3.471
lnCLr	Severe	8	6.33520	6.90005		6.91587	7.44666	0.40512	5.871
lnLambda_z	Normal	8	-2.14023	-1.79985		-1.70282	-1.47258	0.25630	-14.240
lnLambda_z	Severe	8	-2.26576	-1.85473		-1.72670	-1.51796	0.32714	-17.638
lnCl_F	Normal	8	4.46844	4.82858		4.71073	5.76920	0.42099	8.719
lnCl_F	Severe	8	4.08212	4.66241		4.70723	5.18996	0.31634	6.785
lnfe	Normal	8	0.31766	0.84117		0.83303	1.28608	0.34855	41.436
lnfe	Severe	8	-0.69920	-0.07743		-0.01178	0.57609	0.42809	-552.861
lnVz_F	Normal	8	6.12064	6.62843		6.66639	7.39239	0.38927	5.873
lnVz_F	Severe	8	6.20863	6.51714		6.51572	6.81367	0.24404	3.745
RkTmax	Normal	8	3.50000	9.43750	8.58239	10.00000	14.50000	3.95002	41.855
RkTmax	Severe	8	1.50000	7.56250	5.49765	6.50000	14.50000	5.46049	72.205

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnCmax
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.07015	0.07015	0.48 0.4992
Error	14	2.04054	0.14575	
Corrected Total	15	2.11069		

Root MSE	0.38178	R-Square	0.0332
Dependent Mean	5.61879	Adj R-Sq	-0.0358
Coeff Var	6.79463		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	5.72061	0.17508	32.67	<.0001	5.34511 6.09611
eGFR	eGFR	1	-0.00157	0.00226	-0.69	0.4992	-0.00641 0.00328

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=13 Param=lnCmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	5.6630	5.5405	0.1478	0.1225	0.352	0.348						0.011
2	5.7137	5.5608	0.1268	0.1529	0.360	0.425						0.011
3	6.2422	5.5734	0.1157	0.6689	0.364	1.839				***		0.171
4	5.7869	5.5499	0.1378	0.2370	0.356	0.666				*		0.033
5	4.8363	5.5608	0.1268	-0.7245	0.360	-2.012	****					0.251
6	5.6204	5.5389	0.1496	0.0815	0.351	0.232						0.005
7	5.1533	5.5671	0.1211	-0.4138	0.362	-1.143	**					0.073
8	5.4467	5.5358	0.1531	-0.0890	0.350	-0.255						0.006
9	5.8319	5.6799	0.1299	0.1520	0.359	0.423						0.012
10	5.0938	5.6846	0.1346	-0.5908	0.357	-1.654	***					0.194
11	5.4596	5.6799	0.1299	-0.2203	0.359	-0.614	*					0.025
12	5.6836	5.6908	0.1411	-0.007270	0.355	-0.0205						0.000
13	6.0497	5.6783	0.1283	0.3714	0.360	1.033				**		0.068
14	6.1527	5.6955	0.1461	0.4572	0.353	1.296				**		0.144
15	5.5722	5.6877	0.1378	-0.1156	0.356	-0.325						0.008
16	5.5947	5.6768	0.1268	-0.0820	0.360	-0.228						0.003

Sum of Residuals 0
 Sum of Squared Residuals 2.04054
 Predicted Residual SS (PRESS) 2.59787

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=14 Param=lnAUCT
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.08126	0.08126	0.58	0.4595
Error	14	1.96620	0.14044		
Corrected Total	15	2.04746			

Root MSE 0.37476 R-Square 0.0397
 Dependent Mean 7.44946 Adj R-Sq -0.0289
 Coeff Var 5.03067

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	7.55905	0.17186	43.98	<.0001	7.19045 7.92765
eGFR	eGFR	1	-0.00169	0.00222	-0.76	0.4595	-0.00644 0.00307

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=lnAUCT

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	7.4628	7.3652	0.1451	0.0976	0.346	0.283						0.007
2	7.7273	7.3871	0.1245	0.3402	0.353	0.962			*			0.057
3	7.7204	7.4006	0.1136	0.3198	0.357	0.896			*			0.041
4	7.5116	7.3753	0.1352	0.1364	0.350	0.390						0.011
5	6.4271	7.3871	0.1245	-0.9600	0.353	-2.716	*****					0.458
6	7.3228	7.3635	0.1468	-0.0407	0.345	-0.118						0.001
7	7.1914	7.3938	0.1189	-0.2024	0.355	-0.570		*				0.018
8	7.5786	7.3601	0.1503	0.2185	0.343	0.636			*			0.039
9	7.7072	7.5152	0.1275	0.1920	0.352	0.545			*			0.019
10	7.0064	7.5203	0.1321	-0.5138	0.351	-1.465	**					0.152
11	7.6381	7.5152	0.1275	0.1229	0.352	0.349						0.008
12	7.4743	7.5270	0.1385	-0.0528	0.348	-0.151						0.002
13	8.1095	7.5135	0.1260	0.5959	0.353	1.688			***			0.182
14	7.5097	7.5321	0.1434	-0.0224	0.346	-0.0647						0.000
15	7.3495	7.5236	0.1352	-0.1741	0.350	-0.498						0.019
16	7.4548	7.5118	0.1245	-0.0571	0.353	-0.161						0.002

Sum of Residuals 0
 Sum of Squared Residuals 1.96620
 Predicted Residual SS (PRESS) 2.50413

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

 Order=15 Param=lnAUCinf
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.08438	0.08438	0.60 0.4513
Error	14	1.96718	0.14051	
Corrected Total	15	2.05156		

Root MSE	0.37485	R-Square	0.0411
Dependent Mean	7.46058	Adj R-Sq	-0.0274
Coeff Var	5.02441		

Parameter Estimates						
Variable	Label	DF	Parameter Estimate	Standard Error	t Value Pr > t	95% Confidence Limits
Intercept	Intercept	1	7.57226	0.17190	44.05 <.0001	7.20357 7.94095
eGFR	eGFR	1	-0.00172	0.00222	-0.77 0.4513	-0.00647 0.00304

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=15 Param=lnAUCinf

Obs	Dependent Variable	Predicted Value	Output Statistics				-2-1 0 1 2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual		
1	7.4681	7.3747	0.1452	0.0934	0.346	0.270		0.006
2	7.7376	7.3970	0.1245	0.3406	0.354	0.963	*	0.058
3	7.7258	7.4108	0.1136	0.3151	0.357	0.882	*	0.039
4	7.5226	7.3850	0.1353	0.1376	0.350	0.394		0.012
5	6.4369	7.3970	0.1245	-0.9601	0.354	-2.716	*****	0.458
6	7.3281	7.3730	0.1469	-0.0449	0.345	-0.130		0.002
7	7.2106	7.4039	0.1189	-0.1933	0.355	-0.544	*	0.017
8	7.5903	7.3695	0.1503	0.2208	0.343	0.643	*	0.040
9	7.7193	7.5276	0.1275	0.1917	0.352	0.544	*	0.019
10	7.0161	7.5327	0.1321	-0.5166	0.351	-1.473	**	0.154
11	7.6582	7.5276	0.1275	0.1306	0.352	0.370		0.009
12	7.4823	7.5396	0.1385	-0.0573	0.348	-0.165		0.002
13	8.1240	7.5259	0.1260	0.5981	0.353	1.694	***	0.183
14	7.5154	7.5448	0.1435	-0.0294	0.346	-0.0848		0.001
15	7.3678	7.5362	0.1353	-0.1684	0.350	-0.482		0.017
16	7.4663	7.5242	0.1245	-0.0579	0.354	-0.164		0.002

Sum of Residuals 0
 Sum of Squared Residuals 1.96718
 Predicted Residual SS (PRESS) 2.50586

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=16 Param=lnAe

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	3.38108	3.38108	22.25	0.0003
Error	14	2.12750	0.15196		
Corrected Total	15	5.50858			

Root MSE	0.38983	R-Square	0.6138
Dependent Mean	1.07502	Adj R-Sq	0.5862
Coeff Var	36.26232		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	0.36811	0.17877	2.06	0.0586	-0.01531 0.75153
eGFR	eGFR	1	0.01088	0.00231	4.72	0.0003	0.00593 0.01582

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=16 Param=lnAe

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	1.4967	1.6188	0.1510	-0.1221	0.359	-0.340						0.010
2	1.9442	1.4774	0.1295	0.4668	0.368	1.269			**			0.100
3	1.9792	1.3904	0.1182	0.5888	0.371	1.585			***			0.127
4	1.1395	1.5535	0.1407	-0.4141	0.364	-1.139		**				0.097
5	1.0108	1.4774	0.1295	-0.4666	0.368	-1.269		**				0.100
6	1.4170	1.6297	0.1527	-0.2127	0.359	-0.593		*				0.032
7	1.5557	1.4339	0.1236	0.1218	0.370	0.329						0.006
8	1.7315	1.6514	0.1563	0.0801	0.357	0.224						0.005
9	0.6768	0.6509	0.1326	0.0259	0.367	0.0707						0.000
10	0.3865	0.6182	0.1374	-0.2318	0.365	-0.635		*				0.029
11	1.2692	0.6509	0.1326	0.6184	0.367	1.687			***			0.186
12	-0.006052	0.5747	0.1440	-0.5808	0.362	-1.603		***				0.203
13	0.9761	0.6617	0.1311	0.3144	0.367	0.856			*			0.047
14	0.1260	0.5421	0.1492	-0.4161	0.360	-1.155		**				0.115
15	0.8112	0.5965	0.1407	0.2147	0.364	0.591			*			0.026
16	0.6860	0.6726	0.1295	0.0133	0.368	0.0363						0.000

Sum of Residuals 0
 Sum of Squared Residuals 2.12750
 Predicted Residual SS (PRESS) 2.74548

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=17 Param=lnCLr

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	4.51067	4.51067	33.97 <.0001
Error	14	1.85897	0.13278	
Corrected Total	15	6.36964		

Root MSE	0.36439	R-Square	0.7082
Dependent Mean	7.44107	Adj R-Sq	0.6873
Coeff Var	4.89707		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	6.62457	0.16711	39.64	<.0001	6.26616 6.98297
eGFR	eGFR	1	0.01256	0.00216	5.83	<.0001	0.00794 0.01718

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=17 Param=lnCLr

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	7.8494	8.0691	0.1411	-0.2198	0.336	-0.654		*				0.038
2	8.0324	7.9058	0.1211	0.1266	0.344	0.368						0.008
3	8.0744	7.8054	0.1105	0.2690	0.347	0.775			*			0.030
4	7.4433	7.9938	0.1315	-0.5504	0.340	-1.620		***				0.196
5	8.3993	7.9058	0.1211	0.4934	0.344	1.436			**			0.128
6	7.9097	8.0817	0.1428	-0.1720	0.335	-0.513		*				0.024
7	8.1798	7.8556	0.1156	0.3242	0.346	0.938			*			0.049
8	7.9684	8.1068	0.1461	-0.1384	0.334	-0.415						0.016
9	6.7850	6.9512	0.1240	-0.1661	0.343	-0.485						0.015
10	7.1955	6.9135	0.1284	0.2821	0.341	0.827			*			0.049
11	7.4467	6.9512	0.1240	0.4955	0.343	1.446			**			0.137
12	6.3352	6.8632	0.1346	-0.5280	0.339	-1.559		***				0.192
13	6.6821	6.9637	0.1225	-0.2816	0.343	-0.821		*				0.043
14	6.4318	6.8256	0.1395	-0.3937	0.337	-1.170		**				0.117
15	7.2772	6.8884	0.1315	0.3889	0.340	1.144			**			0.098
16	7.0467	6.9763	0.1211	0.0704	0.344	0.205						0.003

Sum of Residuals 0
 Sum of Squared Residuals 1.85897
 Predicted Residual SS (PRESS) 2.42809

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
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 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=18 Param=lnLambda_z
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.00254	0.00254	0.03	0.8668
Error	14	1.21849	0.08703		
Corrected Total	15	1.22103			

Root MSE	0.29502	R-Square	0.0021
Dependent Mean	-1.82729	Adj R-Sq	-0.0692
Coeff Var	-16.14503		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-1.84667	0.13529	-13.65	<.0001	-2.13684 -1.55650
eGFR	eGFR	1	0.00029809	0.00174	0.17	0.8668	-0.00344 0.00404

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=18 Param=lnLambda_z

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	-1.9863	-1.8124	0.1142	-0.1739	0.272	-0.639	*					0.036
2	-2.1400	-1.8163	0.0980	-0.3237	0.278	-1.163	**					0.084
3	-1.6404	-1.8186	0.0894	0.1783	0.281	0.634		*				0.020
4	-1.6309	-1.8142	0.1065	0.1833	0.275	0.666		*				0.033
5	-1.6232	-1.8163	0.0980	0.1931	0.278	0.694		*				0.030
6	-1.4726	-1.8121	0.1156	0.3395	0.271	1.251		**				0.142
7	-1.7653	-1.8175	0.0936	0.0522	0.280	0.187						0.002
8	-2.1402	-1.8115	0.1183	-0.3287	0.270	-1.216	**					0.142
9	-2.2056	-1.8389	0.1004	-0.3667	0.277	-1.322	**					0.114
10	-1.5948	-1.8398	0.1040	0.2450	0.276	0.888		*				0.056
11	-2.2658	-1.8389	0.1004	-0.4268	0.277	-1.539	***					0.155
12	-1.5666	-1.8410	0.1090	0.2744	0.274	1.001		**				0.079
13	-2.2337	-1.8386	0.0992	-0.3951	0.278	-1.422	**					0.129
14	-1.5180	-1.8419	0.1129	0.3239	0.273	1.189		**				0.121
15	-1.8180	-1.8404	0.1065	0.0224	0.275	0.0813						0.000
16	-1.6354	-1.8383	0.0980	0.2029	0.278	0.729		*				0.033

Sum of Residuals 0
 Sum of Squared Residuals 1.21849
 Predicted Residual SS (PRESS) 1.60139

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
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 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=19 Param=lnCl_F

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.08438	0.08438	0.60 0.4513
Error	14	1.96718	0.14051	
Corrected Total	15	2.05156		

Root MSE	0.37485	R-Square	0.0411
Dependent Mean	4.74549	Adj R-Sq	-0.0274
Coeff Var	7.89908		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	4.63381	0.17190	26.96	<.0001	4.26512 5.00250
eGFR	eGFR	1	0.00172	0.00222	0.77	0.4513	-0.00304 0.00647

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=19 Param=lnCl_F

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	4.7380	4.8314	0.1452	-0.0934	0.346	-0.270						0.006
2	4.4684	4.8091	0.1245	-0.3406	0.354	-0.963	*					0.058
3	4.4803	4.7953	0.1136	-0.3151	0.357	-0.882	*					0.039
4	4.6834	4.8211	0.1353	-0.1376	0.350	-0.394						0.012
5	5.7692	4.8091	0.1245	0.9601	0.354	2.716			*****			0.458
6	4.8780	4.8331	0.1469	0.0449	0.345	0.130						0.002
7	4.9955	4.8022	0.1189	0.1933	0.355	0.544		*				0.017
8	4.6158	4.8366	0.1503	-0.2208	0.343	-0.643	*					0.040
9	4.4868	4.6785	0.1275	-0.1917	0.352	-0.544	*					0.019
10	5.1900	4.6733	0.1321	0.5166	0.351	1.473			**			0.154
11	4.5479	4.6785	0.1275	-0.1306	0.352	-0.370						0.009
12	4.7238	4.6665	0.1385	0.0573	0.348	0.165						0.002
13	4.0821	4.6802	0.1260	-0.5981	0.353	-1.694	***					0.183
14	4.6907	4.6613	0.1435	0.0294	0.346	0.0848						0.001
15	4.8383	4.6699	0.1353	0.1684	0.350	0.482						0.017
16	4.7398	4.6819	0.1245	0.0579	0.354	0.164						0.002

Sum of Residuals 0
 Sum of Squared Residuals 1.96718
 Predicted Residual SS (PRESS) 2.50586

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=20 Param=lnfe

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	3.38108	3.38108	22.25 0.0003
Error	14	2.12750	0.15196	
Corrected Total	15	5.50858		

Root MSE	0.38983	R-Square	0.6138
Dependent Mean	0.38187	Adj R-Sq	0.5862
Coeff Var	102.08357		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-0.32504	0.17877	-1.82	0.0905	-0.70846 0.05838
eGFR	eGFR	1	0.01088	0.00231	4.72	0.0003	0.00593 0.01582

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=20 Param=lnfe

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	0.8035	0.9256	0.1510	-0.1221	0.359	-0.340						0.010
2	1.2510	0.7843	0.1295	0.4668	0.368	1.269			**			0.100
3	1.2861	0.6973	0.1182	0.5888	0.371	1.585			***			0.127
4	0.4463	0.8604	0.1407	-0.4141	0.364	-1.139	**					0.097
5	0.3177	0.7843	0.1295	-0.4666	0.368	-1.269	**					0.100
6	0.7239	0.9365	0.1527	-0.2127	0.359	-0.593	*					0.032
7	0.8625	0.7408	0.1236	0.1218	0.370	0.329						0.006
8	1.0383	0.9583	0.1563	0.0801	0.357	0.224						0.005
9	-0.0164	-0.0423	0.1326	0.0259	0.367	0.0707						0.000
10	-0.3067	-0.0749	0.1374	-0.2318	0.365	-0.635	*					0.029
11	0.5761	-0.0423	0.1326	0.6184	0.367	1.687			***			0.186
12	-0.6992	-0.1184	0.1440	-0.5808	0.362	-1.603	***					0.203
13	0.2830	-0.0314	0.1311	0.3144	0.367	0.856			*			0.047
14	-0.5671	-0.1510	0.1492	-0.4161	0.360	-1.155	**					0.115
15	0.1181	-0.0967	0.1407	0.2147	0.364	0.591			*			0.026
16	-0.007186	-0.0205	0.1295	0.0133	0.368	0.0363						0.000

Sum of Residuals 0
 Sum of Squared Residuals 2.12750
 Predicted Residual SS (PRESS) 2.74548

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
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 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=21 Param=lnVz_F

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.05764	0.05764	0.55 0.4709
Error	14	1.46951	0.10497	
Corrected Total	15	1.52716		

Root MSE	0.32398	R-Square	0.0377
Dependent Mean	6.57279	Adj R-Sq	-0.0310
Coeff Var	4.92916		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	6.48048	0.14857	43.62	<.0001	6.16182 6.79914
eGFR	eGFR	1	0.00142	0.00192	0.74	0.4709	-0.00269 0.00553

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
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 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=21 Param=lnVz_F

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	6.7243	6.6438	0.1255	0.0805	0.299	0.270						0.006
2	6.6084	6.6253	0.1076	-0.0169	0.306	-0.0552						0.000
3	6.1206	6.6140	0.0982	-0.4933	0.309	-1.598	***					0.129
4	6.3143	6.6353	0.1169	-0.3209	0.302	-1.062	**					0.084
5	7.3924	6.6253	0.1076	0.7671	0.306	2.510			*****			0.391
6	6.3506	6.6452	0.1269	-0.2946	0.298	-0.988	*					0.089
7	6.7607	6.6196	0.1028	0.1411	0.307	0.459						0.012
8	6.7560	6.6480	0.1299	0.1080	0.297	0.364						0.013
9	6.6924	6.5174	0.1102	0.1750	0.305	0.574			*			0.022
10	6.7847	6.5131	0.1142	0.2716	0.303	0.896			*			0.057
11	6.8137	6.5174	0.1102	0.2963	0.305	0.972			*			0.062
12	6.2904	6.5075	0.1197	-0.2171	0.301	-0.721	*					0.041
13	6.3158	6.5188	0.1089	-0.2030	0.305	-0.665	*					0.028
14	6.2086	6.5032	0.1240	-0.2946	0.299	-0.984	*					0.083
15	6.6563	6.5103	0.1169	0.1460	0.302	0.483						0.017
16	6.3752	6.5202	0.1076	-0.1451	0.306	-0.475						0.014

Sum of Residuals 0
 Sum of Squared Residuals 1.46951
 Predicted Residual SS (PRESS) 1.88342

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=22 Param=RkTmax
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	17.88375	17.88375	0.80	0.3871
Error	14	314.11625	22.43687		
Corrected Total	15	332.00000			

Root MSE	4.73676	R-Square	0.0539
Dependent Mean	8.50000	Adj R-Sq	-0.0137
Coeff Var	55.72656		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	6.87420	2.17220	3.16	0.0069	2.21529 11.53312
eGFR	eGFR	1	0.02501	0.02802	0.89	0.3871	-0.03508 0.08510

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=22 Param=RkTmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	8.0000	9.7506	1.8343	-1.7506	4.367	-0.401						0.014
2	14.5000	9.4255	1.5738	5.0745	4.468	1.136			**			0.080
3	5.0000	9.2254	1.4361	-4.2254	4.514	-0.936		*				0.044
4	10.0000	9.6005	1.7093	0.3995	4.418	0.0904						0.001
5	3.5000	9.4255	1.5738	-5.9255	4.468	-1.326		**				0.109
6	10.0000	9.7756	1.8557	0.2244	4.358	0.0515						0.000
7	14.5000	9.3254	1.5023	5.1746	4.492	1.152			**			0.074
8	10.0000	9.8256	1.8992	0.1744	4.339	0.0402						0.000
9	1.5000	7.5245	1.6112	-6.0245	4.454	-1.353		**				0.120
10	14.5000	7.4495	1.6694	7.0505	4.433	1.591			***			0.179
11	14.5000	7.5245	1.6112	6.9755	4.454	1.566			***			0.160
12	7.0000	7.3494	1.7502	-0.3494	4.402	-0.0794						0.000
13	6.0000	7.5495	1.5924	-1.5495	4.461	-0.347						0.008
14	1.5000	7.2744	1.8130	-5.7744	4.376	-1.320		**				0.149
15	3.5000	7.3995	1.7093	-3.8995	4.418	-0.883		*				0.058
16	12.0000	7.5745	1.5738	4.4255	4.468	0.991			*			0.061

Sum of Residuals 0
 Sum of Squared Residuals 314.11625
 Predicted Residual SS (PRESS) 403.50373

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=13 Param=lnCmax

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.17464	0.17464	1.26	0.2800
Error	14	1.93605	0.13829		
Corrected Total	15	2.11069			

Root MSE	0.37187	R-Square	0.0827
Dependent Mean	5.61879	Adj R-Sq	0.0172
Coeff Var	6.61837		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	5.78834	0.17722	32.66	<.0001	5.40824 6.16844
CrCL	CrCL	1	-0.00198	0.00177	-1.12	0.2800	-0.00577 0.00180

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=13 Param=lnCmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	5.6630	5.4633	0.1667	0.1997	0.332	0.601			*			0.045
2	5.7137	5.4851	0.1510	0.2286	0.340	0.673			*			0.045
3	6.2422	5.5891	0.0967	0.6532	0.359	1.819			***			0.120
4	5.7869	5.5417	0.1156	0.2452	0.353	0.694			*			0.026
5	4.8363	5.4805	0.1543	-0.6442	0.338	-1.904	***					0.377
6	5.6204	5.5499	0.1114	0.0705	0.355	0.199						0.002
7	5.1533	5.5574	0.1078	-0.4041	0.356	-1.136	**					0.059
8	5.4467	5.4960	0.1435	-0.0492	0.343	-0.144						0.002
9	5.8319	5.7088	0.1227	0.1231	0.351	0.351						0.008
10	5.0938	5.7298	0.1356	-0.6360	0.346	-1.837	***					0.259
11	5.4596	5.7017	0.1187	-0.2421	0.352	-0.687	*					0.027
12	5.6836	5.7284	0.1347	-0.0448	0.347	-0.129						0.001
13	6.0497	5.7350	0.1390	0.3148	0.345	0.913			*			0.068
14	6.1527	5.7481	0.1479	0.4046	0.341	1.186			**			0.132
15	5.5722	5.7282	0.1346	-0.1560	0.347	-0.450						0.015
16	5.5947	5.6579	0.0993	-0.0631	0.358	-0.176						0.001

Sum of Residuals 0
 Sum of Squared Residuals 1.93605
 Predicted Residual SS (PRESS) 2.54565

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=lnAUCT

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.15435	0.15435	1.14 0.3034
Error	14	1.89311	0.13522	
Corrected Total	15	2.04746		

Root MSE	0.36773	R-Square	0.0754
Dependent Mean	7.44946	Adj R-Sq	0.0093
Coeff Var	4.93627		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	7.60886	0.17524	43.42	<.0001	7.23300 7.98472
CrCL	CrCL	1	-0.00187	0.00175	-1.07	0.3034	-0.00561 0.00188

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=lnAUCT

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	7.4628	7.3032	0.1649	0.1596	0.329	0.485						0.030
2	7.7273	7.3238	0.1493	0.4035	0.336	1.201			**			0.142
3	7.7204	7.4215	0.0956	0.2989	0.355	0.842			*			0.026
4	7.5116	7.3769	0.1143	0.1347	0.350	0.385						0.008
5	6.4271	7.3194	0.1525	-0.8924	0.335	-2.667	*****					0.739
6	7.3228	7.3847	0.1101	-0.0619	0.351	-0.176						0.002
7	7.1914	7.3918	0.1066	-0.2004	0.352	-0.569		*				0.015
8	7.5786	7.3340	0.1419	0.2446	0.339	0.721			*			0.045
9	7.7072	7.5341	0.1213	0.1732	0.347	0.499						0.015
10	7.0064	7.5538	0.1341	-0.5474	0.342	-1.599	***					0.196
11	7.6381	7.5274	0.1174	0.1107	0.348	0.318						0.006
12	7.4743	7.5525	0.1332	-0.0782	0.343	-0.228						0.004
13	8.1095	7.5587	0.1375	0.5508	0.341	1.615			***			0.212
14	7.5097	7.5711	0.1463	-0.0614	0.337	-0.182						0.003
15	7.3495	7.5523	0.1331	-0.2028	0.343	-0.592		*				0.026
16	7.4548	7.4862	0.0981	-0.0314	0.354	-0.0886						0.000

Sum of Residuals 0
 Sum of Squared Residuals 1.89311
 Predicted Residual SS (PRESS) 2.62564

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=15 Param=lnAUCinf

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.15820	0.15820	1.17	0.2977
Error	14	1.89336	0.13524		
Corrected Total	15	2.05156			

Root MSE	0.36775	R-Square	0.0771
Dependent Mean	7.46058	Adj R-Sq	0.0112
Coeff Var	4.92925		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	7.62195	0.17526	43.49	<.0001	7.24607 7.99784
CrCL	CrCL	1	-0.00189	0.00175	-1.08	0.2977	-0.00563 0.00186

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=15 Param=lnAUCinf

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error	Residual	Std Error	Student						
			Mean Predict		Residual	Residual						
1	7.4681	7.3126	0.1649	0.1555	0.329	0.473						0.028
2	7.7376	7.3333	0.1493	0.4043	0.336	1.203			**			0.143
3	7.7258	7.4323	0.0956	0.2935	0.355	0.827			*			0.025
4	7.5226	7.3872	0.1143	0.1355	0.350	0.388						0.008
5	6.4369	7.3289	0.1525	-0.8921	0.335	-2.666	*****					0.738
6	7.3281	7.3950	0.1101	-0.0670	0.351	-0.191						0.002
7	7.2106	7.4022	0.1066	-0.1916	0.352	-0.544		*				0.014
8	7.5903	7.3437	0.1419	0.2466	0.339	0.727			*			0.046
9	7.7193	7.5463	0.1214	0.1731	0.347	0.498						0.015
10	7.0161	7.5662	0.1341	-0.5501	0.342	-1.607	***					0.198
11	7.6582	7.5395	0.1174	0.1187	0.349	0.341						0.007
12	7.4823	7.5649	0.1332	-0.0826	0.343	-0.241						0.004
13	8.1240	7.5712	0.1375	0.5528	0.341	1.621			***			0.213
14	7.5154	7.5837	0.1463	-0.0683	0.337	-0.202						0.004
15	7.3678	7.5647	0.1331	-0.1969	0.343	-0.574		*				0.025
16	7.4663	7.4978	0.0982	-0.0315	0.354	-0.0888						0.000

Sum of Residuals 0
 Sum of Squared Residuals 1.89336
 Predicted Residual SS (PRESS) 2.62664

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=16 Param=lnAe

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	3.06285	3.06285	17.53 0.0009
Error	14	2.44572	0.17469	
Corrected Total	15	5.50858		

Root MSE	0.41796	R-Square	0.5560
Dependent Mean	1.07502	Adj R-Sq	0.5243
Coeff Var	38.87985		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	0.36496	0.19919	1.83	0.0883	-0.06225 0.79217
CrCL	CrCL	1	0.00831	0.00198	4.19	0.0009	0.00405 0.01256

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=16 Param=lnAe

Obs	Output Statistics							-2	-1	0	1	2	Cook's D
	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual							
1	1.4967	1.7263	0.1874	-0.2297	0.374	-0.615		*					0.048
2	1.9442	1.6349	0.1697	0.3093	0.382	0.810			*				0.065
3	1.9792	1.1996	0.1086	0.7797	0.404	1.932				***			0.135
4	1.1395	1.3981	0.1299	-0.2586	0.397	-0.651		*					0.023
5	1.0108	1.6543	0.1734	-0.6435	0.380	-1.692		***					0.297
6	1.4170	1.3635	0.1252	0.0535	0.399	0.134							0.001
7	1.5557	1.3320	0.1212	0.2237	0.400	0.559			*				0.014
8	1.7315	1.5893	0.1613	0.1422	0.386	0.369							0.012
9	0.6768	0.6981	0.1379	-0.0213	0.395	-0.0539							0.000
10	0.3865	0.6101	0.1525	-0.2237	0.389	-0.575		*					0.025
11	1.2692	0.7279	0.1334	0.5414	0.396	1.367				**			0.106
12	-0.006052	0.6160	0.1514	-0.6221	0.390	-1.597		***					0.193
13	0.9761	0.5885	0.1563	0.3876	0.388	1.000			*				0.081
14	0.1260	0.5334	0.1663	-0.4074	0.383	-1.062		**					0.106
15	0.8112	0.6170	0.1513	0.1943	0.390	0.499							0.019
16	0.6860	0.9114	0.1116	-0.2255	0.403	-0.560		*					0.012

Sum of Residuals 0
 Sum of Squared Residuals 2.44572
 Predicted Residual SS (PRESS) 3.18542

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=17 Param=lnCLr

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	4.59236	4.59236	36.18 <.0001
Error	14	1.77728	0.12695	
Corrected Total	15	6.36964		

Root MSE	0.35630	R-Square	0.7210
Dependent Mean	7.44107	Adj R-Sq	0.7010
Coeff Var	4.78827		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	6.57162	0.16980	38.70	<.0001	6.20744 6.93580
CrCL	CrCL	1	0.01017	0.00169	6.01	<.0001	0.00655 0.01380

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=17 Param=lnCLr

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	7.8494	8.2386	0.1597	-0.3892	0.318	-1.222	**					0.188
2	8.0324	8.1266	0.1447	-0.0942	0.326	-0.289						0.008
3	8.0744	7.5936	0.0926	0.4808	0.344	1.397		**				0.071
4	7.4433	7.8366	0.1107	-0.3933	0.339	-1.161	**					0.072
5	8.3993	8.1504	0.1478	0.2489	0.324	0.768		*				0.061
6	7.9097	7.7943	0.1067	0.1154	0.340	0.340						0.006
7	8.1798	7.7557	0.1033	0.4241	0.341	1.244		**				0.071
8	7.9684	8.0708	0.1375	-0.1024	0.329	-0.312						0.008
9	6.7850	6.9795	0.1176	-0.1944	0.336	-0.578	*					0.020
10	7.1955	6.8718	0.1300	0.3237	0.332	0.976		*				0.073
11	7.4467	7.0160	0.1137	0.4307	0.338	1.275		**				0.092
12	6.3352	6.8791	0.1291	-0.5439	0.332	-1.638	***					0.203
13	6.6821	6.8453	0.1332	-0.1631	0.330	-0.494						0.020
14	6.4318	6.7778	0.1418	-0.3460	0.327	-1.058	**					0.105
15	7.2772	6.8802	0.1290	0.3971	0.332	1.195		**				0.108
16	7.0467	7.2407	0.0951	-0.1940	0.343	-0.565	*					0.012

Sum of Residuals 0
 Sum of Squared Residuals 1.77728
 Predicted Residual SS (PRESS) 2.30693

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=18 Param=lnLambda_z
 Number of Observations Read 16
 Number of Observations Used 16

Source	Analysis of Variance			F Value	Pr > F
	DF	Sum of Squares	Mean Square		
Model	1	0.00097722	0.00097722	0.01	0.9172
Error	14	1.22005	0.08715		
Corrected Total	15	1.22103			

Root MSE	0.29521	R-Square	0.0008
Dependent Mean	-1.82729	Adj R-Sq	-0.0706
Coeff Var	-16.15538		

Variable		Label		Parameter Estimates			95% Confidence Limits		
				Parameter Estimate	Standard Error	t Value Pr > t			
Intercept	Intercept	1	-1.81461	0.14068	-12.90	<.0001	-2.11635	-1.51287	
CrCL	CrCL	1	-0.00014841	0.00140	-0.11	0.9172	-0.00315	0.00286	

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=18 Param=lnLambda_z

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	-1.9863	-1.8389	0.1324	-0.1474	0.264	-0.559	*					0.039
2	-2.1400	-1.8373	0.1199	-0.3027	0.270	-1.122	**					0.124
3	-1.6404	-1.8295	0.0767	0.1891	0.285	0.664		*				0.016
4	-1.6309	-1.8331	0.0917	0.2022	0.281	0.721		*				0.028
5	-1.6232	-1.8376	0.1225	0.2145	0.269	0.798		*				0.066
6	-1.4726	-1.8324	0.0884	0.3599	0.282	1.278		**				0.080
7	-1.7653	-1.8319	0.0856	0.0666	0.283	0.236						0.003
8	-2.1402	-1.8365	0.1139	-0.3037	0.272	-1.115	**					0.109
9	-2.2056	-1.8206	0.0974	-0.3851	0.279	-1.382	**					0.117
10	-1.5948	-1.8190	0.1077	0.2242	0.275	0.816		*				0.051
11	-2.2658	-1.8211	0.0942	-0.4447	0.280	-1.589	***					0.143
12	-1.5666	-1.8191	0.1070	0.2525	0.275	0.918		*				0.064
13	-2.2337	-1.8186	0.1104	-0.4151	0.274	-1.516	***					0.187
14	-1.5180	-1.8176	0.1174	0.2997	0.271	1.106		**				0.115
15	-1.8180	-1.8191	0.1068	0.001081	0.275	0.00393						0.000
16	-1.6354	-1.8244	0.0788	0.1890	0.284	0.664		*				0.017

Sum of Residuals 0
 Sum of Squared Residuals 1.22005
 Predicted Residual SS (PRESS) 1.59686

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=19 Param=lnCl_F

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.15820	0.15820	1.17 0.2977
Error	14	1.89336	0.13524	
Corrected Total	15	2.05156		

Root MSE	0.36775	R-Square	0.0771
Dependent Mean	4.74549	Adj R-Sq	0.0112
Coeff Var	7.74947		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	4.58412	0.17526	26.16	<.0001	4.20824 4.96001
CrCL	CrCL	1	0.00189	0.00175	1.08	0.2977	-0.00186 0.00563

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=19 Param=lnCl_F

Obs	Output Statistics							-2	-1	0	1	2	Cook's D
	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual							
1	4.7380	4.8935	0.1649	-0.1555	0.329	-0.473						0.028	
2	4.4684	4.8727	0.1493	-0.4043	0.336	-1.203	**					0.143	
3	4.4803	4.7738	0.0956	-0.2935	0.355	-0.827	*					0.025	
4	4.6834	4.8189	0.1143	-0.1355	0.350	-0.388						0.008	
5	5.7692	4.8771	0.1525	0.8921	0.335	2.666			*****			0.738	
6	4.8780	4.8111	0.1101	0.0670	0.351	0.191						0.002	
7	4.9955	4.8039	0.1066	0.1916	0.352	0.544		*				0.014	
8	4.6158	4.8624	0.1419	-0.2466	0.339	-0.727	*					0.046	
9	4.4868	4.6598	0.1214	-0.1731	0.347	-0.498						0.015	
10	5.1900	4.6398	0.1341	0.5501	0.342	1.607			***			0.198	
11	4.5479	4.6666	0.1174	-0.1187	0.349	-0.341						0.007	
12	4.7238	4.6412	0.1332	0.0826	0.343	0.241						0.004	
13	4.0821	4.6349	0.1375	-0.5528	0.341	-1.621	***					0.213	
14	4.6907	4.6224	0.1463	0.0683	0.337	0.202						0.004	
15	4.8383	4.6414	0.1331	0.1969	0.343	0.574		*				0.025	
16	4.7398	4.7083	0.0982	0.0315	0.354	0.0888						0.000	

Sum of Residuals 0
 Sum of Squared Residuals 1.89336
 Predicted Residual SS (PRESS) 2.62664

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=20 Param=lnfe

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	3.06285	3.06285	17.53 0.0009
Error	14	2.44572	0.17469	
Corrected Total	15	5.50858		

Root MSE	0.41796	R-Square	0.5560
Dependent Mean	0.38187	Adj R-Sq	0.5243
Coeff Var	109.45229		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-0.32818	0.19919	-1.65	0.1217	-0.75540 0.09903
CrCL	CrCL	1	0.00831	0.00198	4.19	0.0009	0.00405 0.01256

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=20 Param=lnfe

Obs	Output Statistics							-2	-1	0	1	2	Cook's D
	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual							
1	0.8035	1.0332	0.1874	-0.2297	0.374	-0.615		*					0.048
2	1.2510	0.9417	0.1697	0.3093	0.382	0.810			*				0.065
3	1.2861	0.5064	0.1086	0.7797	0.404	1.932				***			0.135
4	0.4463	0.7049	0.1299	-0.2586	0.397	-0.651		*					0.023
5	0.3177	0.9611	0.1734	-0.6435	0.380	-1.692		***					0.297
6	0.7239	0.6703	0.1252	0.0535	0.399	0.134							0.001
7	0.8625	0.6389	0.1212	0.2237	0.400	0.559			*				0.014
8	1.0383	0.8962	0.1613	0.1422	0.386	0.369							0.012
9	-0.0164	0.004908	0.1379	-0.0213	0.395	-0.0539							0.000
10	-0.3067	-0.0830	0.1525	-0.2237	0.389	-0.575		*					0.025
11	0.5761	0.0347	0.1334	0.5414	0.396	1.367				**			0.106
12	-0.6992	-0.0771	0.1514	-0.6221	0.390	-1.597		***					0.193
13	0.2830	-0.1047	0.1563	0.3876	0.388	1.000			*				0.081
14	-0.5671	-0.1598	0.1663	-0.4074	0.383	-1.062		**					0.106
15	0.1181	-0.0762	0.1513	0.1943	0.390	0.499							0.019
16	-0.007186	0.2183	0.1116	-0.2255	0.403	-0.560		*					0.012

Sum of Residuals 0
 Sum of Squared Residuals 2.44572
 Predicted Residual SS (PRESS) 3.18542

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=21 Param=lnVz_F

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.18404	0.18404	1.92 0.1877
Error	14	1.34312	0.09594	
Corrected Total	15	1.52716		

Root MSE	0.30974	R-Square	0.1205
Dependent Mean	6.57279	Adj R-Sq	0.0577
Coeff Var	4.71241		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	6.39873	0.14761	43.35	<.0001	6.08214 6.71532
CrCL	CrCL	1	0.00204	0.00147	1.39	0.1877	-0.00112 0.00519

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=21 Param=lnVz_F

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	6.7243	6.7324	0.1389	-0.008103	0.277	-0.0293						0.000
2	6.6084	6.7100	0.1257	-0.1016	0.283	-0.359						0.013
3	6.1206	6.6033	0.0805	-0.4827	0.299	-1.614	***					0.094
4	6.3143	6.6520	0.0963	-0.3376	0.294	-1.147	**					0.070
5	7.3924	6.7148	0.1285	0.6776	0.282	2.404			****			0.601
6	6.3506	6.6435	0.0928	-0.2929	0.296	-0.991	*					0.048
7	6.7607	6.6358	0.0898	0.1249	0.296	0.421						0.008
8	6.7560	6.6989	0.1195	0.0572	0.286	0.200						0.003
9	6.6924	6.4804	0.1022	0.2120	0.292	0.725		*				0.032
10	6.7847	6.4588	0.1130	0.3259	0.288	1.130		**				0.098
11	6.8137	6.4877	0.0988	0.3260	0.294	1.111		**				0.070
12	6.2904	6.4603	0.1122	-0.1699	0.289	-0.588	*					0.026
13	6.3158	6.4535	0.1158	-0.1377	0.287	-0.479						0.019
14	6.2086	6.4400	0.1232	-0.2314	0.284	-0.814	*					0.062
15	6.6563	6.4605	0.1121	0.1958	0.289	0.678		*				0.035
16	6.3752	6.5327	0.0827	-0.1575	0.299	-0.528	*					0.011

Sum of Residuals 0
 Sum of Squared Residuals 1.34312
 Predicted Residual SS (PRESS) 1.76761

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=22 Param=RkTmax

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	21.48686	21.48686	0.97	0.3417
Error	14	310.51314	22.17951		
Corrected Total	15	332.00000			

Root MSE	4.70951	R-Square	0.0647
Dependent Mean	8.50000	Adj R-Sq	-0.0021
Coeff Var	55.40603		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	6.61932	2.24437	2.95	0.0106	1.80563 11.43301
CrCL	CrCL	1	0.02201	0.02236	0.98	0.3417	-0.02595 0.06996

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=22 Param=RkTmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	8.0000	10.2251	2.1114	-2.2251	4.210	-0.529		*				0.035
2	14.5000	9.9828	1.9120	4.5172	4.304	1.050			**			0.109
3	5.0000	8.8299	1.2242	-3.8299	4.548	-0.842		*				0.026
4	10.0000	9.3556	1.4635	0.6444	4.476	0.144						0.001
5	3.5000	10.0343	1.9535	-6.5343	4.285	-1.525		***				0.242
6	10.0000	9.2641	1.4103	0.7359	4.493	0.164						0.001
7	14.5000	9.1807	1.3655	5.3193	4.507	1.180			**			0.064
8	10.0000	9.8622	1.8170	0.1378	4.345	0.0317						0.000
9	1.5000	7.5016	1.5541	-6.0016	4.446	-1.350		**				0.111
10	14.5000	7.2687	1.7179	7.2313	4.385	1.649			***			0.209
11	14.5000	7.5806	1.5029	6.9194	4.463	1.550			***			0.136
12	7.0000	7.2844	1.7064	-0.2844	4.390	-0.0648						0.000
13	6.0000	7.2113	1.7608	-1.2113	4.368	-0.277						0.006
14	1.5000	7.0654	1.8737	-5.5654	4.321	-1.288		**				0.156
15	3.5000	7.2868	1.7046	-3.7868	4.390	-0.863		*				0.056
16	12.0000	8.0667	1.2570	3.9333	4.539	0.867			*			0.029

Sum of Residuals 0
 Sum of Squared Residuals 310.51314
 Predicted Residual SS (PRESS) 408.10127

```

----- SUMMARY REPORT -----
Algorithm Pharma
CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan
(Healthy vs Severe)
ANOVA analysis
NON-PARAMETRIC TEST OF FIXED EFFECT for Tmax parameter
----- SUMMARY REPORT -----

```

The NPAR1WAY Procedure

```

Wilcoxon Scores (Rank Sums) for Variable Value
Classified by Variable Group
Group      N      Sum of      Expected Std Dev      Mean
          Scores Under H0 Under H0      Score
1           8      75.50      68.0 9.409215  9.43750
2           8      60.50      68.0 9.409215  7.56250

```

Average scores were used for ties.

Wilcoxon Two-Sample Test

Statistic 75.5000

Normal Approximation

```

Z                                0.7440
One-Sided Pr > Z                0.2285
Two-Sided Pr > |Z|              0.4569

```

t Approximation

```

One-Sided Pr > Z                0.2342
Two-Sided Pr > |Z|              0.4684

```

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test

```

Chi-Square      0.6354
DF              1
Pr > Chi-Square  0.4254

```

Hodges-Lehmann Estimation

```

Location Shift (1 - 2)      0.3417
Type      90%      Interval      Asymptotic
          Confidence      Midpoint Standard Error
          Limits
Asymptotic (Moses) -0.5000 1.2500  0.3750      0.5320
Exact          -0.5000 1.2500  0.3750

```

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Normal

Obs	Subject	Cmax	Tmax	AUCT	Thalf	AUCinf	Ae	CLr	Lambda z	Cl F	Vz F	fe
1	101	288.00000	2.00000	1742.02000	5.05210	1751.19483	4.46677	2564.12957	0.13720	114.20774	832.41956	2.23338
2	102	303.00000	3.00000	2269.41500	5.89140	2293.04005	6.98788	3079.15256	0.11765	87.22046	741.32912	3.49394
3	103	514.00000	1.25000	2253.80500	3.57464	2266.08474	7.23717	3211.08792	0.19391	88.25795	455.15651	3.61858
4	104	326.00000	2.50000	1829.20892	3.54085	1849.42566	3.12512	1708.45439	0.19576	108.14168	552.42749	1.56256
5	105	126.00000	1.00000	618.34750	3.51372	624.44976	2.74783	4443.82811	0.19727	320.28197	1623.58102	1.37392
6	106	276.00000	2.50000	1514.40000	3.02245	1522.43647	4.12476	2723.68991	0.22933	131.36837	572.82872	2.06238
7	107	173.00000	3.00000	1327.93883	4.05010	1353.72355	4.73839	3568.22610	0.17114	147.74065	863.25825	2.36919
8	108	232.00000	2.50000	1955.87600	5.89271	1978.86981	5.64905	2888.24547	0.11763	101.06779	859.21551	2.82453

Obs	lnCmax	lnAUCT	lnAUCinf	lnAe	lnCLr	lnLambda_z	lnCl_F	lnfe	lnVz_F	RkTmax	eGFR	CrCL
1	5.66296	7.46280	7.46805	1.49666	7.84937	-1.98632	4.73802	0.80352	6.72434	8.0	115.00000	163.85000
2	5.71373	7.72728	7.73763	1.94418	8.03241	-2.14001	4.46844	1.25103	6.60844	14.5	102.00000	152.84000
3	6.24222	7.72038	7.72581	1.97923	8.07437	-1.64038	4.48026	1.28608	6.12064	5.0	94.00000	100.45000
4	5.78690	7.51164	7.52263	1.13947	7.44334	-1.63088	4.68344	0.44633	6.31432	10.0	109.00000	124.34000
5	4.83628	6.42705	6.43687	1.01081	8.39927	-1.62319	5.76920	0.31766	7.39239	3.5	102.00000	155.18000
6	5.62040	7.32277	7.32807	1.41701	7.90974	-1.47258	4.87801	0.72386	6.35059	10.0	116.00000	120.18000
7	5.15329	7.19138	7.21061	1.55570	8.17982	-1.76526	4.99546	0.86255	6.76071	14.5	98.00000	116.39000
8	5.44674	7.57859	7.59028	1.73149	7.96840	-2.14023	4.61579	1.03834	6.75602	10.0	118.00000	147.36000

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Severe

Obs	Subject	Cmax	Tmax	AUCT	Thalf	AUCinf	Ae	CLr	Lambda z	Cl F	Vz F	fe
9	013-01	163.00000	3.00000	1103.70000	3.41530	1114.44994	1.47176	1333.47377	0.20295	179.46073	884.24501	0.73588
10	013-02	424.00000	1.75000	3325.83000	6.47006	3374.34231	2.65410	798.02636	0.10713	59.27081	553.25258	1.32705
11	013-03	235.00000	3.00000	2075.78225	6.68086	2117.85268	3.55816	1714.12729	0.10375	94.43528	910.20931	1.77908
12	013-04	269.00000	2.56667	1728.08917	3.55680	1748.10852	1.98568	1149.06108	0.19488	114.40937	587.07806	0.99284
13	013-05	470.00000	0.75000	1825.62167	3.16277	1836.10995	1.13428	621.31329	0.21916	108.92594	497.02008	0.56714
14	013-06	341.00000	0.75000	2224.39000	6.29100	2251.39127	1.96752	884.51935	0.11018	88.83396	806.25652	0.98376
15	013-07	294.00000	1.81667	1762.09667	3.32045	1776.27542	0.99397	564.08143	0.20875	112.59515	539.37588	0.49698
16	013-08	263.00000	1.00000	1555.42500	4.26959	1584.17584	2.25069	1446.99037	0.16235	126.24861	777.65537	1.12534

Obs	lnCmax	lnAUCT	lnAUCinf	lnAe	lnCLr	lnLambda z	lnCl F	lnfe	lnVz F	RkTmax	eGFR	CrCL
9	5.09375	7.00642	7.01612	0.38646	7.19554	-1.59478	5.18996	-0.30669	6.78473	14.5	23.00000	29.51000
10	6.04973	8.10947	8.12396	0.97611	6.68214	-2.23370	4.08212	0.28296	6.31581	6.0	27.00000	26.90000
11	5.45959	7.63809	7.65816	1.26924	7.44666	-2.26576	4.54791	0.57609	6.81367	14.5	26.00000	43.68000
12	5.59471	7.45477	7.46629	0.68596	7.04670	-1.63537	4.73978	-0.00719	6.37516	12.0	28.00000	65.77000
13	6.15273	7.50968	7.51540	0.12600	6.43184	-1.51796	4.69067	-0.56715	6.20863	1.5	16.00000	20.27000
14	5.83188	7.70724	7.71930	0.67677	6.78504	-2.20563	4.48677	-0.01638	6.69240	1.5	26.00000	40.09000
15	5.68358	7.47426	7.48227	-0.00605	6.33520	-1.56661	4.72380	-0.69920	6.29041	7.0	19.00000	30.22000
16	5.57215	7.34950	7.36782	0.81123	7.27724	-1.81803	4.83825	0.11809	6.65628	3.5	21.00000	30.33000

----- SUMMARY REPORT -----
 Algorithmhe Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 DESCRIPTIVE RESULTS (OVERALL)
 ----- SUMMARY REPORT -----

Parameter	Renal Function Group	n	Min	Mean	Geometric Mean	Median	Max	Standard Deviation	Coefficient of Variation
Cmax	Normal	8	126.00000	279.75000	259.25593	282.00000	514.00000	116.46551	41.632
Cmax	Severe	8	163.00000	307.37500	292.88094	281.50000	470.00000	100.62794	32.738
Tmax	Normal	8	1.00000	2.21875	2.08090	2.50000	3.00000	0.74926	33.769
Tmax	Severe	8	0.75000	1.82917	1.59223	1.78333	3.00000	0.94934	51.900
AUCT	Normal	8	618.34750	1688.87641	1584.04463	1785.61446	2269.41500	542.04977	32.095
AUCT	Severe	8	1103.70000	1950.11684	1865.30538	1793.85917	3325.83000	649.83012	33.323
Thalf	Normal	8	3.02245	4.31725	4.19268	3.81237	5.89271	1.13690	26.334
Thalf	Severe	8	3.16277	4.64585	4.42920	3.91320	6.68086	1.55718	33.518
AUCinf	Normal	8	624.44976	1704.90311	1599.57784	1800.31024	2293.04005	545.49033	31.995
AUCinf	Severe	8	1114.44994	1975.33824	1888.73988	1806.19268	3374.34231	661.00665	33.463
Ae	Normal	8	2.74783	4.88462	4.63816	4.60258	7.23717	1.64654	33.709
Ae	Severe	8	0.99397	2.00202	1.85098	1.97660	3.55816	0.84180	42.048
CLr	Normal	8	1708.45439	3023.35175	2928.05019	2983.69901	4443.82811	792.90521	26.226
CLr	Severe	8	564.08143	1063.94912	992.31982	1016.79021	1714.12729	413.70175	38.884
Lambda_z	Normal	8	0.11763	0.16999	0.16532	0.18252	0.22933	0.04151	24.417
Lambda_z	Severe	8	0.10375	0.16364	0.15649	0.17861	0.21916	0.04968	30.360
Cl_F	Normal	8	87.22046	137.28583	125.03299	111.17471	320.28197	76.75183	55.907
Cl_F	Severe	8	59.27081	110.52248	105.89071	110.76055	179.46073	34.59494	31.301
Vz_F	Normal	8	455.15651	812.52702	756.29525	786.87434	1623.58102	362.69776	44.638
Vz_F	Severe	8	497.02008	694.38660	676.63956	682.36672	910.20931	167.54105	24.128
fe	Normal	8	1.37392	2.44231	2.31908	2.30129	3.61858	0.82327	33.709
fe	Severe	8	0.49698	1.00101	0.92549	0.98830	1.77908	0.42090	42.048
lnCmax	Normal	8	4.83628	5.55782		5.64168	6.24222	0.42372	7.624
lnCmax	Severe	8	5.09375	5.67977		5.63915	6.15273	0.33688	5.931
lnAUCT	Normal	8	6.42705	7.36774		7.48722	7.72728	0.42187	5.726
lnAUCT	Severe	8	7.00642	7.53118		7.49197	8.10947	0.31504	4.183
lnAUCinf	Normal	8	6.43687	7.37750		7.49534	7.73763	0.42099	5.706
lnAUCinf	Severe	8	7.01612	7.54367		7.49884	8.12396	0.31634	4.193
lnAe	Normal	8	1.01081	1.53432		1.52618	1.97923	0.34855	22.717
lnAe	Severe	8	-0.00605	0.61571		0.68137	1.26924	0.42809	69.528
lnCLr	Normal	8	7.44334	7.98209		8.00041	8.39927	0.27709	3.471
lnCLr	Severe	8	6.33520	6.90005		6.91587	7.44666	0.40512	5.871
lnLambda_z	Normal	8	-2.14023	-1.79985		-1.70282	-1.47258	0.25630	-14.240
lnLambda_z	Severe	8	-2.26576	-1.85473		-1.72670	-1.51796	0.32714	-17.638
lnCl_F	Normal	8	4.46844	4.82858		4.71073	5.76920	0.42099	8.719
lnCl_F	Severe	8	4.08212	4.66241		4.70723	5.18996	0.31634	6.785
lnfe	Normal	8	0.31766	0.84117		0.83303	1.28608	0.34855	41.436
lnfe	Severe	8	-0.69920	-0.07743		-0.01178	0.57609	0.42809	-552.861
lnVz_F	Normal	8	6.12064	6.62843		6.66639	7.39239	0.38927	5.873
lnVz_F	Severe	8	6.20863	6.51714		6.51572	6.81367	0.24404	3.745
RkTmax	Normal	8	3.50000	9.43750	8.58239	10.00000	14.50000	3.95002	41.855
RkTmax	Severe	8	1.50000	7.56250	5.49765	6.50000	14.50000	5.46049	72.205

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=1 Param=Cmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	175.20453373	
1	1	175.05551335	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	10126
Residual	FunctionGroup Normal	13564

Fit Statistics

-2 Res Log Likelihood	175.1
AIC (Smaller is Better)	179.1
AICC (Smaller is Better)	180.1
BIC (Smaller is Better)	180.6

Null Model Likelihood

Ratio Test

DF	Chi-Square	Pr > ChiSq
1	0.15	0.6995

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	0.26	0.6196

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	307.38	35.5773	14	8.64	<.0001	0.1	244.71	370.04
FunctionGroup	Normal	279.75	41.1768	14	6.79	<.0001	0.1	207.22	352.28

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	27.6250	54.4176	14	0.51	0.6196	0.1	-68.2213	123.47

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=3 Param=AUCT

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	222.92709703	
1	1	222.69812530	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	422279
Residual	FunctionGroup Normal	293818

Fit Statistics

-2 Res Log Likelihood	222.7
AIC (Smaller is Better)	226.7
AICC (Smaller is Better)	227.8
BIC (Smaller is Better)	228.2

Null Model Likelihood

Ratio Test

DF	Chi-Square	Pr > ChiSq
1	0.23	0.6323

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	0.76	0.3973

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	1950.12	229.75	14	8.49	<.0001	0.1	1545.46	2354.78
FunctionGroup	Normal	1688.88	191.64	14	8.81	<.0001	0.1	1351.33	2026.42

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	261.24	299.19	14	0.87	0.3973	0.1	-265.72	788.20

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=5 Param=AUCinf

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	223.28213516	
1	1	223.02544785	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	436930
Residual	FunctionGroup Normal	297560

Fit Statistics

-2 Res Log Likelihood	223.0
AIC (Smaller is Better)	227.0
AICC (Smaller is Better)	228.1
BIC (Smaller is Better)	228.6

Null Model Likelihood

Ratio Test

DF	Chi-Square	Pr > ChiSq
1	0.26	0.6124

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	0.80	0.3872	

Least Squares Means

Effect	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	Function		Error							
	Group									
FunctionGroup	Severe	1975.34	233.70	14	8.45	<.0001	0.1	1563.72	2386.96	
FunctionGroup	Normal	1704.90	192.86	14	8.84	<.0001	0.1	1365.22	2044.59	

Differences of Least Squares Means

Effect	Renal	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	Function	Function		Error							
	Group	Group									
FunctionGroup	Severe	Normal	270.44	303.00	14	0.89	0.3872	0.1	-263.25	804.12	

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=12 Param=lnCmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	17.00030740	
1	1	16.63533952	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.1135
Residual	FunctionGroup Normal	0.1795

Fit Statistics

-2 Res Log Likelihood	16.6
AIC (Smaller is Better)	20.6
AICC (Smaller is Better)	21.7
BIC (Smaller is Better)	22.2

Null Model Likelihood

Ratio Test

DF	Chi-Square	Pr > ChiSq
1	0.36	0.5458

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	0.41	0.5343

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	5.6798	0.1191	14	47.69	<.0001	0.1	5.4700	5.8895
FunctionGroup	Normal	5.5578	0.1498	14	37.10	<.0001	0.1	5.2940	5.8217

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.1220	0.1914	14	0.64	0.5343	0.1	-0.2151	0.4590

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=13 Param=lnAUCT

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	16.22438554	
1	1	15.63585311	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.09925
Residual	FunctionGroup Normal	0.1780

Fit Statistics

-2 Res Log Likelihood	15.6
AIC (Smaller is Better)	19.6
AICC (Smaller is Better)	20.7
BIC (Smaller is Better)	21.2

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	0.59	0.4430

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	0.77	0.3948

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	7.5312	0.1114	14	67.61	<.0001	0.1	7.3350	7.7274
FunctionGroup	Normal	7.3677	0.1492	14	49.40	<.0001	0.1	7.1050	7.6304

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.1634	0.1862	14	0.88	0.3948	0.1	-0.1644	0.4913

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=14 Param=lnAUCinf

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	16.22800060	
1	1	15.66382424	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.1001
Residual	FunctionGroup Normal	0.1772

Fit Statistics

-2 Res Log Likelihood	15.7
AIC (Smaller is Better)	19.7
AICC (Smaller is Better)	20.8
BIC (Smaller is Better)	21.2

Null Model Likelihood
Ratio Test

DF	Chi-Square	Pr > ChiSq
1	0.56	0.4526

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	0.80	0.3872

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	7.5437	0.1118	14	67.45	<.0001	0.1	7.3467	7.7407
FunctionGroup	Normal	7.3775	0.1488	14	49.57	<.0001	0.1	7.1153	7.6397

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.1662	0.1862	14	0.89	0.3872	0.1	-0.1617	0.4941

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=21 Param=RkTmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	87.60832691	
1	1	86.88680275	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	29.8170
Residual	FunctionGroup Normal	15.6027

Fit Statistics

-2 Res Log Likelihood	86.9
AIC (Smaller is Better)	90.9
AICC (Smaller is Better)	92.0
BIC (Smaller is Better)	92.4

Null Model Likelihood

Ratio Test

DF	Chi-Square	Pr > ChiSq
1	0.72	0.3956

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	0.62	0.4445

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	7.5625	1.9306	14	3.92	0.0015	0.1	4.1622	10.9628
FunctionGroup	Normal	9.4375	1.3965	14	6.76	<.0001	0.1	6.9778	11.8972

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	-1.8750	2.3827	14	-0.79	0.4445	0.1	-6.0717	2.3217

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 Geometric LSmeans
 ----- SUMMARY REPORT -----

Obs	Parameters	Group	GeoLSmeans
1	lnCmax	Severe	292.88
2	lnCmax	Normal	259.26
3	lnAUCT	Severe	1865.31
4	lnAUCT	Normal	1584.04
5	lnAUCinf	Severe	1888.74
6	lnAUCinf	Normal	1599.58

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - Lasmiditan - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RATIO ESTIMATE BASED ON ln-TRANSFORMED PARAMETERS
 ----- SUMMARY REPORT -----

Obs	Parameters	Group	vs Group	Ratio (%)	L90	U90
1	lnCmax	Severe	Normal	112.970	80.643	158.255
2	lnAUCT	Severe	Normal	117.756	84.837	163.447
3	lnAUCinf	Severe	Normal	118.077	85.065	163.901

16.1.9.3 Documentation of statistical analysis – SAS® output of (S)-M8

Legend:

- AUCinf= $AUC_{(0-\infty)}$
- AUCT= $AUC_{(0-tlast)}$
- V_{Z_F}= V_Z/F
- CL_F= CL/F
- LambdaZ = λ_Z
- lCmax= $\ln(C_{max})$
- lAUCT= $\ln(AUC_{(0-tlast)})$
- lAUCinf= $\ln(AUC_{(0-\infty)})$
- lCLF= $\ln(CL/F)$
- lLambdaZ = $\ln(\lambda_Z)$
- lV_{Z_F}= $\ln(V_Z/F)$
- RkTmax= Rank of T_{max}

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Normal

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res_Area	Lambda z	lnCmax	lnAUCT
1	101	418.00000	2.00000	5781.92500	16.77310	86.63720	7258.77076	20.34567	0.04132	6.03548	8.66249
2	102	292.00000	2.50000	5449.00000	14.37083	83.95300	6685.55732	18.49595	0.04823	5.67675	8.60319
3	103	527.00000	2.50000	7332.65000	11.05589	111.32950	8072.40389	9.16399	0.06269	6.26720	8.90009
4	104	482.00000	2.00000	7017.30800	10.73134	75.04500	7829.60165	10.37465	0.06459	6.17794	8.85613
5	105	276.00000	0.75000	2600.95000	22.26073	72.86400	3495.21568	25.58542	0.03114	5.62040	7.86363
6	106	587.00000	2.50000	6180.57500	9.57655	114.41100	6588.78200	6.19549	0.07238	6.37502	8.72917
7	107	368.00000	6.00000	6280.01000	12.05213	93.66040	7234.85257	13.19782	0.05751	5.90808	8.74513
8	108	305.00000	2.50000	5063.21950	14.79742	93.54840	6192.57687	18.23728	0.04684	5.72031	8.52976

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrCL
1	8.8900	4.46173	-3.18629	6.5	115.00000	163.85000
2	8.8077	4.43026	-3.03171	9.5	102.00000	152.84000
3	8.9962	4.71249	-2.76948	9.5	94.00000	100.45000
4	8.9657	4.31809	-2.73968	6.5	109.00000	124.34000
5	8.1592	4.28859	-3.46934	1.5	102.00000	155.18000
6	8.7931	4.73980	-2.62583	9.5	116.00000	120.18000
7	8.8867	4.53968	-2.85575	14.5	98.00000	116.39000
8	8.7311	4.53848	-3.06097	9.5	118.00000	147.36000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Severe

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res Area	Lambda z	lnCmax
9	201	358.00000	1.00000	7425.10000	39.27202	28.24120	15368.01449	51.68471	0.01765	5.88053
10	202	470.00000	1.75000	9428.50000	25.32404	41.78940	15253.32387	38.18724	0.02737	6.15273
11	203	310.00000	4.00000	6700.17250	29.06330	40.12630	12055.64869	44.42296	0.02385	5.73657
12	204	417.00000	6.00000	10078.39167	23.04963	48.17324	15380.50680	34.47295	0.03007	6.03309
13	205	659.00000	6.00000	13860.92500	24.48850	55.44030	21130.95349	34.40464	0.02831	6.49072
14	206	849.00000	0.75000	13271.27500	31.80603	33.06085	23844.88619	44.34331	0.02179	6.74406
15	207	453.00000	1.00000	9315.07500	34.16493	45.28310	17732.59498	47.46919	0.02029	6.11589
16	208	331.00000	6.00000	7604.02333	25.01790	48.79000	12356.74154	38.46255	0.02771	5.80212

Obs	lnAUCT	lnAUCinf	lnAe	lnLambda_z	RkTmax	eGFR	CrCL
9	8.91262	9.6400	3.34078	-4.03703	3.5	26.00000	40.09000
10	9.15149	9.6326	3.73264	-3.59827	5.0	23.00000	29.51000
11	8.80989	9.3973	3.69203	-3.73599	12.0	26.00000	43.68000
12	9.21815	9.6409	3.87480	-3.50416	14.5	19.00000	30.22000
13	9.53683	9.9585	4.01531	-3.56472	14.5	27.00000	26.90000
14	9.49336	10.0793	3.49835	-3.82617	1.5	16.00000	20.27000
15	9.13939	9.7832	3.81293	-3.89771	3.5	21.00000	30.33000
16	8.93643	9.4220	3.88753	-3.58610	14.5	28.00000	65.77000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 DESCRIPTIVE RESULTS (OVERALL)
 ----- SUMMARY REPORT -----

Parameter	Renal Function Group	n	Min	Mean	Geometric Mean	Median	Max	Standard Deviation	Coefficient of Variation
Cmax	Normal	8	276.00000	406.87500	392.54455	393.00000	587.00000	116.40869	28.6104
Cmax	Severe	8	310.00000	480.87500	454.62126	435.00000	849.00000	184.76969	38.4236
Tmax	Normal	8	0.75000	2.59375	2.26923	2.50000	6.00000	1.49963	57.8170
Tmax	Severe	8	0.75000	3.31250	2.40894	2.87500	6.00000	2.44493	73.8092
AUCT	Normal	8	2600.95000	5713.20469	5492.82916	5981.25000	7332.65000	1466.09922	25.6616
AUCT	Severe	8	6700.17250	9710.43281	9412.27480	9371.78750	13860.9250	2645.71741	27.2461
Thalf	Normal	8	9.57655	13.95225	13.47543	13.21148	22.26073	4.12999	29.6009
Thalf	Severe	8	23.04963	29.02329	28.56709	27.19367	39.27202	5.67192	19.5427
Ae	Normal	8	72.86400	91.43106	90.34533	90.09280	114.41100	15.23914	16.6674
Ae	Severe	8	28.24120	42.61305	41.75407	43.53625	55.44030	8.82686	20.7140
AUCinf	Normal	8	3495.21568	6669.72009	6494.42091	6960.20495	8072.40389	1428.84310	21.4228
AUCinf	Severe	8	12055.6487	16640.3338	16223.39570	15374.2606	23844.8862	4101.61174	24.6486
Res_Area	Normal	8	6.19549	15.19953	13.86411	15.71755	25.58542	6.53814	43.0154
Res_Area	Severe	8	34.40464	41.68095	41.27221	41.40293	51.68471	6.27523	15.0554
Lambda_z	Normal	8	0.03114	0.05309	0.05144	0.05287	0.07238	0.01362	25.6606
Lambda_z	Severe	8	0.01765	0.02463	0.02426	0.02561	0.03007	0.00441	17.9180
lnCmax	Normal	8	5.62040	5.97265		5.97178	6.37502	0.28642	4.7954
lnCmax	Severe	8	5.73657	6.11946		6.07449	6.74406	0.34660	5.6639
lnAUCT	Normal	8	7.86363	8.61120		8.69583	8.90009	0.32590	3.7846
lnAUCT	Severe	8	8.80989	9.14977		9.14544	9.53683	0.26455	2.8914
lnAUCinf	Normal	8	8.15915	8.77870		8.84719	8.99621	0.26551	3.0244
lnAUCinf	Severe	8	9.39729	9.69421		9.64045	10.07933	0.23843	2.4595
lnAe	Normal	8	4.28859	4.50364		4.50010	4.73980	0.16463	3.6555
lnAe	Severe	8	3.34078	3.73180		3.77279	4.01531	0.22060	5.9112
lnLambda_z	Normal	8	-3.46934	-2.96738		-2.94373	-2.62583	0.27592	-9.2983
lnLambda_z	Severe	8	-4.03703	-3.71877		-3.66713	-3.50416	0.18786	-5.0518
RkTmax	Normal	8	1.50000	8.37500	7.23224	9.50000	14.50000	3.72012	44.4193
RkTmax	Severe	8	1.50000	8.62500	6.54350	8.50000	14.50000	5.74922	66.6577

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=9 Param=lnCmax
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.09927	0.09927	0.99 0.3363
Error	14	1.40212	0.10015	
Corrected Total	15	1.50139		

Root MSE	0.31647	R-Square	0.0661
Dependent Mean	6.04606	Adj R-Sq	-0.0006
Coeff Var	5.23427		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	6.16719	0.14513	42.50	<.0001	5.85592 6.47845
eGFR	eGFR	1	-0.00186	0.00187	-1.00	0.3363	-0.00588 0.00215

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Obs	Output Statistics							-2	-1	0	1	2	Cook's D
	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual							
1	6.0355	5.9529	0.1225	0.0826	0.292	0.283						0.007	
2	5.6768	5.9771	0.1051	-0.3004	0.298	-1.006	**					0.063	
3	6.2672	5.9920	0.0959	0.2752	0.302	0.913		*				0.042	
4	6.1779	5.9641	0.1142	0.2139	0.295	0.725		*				0.039	
5	5.6204	5.9771	0.1051	-0.3567	0.298	-1.195	**					0.089	
6	6.3750	5.9510	0.1240	0.4240	0.291	1.456			**			0.192	
7	5.9081	5.9846	0.1004	-0.0765	0.300	-0.255						0.004	
8	5.7203	5.9473	0.1269	-0.2270	0.290	-0.783	*					0.059	
9	5.8805	6.1187	0.1076	-0.2382	0.298	-0.800	*					0.042	
10	6.1527	6.1243	0.1115	0.0284	0.296	0.0959						0.001	
11	5.7366	6.1187	0.1076	-0.3822	0.298	-1.284	**					0.108	
12	6.0331	6.1318	0.1169	-0.0987	0.294	-0.336						0.009	
13	6.4907	6.1169	0.1064	0.3739	0.298	1.254			**			0.100	
14	6.7441	6.1374	0.1211	0.6067	0.292	2.075			****			0.370	
15	6.1159	6.1281	0.1142	-0.0122	0.295	-0.0412						0.000	
16	5.8021	6.1150	0.1051	-0.3129	0.298	-1.048	**					0.068	

Sum of Residuals 0
 Sum of Squared Residuals 1.40212
 Predicted Residual SS (PRESS) 1.84804

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

 Order=10 Param=lnAUCT

 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.18316	1.18316	13.68	0.0024
Error	14	1.21049	0.08646		
Corrected Total	15	2.39365			

Root MSE 0.29405 R-Square 0.4943
 Dependent Mean 8.88048 Adj R-Sq 0.4582
 Coeff Var 3.31116

Parameter Estimates								
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits	
Intercept	Intercept	1	9.29866	0.13485	68.96	<.0001	9.00945	9.58787
eGFR	eGFR	1	-0.00643	0.00174	-3.70	0.0024	-0.01016	-0.00270

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Obs	Dependent Variable	Output Statistics								Cook's D
		Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual	-2	-1	0	
1	8.6625	8.5588	0.1139	0.1037	0.271	0.382				0.013
2	8.6032	8.6424	0.0977	-0.0393	0.277	-0.142				0.001
3	8.9001	8.6939	0.0892	0.2062	0.280	0.736			*	0.027
4	8.8561	8.5974	0.1061	0.2587	0.274	0.943			*	0.067
5	7.8636	8.6424	0.0977	-0.7788	0.277	-2.808	*****			0.489
6	8.7292	8.5524	0.1152	0.1768	0.271	0.653			*	0.039
7	8.7451	8.6682	0.0933	0.0769	0.279	0.276				0.004
8	8.5298	8.5395	0.1179	-0.009753	0.269	-0.0362				0.000
9	8.9126	9.1314	0.1000	-0.2188	0.277	-0.791			*	0.041
10	9.1515	9.1507	0.1036	0.000802	0.275	0.00292				0.000
11	8.8099	9.1314	0.1000	-0.3215	0.277	-1.163	**			0.088
12	9.2181	9.1764	0.1086	0.0417	0.273	0.153				0.002
13	9.5368	9.1250	0.0989	0.4119	0.277	1.487			**	0.141
14	9.4934	9.1957	0.1125	0.2976	0.272	1.096			**	0.103
15	9.1394	9.1636	0.1061	-0.0242	0.274	-0.0881				0.001
16	8.9364	9.1185	0.0977	-0.1821	0.277	-0.657	*			0.027

Sum of Residuals 0
 Sum of Squared Residuals 1.21049
 Predicted Residual SS (PRESS) 1.54997

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	3.35690	3.35690	52.98 <.0001
Error	14	0.88714	0.06337	
Corrected Total	15	4.24404		

Root MSE	0.25173	R-Square	0.7910
Dependent Mean	9.23645	Adj R-Sq	0.7760
Coeff Var	2.72538		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	9.94083	0.11544	86.11	<.0001	9.69324 10.18842
eGFR	eGFR	1	-0.01084	0.00149	-7.28	<.0001	-0.01403 -0.00764

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	8.8900	8.6946	0.0975	0.1953	0.232	0.842			*			0.062
2	8.8077	8.8355	0.0836	-0.0278	0.237	-0.117						0.001
3	8.9962	8.9222	0.0763	0.0740	0.240	0.309						0.005
4	8.9657	8.7596	0.0908	0.2060	0.235	0.878			*			0.058
5	8.1592	8.8355	0.0836	-0.6764	0.237	-2.849	*****					0.503
6	8.7931	8.6838	0.0986	0.1093	0.232	0.472						0.020
7	8.8867	8.8788	0.0798	0.007818	0.239	0.0327						0.000
8	8.7311	8.6621	0.1009	0.0690	0.231	0.299						0.009
9	9.6400	9.6591	0.0856	-0.0190	0.237	-0.0804						0.000
10	9.6326	9.6916	0.0887	-0.0590	0.236	-0.251						0.004
11	9.3973	9.6591	0.0856	-0.2618	0.237	-1.106	**					0.080
12	9.6409	9.7349	0.0930	-0.0941	0.234	-0.402						0.013
13	9.9585	9.6482	0.0846	0.3102	0.237	1.309			**			0.109
14	10.0793	9.7674	0.0963	0.3119	0.233	1.341			**			0.154
15	9.7832	9.7133	0.0908	0.0699	0.235	0.298						0.007
16	9.4220	9.6374	0.0836	-0.2155	0.237	-0.907	*					0.051

Sum of Residuals 0
 Sum of Squared Residuals 0.88714
 Predicted Residual SS (PRESS) 1.14358

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	2.35608	2.35608	59.19 <.0001
Error	14	0.55724	0.03980	
Corrected Total	15	2.91332		

Root MSE	0.19951	R-Square	0.8087
Dependent Mean	4.11772	Adj R-Sq	0.7951
Coeff Var	4.84506		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	3.52761	0.09149	38.56	<.0001	3.33138 3.72384
eGFR	eGFR	1	0.00908	0.00118	7.69	<.0001	0.00655 0.01161

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Obs	Dependent Variable	Predicted Value	Output Statistics					-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual							
1	4.4617	4.5716	0.0773	-0.1099	0.184	-0.598	*						0.031
2	4.4303	4.4536	0.0663	-0.0234	0.188	-0.124							0.001
3	4.7125	4.3810	0.0605	0.3315	0.190	1.744			***				0.154
4	4.3181	4.5172	0.0720	-0.1991	0.186	-1.070	**						0.086
5	4.2886	4.4536	0.0663	-0.1650	0.188	-0.877	*						0.048
6	4.7398	4.5807	0.0782	0.1591	0.184	0.867		*					0.068
7	4.5397	4.4173	0.0633	0.1224	0.189	0.647		*					0.023
8	4.5385	4.5989	0.0800	-0.0604	0.183	-0.330							0.010
9	3.3408	3.7637	0.0679	-0.4229	0.188	-2.254	****						0.332
10	3.7326	3.7364	0.0703	-0.003775	0.187	-0.0202							0.000
11	3.6920	3.7637	0.0679	-0.0716	0.188	-0.382							0.010
12	3.8748	3.7001	0.0737	0.1747	0.185	0.942		*					0.070
13	4.0153	3.7727	0.0671	0.2426	0.188	1.291			**				0.106
14	3.4983	3.6729	0.0764	-0.1745	0.184	-0.947	*						0.077
15	3.8129	3.7183	0.0720	0.0947	0.186	0.509		*					0.019
16	3.8875	3.7818	0.0663	0.1057	0.188	0.562		*					0.020

Sum of Residuals 0
 Sum of Squared Residuals 0.55724
 Predicted Residual SS (PRESS) 0.71524

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	2.21253	2.21253	37.51 <.0001
Error	14	0.82576	0.05898	
Corrected Total	15	3.03829		

Root MSE	0.24286	R-Square	0.7282
Dependent Mean	-3.34307	Adj R-Sq	0.7088
Coeff Var	-7.26467		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-3.91492	0.11137	-35.15	<.0001	-4.15380 -3.67605
eGFR	eGFR	1	0.00880	0.00144	6.12	<.0001	0.00572 0.01188

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	-3.1863	-2.9032	0.0940	-0.2831	0.224	-1.264	**					0.141
2	-3.0317	-3.0176	0.0807	-0.0142	0.229	-0.0618						0.000
3	-2.7695	-3.0879	0.0736	0.3185	0.231	1.376			**			0.096
4	-2.7397	-2.9560	0.0876	0.2163	0.226	0.955			*			0.068
5	-3.4693	-3.0176	0.0807	-0.4518	0.229	-1.972	***					0.241
6	-2.6258	-2.8944	0.0951	0.2686	0.223	1.202			**			0.131
7	-2.8558	-3.0528	0.0770	0.1970	0.230	0.855			*			0.041
8	-3.0610	-2.8768	0.0974	-0.1842	0.222	-0.828	*					0.066
9	-4.0370	-3.6862	0.0826	-0.3508	0.228	-1.536	***					0.154
10	-3.5983	-3.7126	0.0856	0.1143	0.227	0.503			*			0.018
11	-3.7360	-3.6862	0.0826	-0.0498	0.228	-0.218						0.003
12	-3.5042	-3.7478	0.0897	0.2436	0.226	1.079			**			0.092
13	-3.5647	-3.6774	0.0816	0.1127	0.229	0.493						0.015
14	-3.8262	-3.7742	0.0930	-0.0520	0.224	-0.232						0.005
15	-3.8977	-3.7302	0.0876	-0.1675	0.226	-0.740	*					0.041
16	-3.5861	-3.6686	0.0807	0.0825	0.229	0.360						0.008

Sum of Residuals 0
 Sum of Squared Residuals 0.82576
 Predicted Residual SS (PRESS) 1.07344

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.04660	0.04660	0.00	0.9651
Error	14	328.45340	23.46096		
Corrected Total	15	328.50000			

Root MSE	4.84365	R-Square	0.0001
Dependent Mean	8.50000	Adj R-Sq	-0.0713
Coeff Var	56.98413		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	8.58300	2.22122	3.86	0.0017	3.81895 13.34704
eGFR	eGFR	1	-0.00128	0.02865	-0.04	0.9651	-0.06272 0.06017

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	6.5000	8.4362	1.8757	-1.9362	4.466	-0.434						0.017
2	9.5000	8.4528	1.6093	1.0472	4.568	0.229						0.003
3	9.5000	8.4630	1.4685	1.0370	4.616	0.225						0.003
4	6.5000	8.4438	1.7479	-1.9438	4.517	-0.430						0.014
5	1.5000	8.4528	1.6093	-6.9528	4.568	-1.522	***					0.144
6	9.5000	8.4349	1.8976	1.0651	4.456	0.239						0.005
7	14.5000	8.4579	1.5363	6.0421	4.594	1.315		**				0.097
8	9.5000	8.4323	1.9421	1.0677	4.437	0.241						0.006
9	3.5000	8.5498	1.6476	-5.0498	4.555	-1.109	**					0.080
10	5.0000	8.5536	1.7071	-3.5536	4.533	-0.784	*					0.044
11	12.0000	8.5498	1.6476	3.4502	4.555	0.757		*				0.038
12	14.5000	8.5587	1.7897	5.9413	4.501	1.320		**				0.138
13	14.5000	8.5485	1.6283	5.9515	4.562	1.305		**				0.108
14	1.5000	8.5626	1.8539	-7.0626	4.475	-1.578	***					0.214
15	3.5000	8.5562	1.7479	-5.0562	4.517	-1.119	**					0.094
16	14.5000	8.5472	1.6093	5.9528	4.568	1.303		**				0.105

Sum of Residuals 0
 Sum of Squared Residuals 328.45340
 Predicted Residual SS (PRESS) 425.98888

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.29993	0.29993	3.49	0.0826
Error	14	1.20146	0.08582		
Corrected Total	15	1.50139			

Root MSE	0.29295	R-Square	0.1998
Dependent Mean	6.04606	Adj R-Sq	0.1426
Coeff Var	4.84527		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	6.26825	0.13961	44.90	<.0001	5.96883 6.56768
CrCL	CrCL	1	-0.00260	0.00139	-1.87	0.0826	-0.00558 0.00038289

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	6.0355	5.8422	0.1313	0.1932	0.262	0.738		*				0.068
2	5.6768	5.8709	0.1189	-0.1941	0.268	-0.725		*				0.052
3	6.2672	6.0071	0.0761	0.2601	0.283	0.920			*			0.031
4	6.1779	5.9450	0.0910	0.2330	0.278	0.837			*			0.037
5	5.6204	5.8648	0.1215	-0.2444	0.267	-0.917		*				0.087
6	6.3750	5.9558	0.0877	0.4192	0.280	1.500			**			0.111
7	5.9081	5.9656	0.0849	-0.0576	0.280	-0.205						0.002
8	5.7203	5.8851	0.1130	-0.1648	0.270	-0.610		*				0.033
9	5.8805	6.1640	0.0967	-0.2835	0.277	-1.025		**				0.064
10	6.1527	6.1915	0.1069	-0.0388	0.273	-0.142						0.002
11	5.7366	6.1547	0.0935	-0.4181	0.278	-1.506	***					0.129
12	6.0331	6.1897	0.1061	-0.1566	0.273	-0.574		*				0.025
13	6.4907	6.1983	0.1095	0.2924	0.272	1.076			**			0.094
14	6.7441	6.2156	0.1165	0.5285	0.269	1.966			***			0.364
15	6.1159	6.1894	0.1060	-0.0735	0.273	-0.269						0.005
16	5.8021	6.0973	0.0782	-0.2951	0.282	-1.045		**				0.042

Sum of Residuals 0
 Sum of Squared Residuals 1.20146
 Predicted Residual SS (PRESS) 1.56784

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.57752	1.57752	27.06	0.0001
Error	14	0.81613	0.05830		
Corrected Total	15	2.39365			

Root MSE	0.24144	R-Square	0.6590
Dependent Mean	8.88048	Adj R-Sq	0.6347
Coeff Var	2.71881		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	9.39007	0.11506	81.61	<.0001	9.14328 9.63685
CrCL	CrCL	1	-0.00596	0.00115	-5.20	0.0001	-0.00842 -0.00350

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	8.6625	8.4131	0.1082	0.2494	0.216	1.156			**			0.168
2	8.6032	8.4787	0.0980	0.1245	0.221	0.564			*			0.031
3	8.9001	8.7911	0.0628	0.1090	0.233	0.467						0.008
4	8.8561	8.6486	0.0750	0.2075	0.229	0.904			*			0.044
5	7.8636	8.4648	0.1002	-0.6011	0.220	-2.736	*****					0.778
6	8.7292	8.6735	0.0723	0.0557	0.230	0.242						0.003
7	8.7451	8.6961	0.0700	0.0491	0.231	0.212						0.002
8	8.5298	8.5114	0.0932	0.0184	0.223	0.0825						0.001
9	8.9126	9.1510	0.0797	-0.2384	0.228	-1.046		**				0.067
10	9.1515	9.2141	0.0881	-0.0626	0.225	-0.279						0.006
11	8.8099	9.1296	0.0771	-0.3197	0.229	-1.397		**				0.111
12	9.2181	9.2099	0.0875	0.008278	0.225	0.0368						0.000
13	9.5368	9.2297	0.0903	0.3072	0.224	1.372			**			0.153
14	9.4934	9.2692	0.0961	0.2242	0.222	1.012			**			0.096
15	9.1394	9.2092	0.0874	-0.0698	0.225	-0.310						0.007
16	8.9364	8.9979	0.0644	-0.0615	0.233	-0.264						0.003

Sum of Residuals 0
 Sum of Squared Residuals 0.81613
 Predicted Residual SS (PRESS) 1.13316

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	3.66660	3.66660	88.90 <.0001
Error	14	0.57744	0.04125	
Corrected Total	15	4.24404		

Root MSE	0.20309	R-Square	0.8639
Dependent Mean	9.23645	Adj R-Sq	0.8542
Coeff Var	2.19880		

Parameter Estimates						
Variable	Label	DF	Parameter Estimate	Standard Error	t Value Pr > t	95% Confidence Limits
Intercept	Intercept	1	10.01334	0.09679	103.46 <.0001	9.80576 10.22093
CrCL	CrCL	1	-0.00909	0.00096417	-9.43 <.0001	-0.01116 -0.00702

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	8.8900	8.5238	0.0911	0.3661	0.182	2.017			****			0.512
2	8.8077	8.6239	0.0825	0.1838	0.186	0.990			*			0.097
3	8.9962	9.1002	0.0528	-0.1040	0.196	-0.530		*				0.010
4	8.9657	8.8830	0.0631	0.0827	0.193	0.428						0.010
5	8.1592	8.6027	0.0842	-0.4435	0.185	-2.400		****				0.598
6	8.7931	8.9208	0.0608	-0.1277	0.194	-0.659		*				0.021
7	8.8867	8.9553	0.0589	-0.0686	0.194	-0.353						0.006
8	8.7311	8.6737	0.0784	0.0574	0.187	0.306						0.008
9	9.6400	9.6489	0.0670	-0.008855	0.192	-0.0462						0.000
10	9.6326	9.7451	0.0741	-0.1125	0.189	-0.595		*				0.027
11	9.3973	9.6163	0.0648	-0.2190	0.192	-1.138		**				0.073
12	9.6409	9.7386	0.0736	-0.0978	0.189	-0.516		*				0.020
13	9.9585	9.7688	0.0759	0.1897	0.188	1.007			**			0.082
14	10.0793	9.8291	0.0808	0.2502	0.186	1.343			**			0.170
15	9.7832	9.7376	0.0735	0.0455	0.189	0.241						0.004
16	9.4220	9.4154	0.0542	0.006507	0.196	0.0332						0.000

Sum of Residuals 0
 Sum of Squared Residuals 0.57744
 Predicted Residual SS (PRESS) 0.82485

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.93556	1.93556	27.71	0.0001
Error	14	0.97775	0.06984		
Corrected Total	15	2.91332			

Root MSE	0.26427	R-Square	0.6644
Dependent Mean	4.11772	Adj R-Sq	0.6404
Coeff Var	6.41791		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	3.55326	0.12594	28.21	<.0001	3.28314 3.82338
CrCL	CrCL	1	0.00660	0.00125	5.26	0.0001	0.00391 0.00930

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	4.4617	4.6355	0.1185	-0.1738	0.236	-0.736		*				0.068
2	4.4303	4.5628	0.1073	-0.1325	0.242	-0.549		*				0.030
3	4.7125	4.2167	0.0687	0.4958	0.255	1.943			***			0.137
4	4.3181	4.3745	0.0821	-0.0564	0.251	-0.225						0.003
5	4.2886	4.5782	0.1096	-0.2896	0.240	-1.204		**				0.151
6	4.7398	4.3470	0.0791	0.3928	0.252	1.558			***			0.119
7	4.5397	4.3220	0.0766	0.2177	0.253	0.861			*			0.034
8	4.5385	4.5266	0.1020	0.0119	0.244	0.0489						0.000
9	3.3408	3.8181	0.0872	-0.4773	0.249	-1.913		***				0.224
10	3.7326	3.7482	0.0964	-0.0155	0.246	-0.0631						0.000
11	3.6920	3.8418	0.0843	-0.1497	0.250	-0.598		*				0.020
12	3.8748	3.7529	0.0958	0.1219	0.246	0.495						0.019
13	4.0153	3.7309	0.0988	0.2844	0.245	1.160			**			0.109
14	3.4983	3.6871	0.1051	-0.1888	0.242	-0.779		*				0.057
15	3.8129	3.7536	0.0957	0.0593	0.246	0.241						0.004
16	3.8875	3.9877	0.0705	-0.1001	0.255	-0.393						0.006

Sum of Residuals 0
 Sum of Squared Residuals 0.97775
 Predicted Residual SS (PRESS) 1.23480

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.58129	1.58129	15.19	0.0016
Error	14	1.45699	0.10407		
Corrected Total	15	3.03829			

Root MSE	0.32260	R-Square	0.5205
Dependent Mean	-3.34307	Adj R-Sq	0.4862
Coeff Var	-9.64981		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-3.85327	0.15374	-25.06	<.0001	-4.18300 -3.52353
CrCL	CrCL	1	0.00597	0.00153	3.90	0.0016	0.00269 0.00925

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z

Output Statistics									
Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual	-2 -1 0 1 2	Cook's D	
1	-3.1863	-2.8751	0.1446	-0.3112	0.288	-1.079	**		0.146
2	-3.0317	-2.9408	0.1310	-0.0909	0.295	-0.308			0.009
3	-2.7695	-3.2536	0.0839	0.4841	0.312	1.554		***	0.087
4	-2.7397	-3.1110	0.1003	0.3713	0.307	1.211		**	0.078
5	-3.4693	-2.9268	0.1338	-0.5425	0.294	-1.848	***		0.355
6	-2.6258	-3.1358	0.0966	0.5100	0.308	1.657		***	0.135
7	-2.8558	-3.1584	0.0935	0.3027	0.309	0.980		*	0.044
8	-3.0610	-2.9735	0.1245	-0.0874	0.298	-0.294			0.008
9	-4.0370	-3.6139	0.1065	-0.4231	0.305	-1.389	**		0.118
10	-3.5983	-3.6771	0.1177	0.0788	0.300	0.262			0.005
11	-3.7360	-3.5925	0.1030	-0.1435	0.306	-0.469			0.012
12	-3.5042	-3.6729	0.1169	0.1687	0.301	0.561		*	0.024
13	-3.5647	-3.6927	0.1206	0.1280	0.299	0.428			0.015
14	-3.8262	-3.7323	0.1283	-0.0939	0.296	-0.317			0.009
15	-3.8977	-3.6722	0.1168	-0.2255	0.301	-0.750	*		0.042
16	-3.5861	-3.4606	0.0861	-0.1255	0.311	-0.404			0.006

Sum of Residuals 0
 Sum of Squared Residuals 1.45699
 Predicted Residual SS (PRESS) 1.88199

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.51068	0.51068	0.02	0.8847
Error	14	327.98932	23.42781		
Corrected Total	15	328.50000			

Root MSE	4.84023	R-Square	0.0016
Dependent Mean	8.50000	Adj R-Sq	-0.0698
Coeff Var	56.94386		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	8.78994	2.30666	3.81	0.0019	3.84264 13.73724
CrCL	CrCL	1	-0.00339	0.02298	-0.15	0.8847	-0.05268 0.04589

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	6.5000	8.2340	2.1700	-1.7340	4.327	-0.401						0.020
2	9.5000	8.2714	1.9651	1.2286	4.423	0.278						0.008
3	9.5000	8.4491	1.2581	1.0509	4.674	0.225						0.002
4	6.5000	8.3681	1.5041	-1.8681	4.601	-0.406						0.009
5	1.5000	8.2635	2.0077	-6.7635	4.404	-1.536	***					0.245
6	9.5000	8.3822	1.4494	1.1178	4.618	0.242						0.003
7	14.5000	8.3951	1.4033	6.1049	4.632	1.318		**				0.080
8	9.5000	8.2900	1.8675	1.2100	4.465	0.271						0.006
9	3.5000	8.6539	1.5972	-5.1539	4.569	-1.128	**					0.078
10	5.0000	8.6898	1.7656	-3.6898	4.507	-0.819	*					0.051
11	12.0000	8.6417	1.5447	3.3583	4.587	0.732		*				0.030
12	14.5000	8.6874	1.7537	5.8126	4.511	1.288		**				0.125
13	14.5000	8.6987	1.8097	5.8013	4.489	1.292		**				0.136
14	1.5000	8.7212	1.9257	-7.2212	4.441	-1.626	***					0.249
15	3.5000	8.6870	1.7519	-5.1870	4.512	-1.150	**					0.100
16	14.5000	8.5668	1.2919	5.9332	4.665	1.272		**				0.062

Sum of Residuals 0
 Sum of Squared Residuals 327.98932
 Predicted Residual SS (PRESS) 432.94522

```

----- SUMMARY REPORT -----
Algorithm Pharma
CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8
(Healthy vs Severe)
ANOVA analysis
NON-PARAMETRIC TEST OF FIXED EFFECT for Tmax parameter
----- SUMMARY REPORT -----

```

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable Value
Classified by Variable Group

Group	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
1	8	67.0	68.0	9.359487	8.3750
2	8	69.0	68.0	9.359487	8.6250

Average scores were used for ties.

Wilcoxon Two-Sample Test

Statistic 67.0000

Normal Approximation

Z	-0.0534
One-Sided Pr < Z	0.4787
Two-Sided Pr > Z	0.9574

t Approximation

One-Sided Pr < Z	0.4791
Two-Sided Pr > Z	0.9581

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test

Chi-Square	0.0114
DF	1
Pr > Chi-Square	0.9149

Hodges-Lehmann Estimation

Location Shift (1 - 2) 0.0000

Type	90% Confidence Limits	Interval Midpoint	Asymptotic Standard Error
Asymptotic (Moses)	-3.5000 1.5000	-1.0000	1.5199
Exact	-3.5000 1.5000	-1.0000	

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Normal

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res_Area	Lambda z	lnCmax	lnAUCT
1	101	418.00000	2.00000	5781.92500	16.77310	86.63720	7258.77076	20.34567	0.04132	6.03548	8.66249
2	102	292.00000	2.50000	5449.00000	14.37083	83.95300	6685.55732	18.49595	0.04823	5.67675	8.60319
3	103	527.00000	2.50000	7332.65000	11.05589	111.32950	8072.40389	9.16399	0.06269	6.26720	8.90009
4	104	482.00000	2.00000	7017.30800	10.73134	75.04500	7829.60165	10.37465	0.06459	6.17794	8.85613
5	105	276.00000	0.75000	2600.95000	22.26073	72.86400	3495.21568	25.58542	0.03114	5.62040	7.86363
6	106	587.00000	2.50000	6180.57500	9.57655	114.41100	6588.78200	6.19549	0.07238	6.37502	8.72917
7	107	368.00000	6.00000	6280.01000	12.05213	93.66040	7234.85257	13.19782	0.05751	5.90808	8.74513
8	108	305.00000	2.50000	5063.21950	14.79742	93.54840	6192.57687	18.23728	0.04684	5.72031	8.52976

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrCL
1	8.8900	4.46173	-3.18629	6.5	115.00000	163.85000
2	8.8077	4.43026	-3.03171	9.5	102.00000	152.84000
3	8.9962	4.71249	-2.76948	9.5	94.00000	100.45000
4	8.9657	4.31809	-2.73968	6.5	109.00000	124.34000
5	8.1592	4.28859	-3.46934	1.5	102.00000	155.18000
6	8.7931	4.73980	-2.62583	9.5	116.00000	120.18000
7	8.8867	4.53968	-2.85575	14.5	98.00000	116.39000
8	8.7311	4.53848	-3.06097	9.5	118.00000	147.36000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Severe

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res Area	Lambda_z	lnCmax
9	013-01	470.00000	1.75000	9428.50000	25.32404	41.78940	15253.32387	38.18724	0.02737	6.15273
10	013-02	659.00000	6.00000	13860.92500	24.48850	55.44030	21130.95349	34.40464	0.02831	6.49072
11	013-03	310.00000	4.00000	6700.17250	29.06330	40.12630	12055.64869	44.42296	0.02385	5.73657
12	013-04	331.00000	6.00000	7604.02333	25.01790	48.79000	12356.74154	38.46255	0.02771	5.80212
13	013-05	849.00000	0.75000	13271.27500	31.80603	33.06085	23844.88619	44.34331	0.02179	6.74406
14	013-06	358.00000	1.00000	7425.10000	39.27202	28.24120	15368.01449	51.68471	0.01765	5.88053
15	013-07	417.00000	6.00000	10078.39167	23.04963	48.17324	15380.50680	34.47295	0.03007	6.03309
16	013-08	453.00000	1.00000	9315.07500	34.16493	45.28310	17732.59498	47.46919	0.02029	6.11589

Obs	lnAUCT	lnAUCinf	lnAe	lnLambda_z	RkTmax	eGFR	CrCL
9	9.15149	9.6326	3.73264	-3.59827	5.0	23.00000	29.51000
10	9.53683	9.9585	4.01531	-3.56472	14.5	27.00000	26.90000
11	8.80989	9.3973	3.69203	-3.73599	12.0	26.00000	43.68000
12	8.93643	9.4220	3.88753	-3.58610	14.5	28.00000	65.77000
13	9.49336	10.0793	3.49835	-3.82617	1.5	16.00000	20.27000
14	8.91262	9.6400	3.34078	-4.03703	3.5	26.00000	40.09000
15	9.21815	9.6409	3.87480	-3.50416	14.5	19.00000	30.22000
16	9.13939	9.7832	3.81293	-3.89771	3.5	21.00000	30.33000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 DESCRIPTIVE RESULTS (OVERALL)
 ----- SUMMARY REPORT -----

Parameter	Renal Function Group	n	Min	Mean	Geometric Mean	Median	Max	Standard Deviation	Coefficient of Variation
Cmax	Normal	8	276.00000	406.87500	392.54455	393.00000	587.00000	116.40869	28.6104
Cmax	Severe	8	310.00000	480.87500	454.62126	435.00000	849.00000	184.76969	38.4236
Tmax	Normal	8	0.75000	2.59375	2.26923	2.50000	6.00000	1.49963	57.8170
Tmax	Severe	8	0.75000	3.31250	2.40894	2.87500	6.00000	2.44493	73.8092
AUCT	Normal	8	2600.95000	5713.20469	5492.82916	5981.25000	7332.65000	1466.09922	25.6616
AUCT	Severe	8	6700.17250	9710.43281	9412.27480	9371.78750	13860.9250	2645.71741	27.2461
Thalf	Normal	8	9.57655	13.95225	13.47543	13.21148	22.26073	4.12999	29.6009
Thalf	Severe	8	23.04963	29.02329	28.56709	27.19367	39.27202	5.67192	19.5427
Ae	Normal	8	72.86400	91.43106	90.34533	90.09280	114.41100	15.23914	16.6674
Ae	Severe	8	28.24120	42.61305	41.75407	43.53625	55.44030	8.82686	20.7140
AUCinf	Normal	8	3495.21568	6669.72009	6494.42091	6960.20495	8072.40389	1428.84310	21.4228
AUCinf	Severe	8	12055.6487	16640.3338	16223.39570	15374.2606	23844.8862	4101.61174	24.6486
Res_Area	Normal	8	6.19549	15.19953	13.86411	15.71755	25.58542	6.53814	43.0154
Res_Area	Severe	8	34.40464	41.68095	41.27221	41.40293	51.68471	6.27523	15.0554
Lambda_z	Normal	8	0.03114	0.05309	0.05144	0.05287	0.07238	0.01362	25.6606
Lambda_z	Severe	8	0.01765	0.02463	0.02426	0.02561	0.03007	0.00441	17.9180
lnCmax	Normal	8	5.62040	5.97265		5.97178	6.37502	0.28642	4.7954
lnCmax	Severe	8	5.73657	6.11946		6.07449	6.74406	0.34660	5.6639
lnAUCT	Normal	8	7.86363	8.61120		8.69583	8.90009	0.32590	3.7846
lnAUCT	Severe	8	8.80989	9.14977		9.14544	9.53683	0.26455	2.8914
lnAUCinf	Normal	8	8.15915	8.77870		8.84719	8.99621	0.26551	3.0244
lnAUCinf	Severe	8	9.39729	9.69421		9.64045	10.07933	0.23843	2.4595
lnAe	Normal	8	4.28859	4.50364		4.50010	4.73980	0.16463	3.6555
lnAe	Severe	8	3.34078	3.73180		3.77279	4.01531	0.22060	5.9112
lnLambda_z	Normal	8	-3.46934	-2.96738		-2.94373	-2.62583	0.27592	-9.2983
lnLambda_z	Severe	8	-4.03703	-3.71877		-3.66713	-3.50416	0.18786	-5.0518
RkTmax	Normal	8	1.50000	8.37500	7.23224	9.50000	14.50000	3.72012	44.4193
RkTmax	Severe	8	1.50000	8.62500	6.54350	8.50000	14.50000	5.74922	66.6577

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=1 Param=Cmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	185.00002078	
1	1	183.55620418	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	34140
Residual	FunctionGroup Normal	13551

Fit Statistics

-2 Res Log Likelihood	183.6
AIC (Smaller is Better)	187.6
AICC (Smaller is Better)	188.6
BIC (Smaller is Better)	189.1

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	1.44	0.2295

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	0.92	0.3541

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	480.88	65.3260	14	7.36	<.0001	0.1	365.82	595.93
FunctionGroup	Normal	406.88	41.1567	14	9.89	<.0001	0.1	334.39	479.36

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	74.0000	77.2098	14	0.96	0.3541	0.1	-61.9904	209.99

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=3 Param=AUCT

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	258.59368283	
1	1	256.28397540	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	6999821
Residual	FunctionGroup Normal	2149447

Fit Statistics

-2 Res Log Likelihood	256.3
AIC (Smaller is Better)	260.3
AICC (Smaller is Better)	261.4
BIC (Smaller is Better)	261.8

Null Model Likelihood

DF	Chi-Square	Pr > ChiSq
1	2.31	0.1286

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	13.97	0.0022

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	9710.43	935.40	14	10.38	<.0001	0.1	8062.90	11358
FunctionGroup	Normal	5713.20	518.34	14	11.02	<.0001	0.1	4800.24	6626.17

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	3997.23	1069.42	14	3.74	0.0022	0.1	2113.65	5880.81

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=6 Param=AUCinf

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	268.72442632	
1	1	262.06174118	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	16823219
Residual	FunctionGroup Normal	2041593

Fit Statistics

-2 Res Log Likelihood	262.1
AIC (Smaller is Better)	266.1
AICC (Smaller is Better)	267.2
BIC (Smaller is Better)	267.6

Null Model Likelihood

DF	Chi-Square	Pr > ChiSq
1	6.66	0.0098

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	42.16	<.0001

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	16640	1450.14	14	11.47	<.0001	0.1	14086	19194
FunctionGroup	Normal	6669.72	505.17	14	13.20	<.0001	0.1	5779.95	7559.49

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	9970.61	1535.61	14	6.49	<.0001	0.1	7265.93	12675

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=9 Param=lnCmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	11.80387731	
1	1	11.55074238	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.1201
Residual	FunctionGroup Normal	0.08203

Fit Statistics

-2 Res Log Likelihood	11.6
AIC (Smaller is Better)	15.6
AICC (Smaller is Better)	16.6
BIC (Smaller is Better)	17.1

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	0.25	0.6149

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	0.85	0.3714

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	6.1195	0.1225	14	49.94	<.0001	0.1	5.9036	6.3353
FunctionGroup	Normal	5.9727	0.1013	14	58.98	<.0001	0.1	5.7943	6.1510

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.1468	0.1590	14	0.92	0.3714	0.1	-0.1332	0.4268

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=10 Param=lnAUCT

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	9.87937378	
1	1	9.57709878	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.06999
Residual	FunctionGroup Normal	0.1062

Fit Statistics

-2 Res Log Likelihood	9.6
AIC (Smaller is Better)	13.6
AICC (Smaller is Better)	14.7
BIC (Smaller is Better)	15.1

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	0.30	0.5825

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	13.17	0.0027

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	9.1498	0.09353	14	97.82	<.0001	0.1	8.9850	9.3145
FunctionGroup	Normal	8.6112	0.1152	14	74.73	<.0001	0.1	8.4083	8.8141

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.5386	0.1484	14	3.63	0.0027	0.1	0.2772	0.8000

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=11 Param=lnAUCinf

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	5.33283729	
1	1	5.25199201	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.05685
Residual	FunctionGroup Normal	0.07049

Fit Statistics

-2 Res Log Likelihood	5.3
AIC (Smaller is Better)	9.3
AICC (Smaller is Better)	10.3
BIC (Smaller is Better)	10.8

Null Model Likelihood

DF	Chi-Square	Pr > ChiSq
1	0.08	0.7762

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	52.66	<.0001

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	9.6942	0.08430	14	115.00	<.0001	0.1	9.5457	9.8427
FunctionGroup	Normal	8.7787	0.09387	14	93.52	<.0001	0.1	8.6134	8.9440

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.9155	0.1262	14	7.26	<.0001	0.1	0.6933	1.1377

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=14 Param=RkTmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	88.05521658	
1	1	86.76864874	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	33.0536
Residual	FunctionGroup Normal	13.8393

Fit Statistics

-2 Res Log Likelihood	86.8
AIC (Smaller is Better)	90.8
AICC (Smaller is Better)	91.9
BIC (Smaller is Better)	92.3

Null Model Likelihood

Ratio Test

DF	Chi-Square	Pr > ChiSq
1	1.29	0.2567

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
FunctionGroup	1	14	0.01	0.9192	

Least Squares Means

Effect	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	Function Group		Error							
FunctionGroup	Severe	8.6250	2.0327	14	4.24	0.0008	0.1	5.0449	12.2051	
FunctionGroup	Normal	8.3750	1.3153	14	6.37	<.0001	0.1	6.0584	10.6916	

Differences of Least Squares Means

Effect	Renal	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	Function Group	Function Group		Error							
FunctionGroup	Severe	Normal	0.2500	2.4211	14	0.10	0.9192	0.1	-4.0143	4.5143	

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 Geometric LSmeans
 ----- SUMMARY REPORT -----

Obs	Parameters	Group	GeoLSmeans
1	lnCmax	Severe	454.62
2	lnCmax	Normal	392.54
3	lnAUCT	Severe	9412.27
4	lnAUCT	Normal	5492.83
5	lnAUCinf	Severe	16223
6	lnAUCinf	Normal	6494.42

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M8 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RATIO ESTIMATE BASED ON ln-TRANSFORMED PARAMETERS
 ----- SUMMARY REPORT -----

Obs	Parameters	Group	vs Group	Ratio (%)	L90	U90
1	lnCmax	Severe	Normal	115.814	87.531	153.236
2	lnAUCT	Severe	Normal	171.356	131.940	222.546
3	lnAUCinf	Severe	Normal	249.805	200.029	311.967

16.1.9.4 Documentation of statistical analysis – SAS® output of (S,R)-M18

Legend:

- AUCinf= $AUC_{(0-\infty)}$
- AUCT= $AUC_{(0-tlast)}$
- V_{Z_F}= V_Z/F
- CL_F= CL/F
- LambdaZ = λ_Z
- lCmax= $\ln(C_{max})$
- lAUCT= $\ln(AUC_{(0-tlast)})$
- lAUCinf= $\ln(AUC_{(0-\infty)})$
- lCLF= $\ln(CL/F)$
- lLambdaZ = $\ln(\lambda_Z)$
- lV_{Z_F}= $\ln(V_Z/F)$
- RkTmax= Rank of T_{max}

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Normal

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res_Area	Lambda z	lnCmax	lnAUCT
1	101	65.40000	8.00000	1622.48750	14.31625	1.81632	2046.25114	20.70927	0.04842	4.18052	7.39172
2	102	60.80000	8.00000	1421.13750	12.64878	1.79845	1712.48846	17.01331	0.05480	4.10759	7.25921
3	103	89.90000	8.00000	1765.70500	8.55370	2.26527	1905.63475	7.34295	0.08103	4.49870	7.47631
4	104	77.00000	8.00000	1578.40617	8.71141	1.59174	1717.79161	8.11422	0.07957	4.34381	7.36417
5	105	34.50000	4.00000	629.62000	12.80730	0.70113	737.98538	14.68395	0.05412	3.54096	6.44512
6	106	70.90000	4.00000	1267.15500	8.04806	1.79999	1351.60507	6.24813	0.08613	4.26127	7.14453
7	107	69.10000	8.03333	1439.94250	10.72780	1.79353	1649.92717	12.72691	0.06461	4.23555	7.27236
8	108	55.50000	8.00000	1336.16300	12.46407	1.43729	1629.00185	17.97658	0.05561	4.01638	7.19756

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrCL
1	7.62376	0.59681	-3.02791	8.0	115.00000	163.85000
2	7.44570	0.58692	-2.90407	8.0	102.00000	152.84000
3	7.55257	0.81769	-2.51288	8.0	94.00000	100.45000
4	7.44879	0.46483	-2.53115	8.0	109.00000	124.34000
5	6.60392	-0.35506	-2.91653	1.5	102.00000	155.18000
6	7.20905	0.58778	-2.45194	1.5	116.00000	120.18000
7	7.40849	0.58418	-2.73935	12.0	98.00000	116.39000
8	7.39572	0.36276	-2.88936	8.0	118.00000	147.36000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Severe

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res_Area	Lambda_z	lnCmax	lnAUCT
9	201	93.10000	12.00000	2726.85000	42.77174	0.58419	6704.18507	59.32615	0.01621	4.53367	7.91090
10	202	68.30000	8.00000	1748.49750	24.77645	0.51524	2863.39423	38.93619	0.02798	4.22391	7.46651
11	203	71.60000	12.00000	2002.04000	26.20845	1.48157	3518.28125	43.09608	0.02645	4.27110	7.60192
12	204	132.00000	12.00000	3378.34583	18.65050	1.24216	4878.47360	30.74994	0.03717	4.88280	8.12514
13	205	90.70000	6.00000	2073.23500	19.35086	0.42887	2955.06339	29.84127	0.03582	4.50756	7.63687
14	206	77.40000	6.00000	1736.29833	23.54602	0.31198	2671.16709	34.99851	0.02944	4.34899	7.45951
15	207	81.70000	8.00000	2231.73750	25.49687	0.99874	3825.46501	41.66101	0.02719	4.40305	7.71054
16	208	86.90000	12.08333	2299.13583	45.55366	0.65712	5991.68955	61.62792	0.01522	4.46476	7.74029

Obs	lnAUCinf	lnAe	lnLambda_z	RkTmax	eGFR	CrCL
9	8.81049	-0.53754	-4.12239	14.0	26.00000	40.09000
10	7.95976	-0.66312	-3.57641	8.0	23.00000	29.51000
11	8.16573	0.39310	-3.63259	14.0	26.00000	43.68000
12	8.49259	0.21685	-3.29239	14.0	19.00000	30.22000
13	7.99128	-0.84661	-3.32925	3.5	27.00000	26.90000
14	7.89027	-1.16481	-3.52547	3.5	16.00000	20.27000
15	8.24944	-0.00126	-3.60507	8.0	21.00000	30.33000
16	8.69813	-0.41989	-4.18540	16.0	28.00000	65.77000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 DESCRIPTIVE RESULTS (OVERALL)
 ----- SUMMARY REPORT -----

Parameter	Renal Function Group	n	Min	Mean	Geometric Mean	Median	Max	Standard Deviation	Coefficient of Variation
Cmax	Normal	8	34.50000	65.38750	63.31345	67.25000	89.90000	16.26885	24.881
Cmax	Severe	8	68.30000	87.71250	86.01138	84.30000	132.00000	19.92468	22.716
Tmax	Normal	8	4.00000	7.00417	6.73067	8.00000	8.03333	1.85425	26.473
Tmax	Severe	8	6.00000	9.51042	9.12592	10.00000	12.08333	2.78831	29.318
AUCT	Normal	8	629.62000	1382.57708	1331.24627	1430.54000	1765.70500	344.31954	24.904
AUCT	Severe	8	1736.29833	2274.51750	2222.65966	2152.48625	3378.34583	548.58434	24.119
Thalf	Normal	8	8.04806	11.03467	10.80637	11.59593	14.31625	2.36420	21.425
Thalf	Severe	8	18.65050	28.29432	26.89951	25.13666	45.55366	10.19501	36.032
Ae	Normal	8	0.70113	1.65046	1.57734	1.79599	2.26527	0.45045	27.292
Ae	Severe	8	0.31198	0.77748	0.68529	0.62065	1.48157	0.41738	53.684
AUCinf	Normal	8	737.98538	1593.83568	1534.56427	1681.20781	2046.25114	401.22674	25.174
AUCinf	Severe	8	2671.16709	4175.96490	3952.91869	3671.87313	6704.18507	1522.00659	36.447
Res_Area	Normal	8	6.24813	13.10191	12.03682	13.70543	20.70927	5.40626	41.263
Res_Area	Severe	8	29.84127	42.52964	41.14168	40.29860	61.62792	12.05540	28.346
Lambda_z	Normal	8	0.04842	0.06554	0.06414	0.06011	0.08613	0.01463	22.329
Lambda_z	Severe	8	0.01522	0.02693	0.02577	0.02758	0.03717	0.00796	29.562
lnCmax	Normal	8	3.54096	4.14810		4.20804	4.49870	0.28544	6.881
lnCmax	Severe	8	4.22391	4.45448		4.43391	4.88280	0.20467	4.595
lnAUCT	Normal	8	6.44512	7.19387		7.26579	7.47631	0.32103	4.463
lnAUCT	Severe	8	7.45951	7.70646		7.67370	8.12514	0.22443	2.912
lnAUCinf	Normal	8	6.60392	7.33600		7.42709	7.62376	0.31967	4.358
lnAUCinf	Severe	8	7.89027	8.28221		8.20758	8.81049	0.34912	4.215
lnAe	Normal	8	-0.35506	0.45574		0.58555	0.81769	0.35217	77.275
lnAe	Severe	8	-1.16481	-0.37791		-0.47871	0.39310	0.53952	-142.764
lnLambda_z	Normal	8	-3.02791	-2.74665		-2.81436	-2.45194	0.22075	-8.037
lnLambda_z	Severe	8	-4.18540	-3.65862		-3.59074	-3.29239	0.33020	-9.025
RkTmax	Normal	8	1.50000	6.87500	5.53798	8.00000	12.00000	3.59315	52.264
RkTmax	Severe	8	3.50000	10.12500	8.75190	11.00000	16.00000	5.01960	49.576

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=9 Param=lnCmax
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.38670	0.38670	6.35	0.0245
Error	14	0.85234	0.06088		
Corrected Total	15	1.23904			

Root MSE	0.24674	R-Square	0.3121
Dependent Mean	4.30129	Adj R-Sq	0.2630
Coeff Var	5.73646		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	4.54036	0.11315	40.13	<.0001	4.29767 4.78304
eGFR	eGFR	1	-0.00368	0.00146	-2.52	0.0245	-0.00681 -0.00054793

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	4.1805	4.1174	0.0955	0.0631	0.227	0.278						0.007
2	4.1076	4.1652	0.0820	-0.0576	0.233	-0.248						0.004
3	4.4987	4.1946	0.0748	0.3041	0.235	1.293			**			0.085
4	4.3438	4.1395	0.0890	0.2043	0.230	0.888			*			0.059
5	3.5410	4.1652	0.0820	-0.6242	0.233	-2.682	*****					0.446
6	4.2613	4.1137	0.0967	0.1476	0.227	0.650			*			0.038
7	4.2356	4.1799	0.0783	0.0556	0.234	0.238						0.003
8	4.0164	4.1064	0.0989	-0.0900	0.226	-0.398						0.015
9	4.5337	4.4447	0.0839	0.0889	0.232	0.383						0.010
10	4.2239	4.4558	0.0870	-0.2319	0.231	-1.004	**					0.071
11	4.2711	4.4447	0.0839	-0.1736	0.232	-0.748	*					0.037
12	4.8828	4.4705	0.0912	0.4123	0.229	1.798			***			0.256
13	4.5076	4.4411	0.0829	0.0665	0.232	0.286						0.005
14	4.3490	4.4815	0.0944	-0.1325	0.228	-0.581	*					0.029
15	4.4031	4.4631	0.0890	-0.0601	0.230	-0.261						0.005
16	4.4648	4.4374	0.0820	0.0274	0.233	0.118						0.001

Sum of Residuals 0
 Sum of Squared Residuals 0.85234
 Predicted Residual SS (PRESS) 1.09736

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=10 Param=lnAUCT
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.01586	1.01586	12.82	0.0030
Error	14	1.10914	0.07922		
Corrected Total	15	2.12500			

Root MSE 0.28147 R-Square 0.4781
 Dependent Mean 7.45017 Adj R-Sq 0.4408
 Coeff Var 3.77800

Parameter Estimates

Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	7.83765	0.12908	60.72	<.0001	7.56081 8.11449
eGFR	eGFR	1	-0.00596	0.00166	-3.58	0.0030	-0.00953 -0.00239

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	7.3917	7.1521	0.1090	0.2396	0.260	0.923			*			0.075
2	7.2592	7.2296	0.0935	0.0296	0.265	0.112						0.001
3	7.4763	7.2773	0.0853	0.1990	0.268	0.742			*			0.028
4	7.3642	7.1879	0.1016	0.1763	0.263	0.672			*			0.034
5	6.4451	7.2296	0.0935	-0.7845	0.265	-2.955	*****					0.542
6	7.1445	7.1461	0.1103	-0.001610	0.259	-0.0062						0.000
7	7.2724	7.2534	0.0893	0.0189	0.267	0.0709						0.000
8	7.1976	7.1342	0.1129	0.0633	0.258	0.246						0.006
9	7.9109	7.6827	0.0957	0.2282	0.265	0.862			*			0.049
10	7.4665	7.7005	0.0992	-0.2340	0.263	-0.888		*				0.056
11	7.6019	7.6827	0.0957	-0.0807	0.265	-0.305						0.006
12	8.1251	7.7244	0.1040	0.4008	0.262	1.532				***		0.186
13	7.6369	7.6767	0.0946	-0.0398	0.265	-0.150						0.001
14	7.4595	7.7423	0.1077	-0.2828	0.260	-1.087		**				0.101
15	7.7105	7.7125	0.1016	-0.001927	0.263	-0.0073						0.000
16	7.7403	7.6707	0.0935	0.0696	0.265	0.262						0.004

Sum of Residuals 0
 Sum of Squared Residuals 1.10914
 Predicted Residual SS (PRESS) 1.43310

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

 Order=11 Param=lnAUCinf
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	3.36674	3.36674	26.43	0.0001
Error	14	1.78304	0.12736		
Corrected Total	15	5.14978			

Root MSE	0.35687	R-Square	0.6538
Dependent Mean	7.80911	Adj R-Sq	0.6290
Coeff Var	4.56998		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	8.51452	0.16366	52.03	<.0001	8.16351 8.86553
eGFR	eGFR	1	-0.01085	0.00211	-5.14	0.0001	-0.01538 -0.00633

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error	Residual	Std Error	Student						
			Mean Predict		Residual	Residual						
1	7.6238	7.2665	0.1382	0.3573	0.329	1.086			**			0.104
2	7.4457	7.4076	0.1186	0.0381	0.337	0.113						0.001
3	7.5526	7.4944	0.1082	0.0582	0.340	0.171						0.001
4	7.4488	7.3316	0.1288	0.1172	0.333	0.352						0.009
5	6.6039	7.4076	0.1186	-0.8036	0.337	-2.388	****					0.354
6	7.2090	7.2556	0.1398	-0.0466	0.328	-0.142						0.002
7	7.4085	7.4510	0.1132	-0.0425	0.338	-0.126						0.001
8	7.3957	7.2339	0.1431	0.1618	0.327	0.495						0.023
9	8.8105	8.2324	0.1214	0.5781	0.336	1.723			***			0.194
10	7.9598	8.2649	0.1258	-0.3051	0.334	-0.914	*					0.059
11	8.1657	8.2324	0.1214	-0.0666	0.336	-0.199						0.003
12	8.4926	8.3083	0.1319	0.1843	0.332	0.556			*			0.024
13	7.9913	8.2215	0.1200	-0.2302	0.336	-0.685		*				0.030
14	7.8903	8.3409	0.1366	-0.4506	0.330	-1.367	**					0.160
15	8.2494	8.2866	0.1288	-0.0372	0.333	-0.112						0.001
16	8.6981	8.2106	0.1186	0.4875	0.337	1.448			**			0.130

Sum of Residuals 0
 Sum of Squared Residuals 1.78304
 Predicted Residual SS (PRESS) 2.30750

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	2.73112	2.73112	12.94	0.0029
Error	14	2.95449	0.21103		
Corrected Total	15	5.68561			

Root MSE	0.45939	R-Square	0.4804
Dependent Mean	0.03892	Adj R-Sq	0.4432
Coeff Var	1180.46320		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-0.59643	0.21067	-2.83	0.0133	-1.04826 -0.14459
eGFR	eGFR	1	0.00977	0.00272	3.60	0.0029	0.00395 0.01560

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Obs	Dependent Variable		Output Statistics		Std Error		Student	-2 -1 0 1 2				Cook's D
			Predicted Value	Mean Predict	Residual	Std Error Residual		Residual	Residual	Residual	Residual	
1	0.5968	0.5276	0.1779	0.0692	0.424	0.163						0.002
2	0.5869	0.4006	0.1526	0.1864	0.433	0.430						0.011
3	0.8177	0.3224	0.1393	0.4953	0.438	1.131			**			0.065
4	0.4648	0.4690	0.1658	-0.004164	0.428	-0.0097						0.000
5	-0.3551	0.4006	0.1526	-0.7556	0.433	-1.744		***				0.189
6	0.5878	0.5374	0.1800	0.0504	0.423	0.119						0.001
7	0.5842	0.3615	0.1457	0.2227	0.436	0.511			*			0.015
8	0.3628	0.5570	0.1842	-0.1942	0.421	-0.461						0.020
9	-0.5375	-0.3423	0.1563	-0.1952	0.432	-0.452						0.013
10	-0.6631	-0.3716	0.1619	-0.2915	0.430	-0.678		*				0.033
11	0.3931	-0.3423	0.1563	0.7354	0.432	1.702			***			0.190
12	0.2169	-0.4107	0.1697	0.6276	0.427	1.470			**			0.171
13	-0.8466	-0.3325	0.1544	-0.5141	0.433	-1.188		**				0.090
14	-1.1648	-0.4400	0.1758	-0.7248	0.424	-1.708		***				0.250
15	-0.001261	-0.3912	0.1658	0.3899	0.428	0.910			*			0.062
16	-0.4199	-0.3227	0.1526	-0.0971	0.433	-0.224						0.003

Sum of Residuals 0
 Sum of Squared Residuals 2.95449
 Predicted Residual SS (PRESS) 3.83717

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	3.09115	3.09115	32.30 <.0001
Error	14	1.33996	0.09571	
Corrected Total	15	4.43111		

Root MSE	0.30937	R-Square	0.6976
Dependent Mean	-3.20264	Adj R-Sq	0.6760
Coeff Var	-9.65995		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-3.87856	0.14187	-27.34	<.0001	-4.18285 -3.57427
eGFR	eGFR	1	0.01040	0.00183	5.68	<.0001	0.00647 0.01432

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	-3.0279	-2.6827	0.1198	-0.3452	0.285	-1.210	**					0.129
2	-2.9041	-2.8179	0.1028	-0.0862	0.292	-0.295						0.005
3	-2.5129	-2.9011	0.0938	0.3882	0.295	1.317		**				0.088
4	-2.5311	-2.7451	0.1116	0.2139	0.289	0.741		*				0.041
5	-2.9165	-2.8179	0.1028	-0.0986	0.292	-0.338						0.007
6	-2.4519	-2.6723	0.1212	0.2204	0.285	0.774		*				0.054
7	-2.7394	-2.8595	0.0981	0.1201	0.293	0.409						0.009
8	-2.8894	-2.6515	0.1240	-0.2379	0.283	-0.839	*					0.067
9	-4.1224	-3.6082	0.1052	-0.5142	0.291	-1.767	***					0.204
10	-3.5764	-3.6394	0.1090	0.0630	0.290	0.218						0.003
11	-3.6326	-3.6082	0.1052	-0.0244	0.291	-0.0839						0.000
12	-3.2924	-3.6810	0.1143	0.3886	0.287	1.352		**				0.144
13	-3.3292	-3.5978	0.1040	0.2685	0.291	0.922		*				0.054
14	-3.5255	-3.7122	0.1184	0.1867	0.286	0.653		*				0.037
15	-3.6051	-3.6602	0.1116	0.0551	0.289	0.191						0.003
16	-4.1854	-3.5874	0.1028	-0.5980	0.292	-2.049	****					0.261

Sum of Residuals 0
 Sum of Squared Residuals 1.33996
 Predicted Residual SS (PRESS) 1.73778

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

 Order=14 Param=RkTmax

 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	41.44799	41.44799	2.17	0.1630
Error	14	267.55201	19.11086		
Corrected Total	15	309.00000			

Root MSE	4.37160	R-Square	0.1341
Dependent Mean	8.50000	Adj R-Sq	0.0723
Coeff Var	51.43055		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	10.97508	2.00475	5.47	<.0001	6.67532 15.27483
eGFR	eGFR	1	-0.03808	0.02586	-1.47	0.1630	-0.09353 0.01738

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	8.0000	6.5961	1.6929	1.4039	4.031	0.348						0.011
2	8.0000	7.0911	1.4525	0.9089	4.123	0.220						0.003
3	8.0000	7.3957	1.3254	0.6043	4.166	0.145						0.001
4	8.0000	6.8246	1.5776	1.1754	4.077	0.288						0.006
5	1.5000	7.0911	1.4525	-5.5911	4.123	-1.356	**					0.114
6	1.5000	6.5580	1.7127	-5.0580	4.022	-1.258	**					0.143
7	12.0000	7.2434	1.3865	4.7566	4.146	1.147		**				0.074
8	8.0000	6.4819	1.7528	1.5181	4.005	0.379						0.014
9	14.0000	9.9850	1.4870	4.0150	4.111	0.977		*				0.062
10	8.0000	10.0993	1.5407	-2.0993	4.091	-0.513	*					0.019
11	14.0000	9.9850	1.4870	4.0150	4.111	0.977		*				0.062
12	14.0000	10.2516	1.6153	3.7484	4.062	0.923		*				0.067
13	3.5000	9.9470	1.4696	-6.4470	4.117	-1.566	***					0.156
14	3.5000	10.3658	1.6732	-6.8658	4.039	-1.700	***					0.248
15	8.0000	10.1754	1.5776	-2.1754	4.077	-0.534	*					0.021
16	16.0000	9.9089	1.4525	6.0911	4.123	1.477		**				0.135

Sum of Residuals 0
 Sum of Squared Residuals 267.55201
 Predicted Residual SS (PRESS) 348.97946

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.52808	0.52808	10.40	0.0061
Error	14	0.71096	0.05078		
Corrected Total	15	1.23904			

Root MSE	0.22535	R-Square	0.4262
Dependent Mean	4.30129	Adj R-Sq	0.3852
Coeff Var	5.23914		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	4.59612	0.10739	42.80	<.0001	4.36579 4.82646
CrCL	CrCL	1	-0.00345	0.00107	-3.22	0.0061	-0.00574 -0.00116

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	4.1805	4.0308	0.1010	0.1497	0.201	0.743			*			0.069
2	4.1076	4.0688	0.0915	0.0388	0.206	0.188						0.003
3	4.4987	4.2496	0.0586	0.2491	0.218	1.145			**			0.047
4	4.3438	4.1672	0.0700	0.1767	0.214	0.825			*			0.036
5	3.5410	4.0608	0.0935	-0.5198	0.205	-2.535	*****					0.668
6	4.2613	4.1815	0.0675	0.0798	0.215	0.371						0.007
7	4.2356	4.1946	0.0653	0.0410	0.216	0.190						0.002
8	4.0164	4.0877	0.0869	-0.0714	0.208	-0.343						0.010
9	4.5337	4.4578	0.0744	0.0759	0.213	0.357						0.008
10	4.2239	4.4943	0.0822	-0.2704	0.210	-1.289	**					0.127
11	4.2711	4.4454	0.0719	-0.1743	0.214	-0.816	*					0.038
12	4.8828	4.4919	0.0816	0.3909	0.210	1.861			***			0.262
13	4.5076	4.5033	0.0843	0.004239	0.209	0.0203						0.000
14	4.3490	4.5262	0.0897	-0.1772	0.207	-0.857	*					0.069
15	4.4031	4.4915	0.0816	-0.0884	0.210	-0.421						0.013
16	4.4648	4.3692	0.0601	0.0955	0.217	0.440						0.007

Sum of Residuals 0
 Sum of Squared Residuals 0.71096
 Predicted Residual SS (PRESS) 0.96773

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.08368	1.08368	14.57	0.0019
Error	14	1.04132	0.07438		
Corrected Total	15	2.12500			

Root MSE	0.27273	R-Square	0.5100
Dependent Mean	7.45017	Adj R-Sq	0.4750
Coeff Var	3.66068		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	7.87252	0.12997	60.57	<.0001	7.59376 8.15128
CrCL	CrCL	1	-0.00494	0.00129	-3.82	0.0019	-0.00772 -0.00217

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Output Statistics												
Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual	-2	-1	0	1	2	Cook's D
1	7.3917	7.0628	0.1223	0.3290	0.244	1.349			**			0.229
2	7.2592	7.1172	0.1107	0.1420	0.249	0.570			*			0.032
3	7.4763	7.3761	0.0709	0.1002	0.263	0.381						0.005
4	7.3642	7.2580	0.0848	0.1062	0.259	0.410						0.009
5	6.4451	7.1056	0.1131	-0.6605	0.248	-2.662	*****					0.736
6	7.1445	7.2786	0.0817	-0.1340	0.260	-0.515		*				0.013
7	7.2724	7.2973	0.0791	-0.0249	0.261	-0.0956						0.000
8	7.1976	7.1442	0.1052	0.0533	0.252	0.212						0.004
9	7.9109	7.6744	0.0900	0.2365	0.257	0.919			*			0.052
10	7.4665	7.7267	0.0995	-0.2602	0.254	-1.025	**					0.081
11	7.6019	7.6566	0.0870	-0.0547	0.258	-0.212						0.003
12	8.1251	7.7232	0.0988	0.4020	0.254	1.581			***			0.189
13	7.6369	7.7396	0.1020	-0.1027	0.253	-0.406						0.013
14	7.4595	7.7723	0.1085	-0.3128	0.250	-1.250	**					0.147
15	7.7105	7.7226	0.0987	-0.0121	0.254	-0.0476						0.000
16	7.7403	7.5475	0.0728	0.1928	0.263	0.734			*			0.021

Sum of Residuals 0
 Sum of Squared Residuals 1.04132
 Predicted Residual SS (PRESS) 1.46054

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	2.98572	2.98572	19.32	0.0006
Error	14	2.16406	0.15458		
Corrected Total	15	5.14978			

Root MSE	0.39316	R-Square	0.5798
Dependent Mean	7.80911	Adj R-Sq	0.5498
Coeff Var	5.03465		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	8.51016	0.18737	45.42	<.0001	8.10830 8.91202
CrCL	CrCL	1	-0.00820	0.00187	-4.39	0.0006	-0.01221 -0.00420

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Obs	Dependent Variable	Predicted Value	Output Statistics				-2-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual					
1	7.6238	7.1660	0.1763	0.4577	0.351	1.302			**		0.213
2	7.4457	7.2564	0.1596	0.1893	0.359	0.527			*		0.027
3	7.5526	7.6861	0.1022	-0.1336	0.380	-0.352					0.004
4	7.4488	7.4902	0.1222	-0.0414	0.374	-0.111					0.001
5	6.6039	7.2372	0.1631	-0.6332	0.358	-1.770		***			0.326
6	7.2090	7.5243	0.1177	-0.3152	0.375	-0.840		*			0.035
7	7.4085	7.5554	0.1140	-0.1469	0.376	-0.390					0.007
8	7.3957	7.3013	0.1517	0.0944	0.363	0.260					0.006
9	8.8105	8.1813	0.1297	0.6292	0.371	1.695			***		0.176
10	7.9598	8.2681	0.1434	-0.3083	0.366	-0.842		*			0.054
11	8.1657	8.1518	0.1255	0.0139	0.373	0.0373					0.000
12	8.4926	8.2623	0.1425	0.2303	0.366	0.629			*		0.030
13	7.9913	8.2895	0.1470	-0.2982	0.365	-0.818		*			0.054
14	7.8903	8.3439	0.1564	-0.4536	0.361	-1.258		**			0.149
15	8.2494	8.2614	0.1423	-0.0119	0.367	-0.0325					0.000
16	8.6981	7.9706	0.1049	0.7275	0.379	1.920			***		0.141

Sum of Residuals 0
 Sum of Squared Residuals 2.16406
 Predicted Residual SS (PRESS) 2.86504

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	2.30470	2.30470	9.54	0.0080
Error	14	3.38091	0.24149		
Corrected Total	15	5.68561			

Root MSE	0.49142	R-Square	0.4054
Dependent Mean	0.03892	Adj R-Sq	0.3629
Coeff Var	1262.78135		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-0.57702	0.23419	-2.46	0.0273	-1.07931 -0.07473
CrCL	CrCL	1	0.00721	0.00233	3.09	0.0080	0.00220 0.01221

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Obs	Output Statistics							-2	-1	0	1	2	Cook's D
	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual							
1	0.5968	0.6039	0.2203	-0.007082	0.439	-0.0161							0.000
2	0.5869	0.5245	0.1995	0.0624	0.449	0.139							0.002
3	0.8177	0.1470	0.1277	0.6707	0.475	1.413			**				0.072
4	0.4648	0.3191	0.1527	0.1457	0.467	0.312							0.005
5	-0.3551	0.5414	0.2038	-0.8965	0.447	-2.005	****						0.418
6	0.5878	0.2892	0.1472	0.2986	0.469	0.637			*				0.020
7	0.5842	0.2618	0.1425	0.3223	0.470	0.685			*				0.022
8	0.3628	0.4850	0.1896	-0.1223	0.453	-0.270							0.006
9	-0.5375	-0.2881	0.1622	-0.2495	0.464	-0.538		*					0.018
10	-0.6631	-0.3643	0.1793	-0.2988	0.458	-0.653		*					0.033
11	0.3931	-0.2622	0.1568	0.6553	0.466	1.407			**				0.112
12	0.2169	-0.3592	0.1781	0.5761	0.458	1.258			**				0.120
13	-0.8466	-0.3831	0.1837	-0.4635	0.456	-1.017		**					0.084
14	-1.1648	-0.4309	0.1955	-0.7339	0.451	-1.628	***						0.249
15	-0.001261	-0.3584	0.1779	0.3572	0.458	0.780			*				0.046
16	-0.4199	-0.1030	0.1312	-0.3169	0.474	-0.669		*					0.017

Sum of Residuals 0
 Sum of Squared Residuals 3.38091
 Predicted Residual SS (PRESS) 4.47864

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	2.10429	2.10429	12.66 0.0031
Error	14	2.32682	0.16620	
Corrected Total	15	4.43111		

Root MSE	0.40768	R-Square	0.4749
Dependent Mean	-3.20264	Adj R-Sq	0.4374
Coeff Var	-12.72947		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-3.79118	0.19428	-19.51	<.0001	-4.20788 -3.37449
CrCL	CrCL	1	0.00689	0.00194	3.56	0.0031	0.00274 0.01104

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z

Output Statistics									
Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual	-2-1 0 1 2	Cook's D	
1	-3.0279	-2.6628	0.1828	-0.3651	0.364	-1.002	**		0.126
2	-2.9041	-2.7386	0.1655	-0.1655	0.373	-0.444			0.019
3	-2.5129	-3.0994	0.1060	0.5865	0.394	1.490		**	0.080
4	-2.5311	-2.9349	0.1267	0.4037	0.387	1.042		**	0.058
5	-2.9165	-2.7225	0.1691	-0.1940	0.371	-0.523	*		0.028
6	-2.4519	-2.9635	0.1221	0.5116	0.389	1.315		**	0.085
7	-2.7394	-2.9896	0.1182	0.2503	0.390	0.641		*	0.019
8	-2.8894	-2.7763	0.1573	-0.1130	0.376	-0.300			0.008
9	-4.1224	-3.5151	0.1345	-0.6073	0.385	-1.578	***		0.152
10	-3.5764	-3.5880	0.1487	0.0115	0.380	0.0304			0.000
11	-3.6326	-3.4904	0.1301	-0.1422	0.386	-0.368			0.008
12	-3.2924	-3.5831	0.1477	0.2907	0.380	0.765		*	0.044
13	-3.3292	-3.6059	0.1524	0.2767	0.378	0.732		*	0.044
14	-3.5255	-3.6516	0.1622	0.1261	0.374	0.337			0.011
15	-3.6051	-3.5823	0.1476	-0.0228	0.380	-0.0599			0.000
16	-4.1854	-3.3382	0.1088	-0.8472	0.393	-2.156	****		0.178

Sum of Residuals 0
 Sum of Squared Residuals 2.32682
 Predicted Residual SS (PRESS) 2.86678

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	22.99752	22.99752	1.13	0.3066
Error	14	286.00248	20.42875		
Corrected Total	15	309.00000			

Root MSE	4.51982	R-Square	0.0744
Dependent Mean	8.50000	Adj R-Sq	0.0083
Coeff Var	53.17432		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	10.44567	2.15397	4.85	0.0003	5.82587 15.06547
CrCL	CrCL	1	-0.02277	0.02146	-1.06	0.3066	-0.06879 0.02326

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2-1	0	1	2	Cook's D
			Std Error	Residual	Std Error	Student Residual					
		Mean Predict									
1	8.0000	6.7153	2.0264	1.2847	4.040	0.318					0.013
2	8.0000	6.9660	1.8350	1.0340	4.131	0.250					0.006
3	8.0000	8.1587	1.1748	-0.1587	4.364	-0.0364					0.000
4	8.0000	7.6148	1.4046	0.3852	4.296	0.0897					0.000
5	1.5000	6.9127	1.8748	-5.4127	4.113	-1.316	**				0.180
6	1.5000	7.7095	1.3535	-6.2095	4.312	-1.440	**				0.102
7	12.0000	7.7958	1.3105	4.2042	4.326	0.972		*			0.043
8	8.0000	7.0907	1.7439	0.9093	4.170	0.218					0.004
9	14.0000	9.5329	1.4915	4.4671	4.267	1.047		**			0.067
10	8.0000	9.7738	1.6487	-1.7738	4.208	-0.421					0.014
11	14.0000	9.4512	1.4424	4.5488	4.283	1.062		**			0.064
12	14.0000	9.7576	1.6376	4.2424	4.213	1.007		**			0.077
13	3.5000	9.8332	1.6899	-6.3332	4.192	-1.511	***				0.185
14	3.5000	9.9842	1.7982	-6.4842	4.147	-1.564	***				0.230
15	8.0000	9.7551	1.6359	-1.7551	4.213	-0.417					0.013
16	16.0000	8.9483	1.2064	7.0517	4.356	1.619		***			0.101

Sum of Residuals 0
 Sum of Squared Residuals 286.00248
 Predicted Residual SS (PRESS) 369.89708

```

----- SUMMARY REPORT -----
Algorithm Pharma
CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18
(Healthy vs Severe)
ANOVA analysis
NON-PARAMETRIC TEST OF FIXED EFFECT for Tmax parameter
----- SUMMARY REPORT -----

```

The NPAR1WAY Procedure

```

Wilcoxon Scores (Rank Sums) for Variable Value
Classified by Variable Group
Group      N      Sum of Expected Std Dev   Mean
          Scores Under H0 Under H0   Score
1             8       55.0      68.0 9.077445   6.8750
2             8       81.0      68.0 9.077445  10.1250

```

Average scores were used for ties.

Wilcoxon Two-Sample Test

```

Statistic                               55.0000

Normal Approximation
Z                                         -1.3770
One-Sided Pr < Z                         0.0843
Two-Sided Pr > |Z|                       0.1685

```

```

t Approximation
One-Sided Pr < Z                         0.0944
Two-Sided Pr > |Z|                       0.1887

```

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test

```

Chi-Square          2.0510
DF                  1
Pr > Chi-Square     0.1521

```

Hodges-Lehmann Estimation

```

Location Shift (1 - 2)    -4.0000
Type      90%      Interval Asymptotic
          Confidence Midpoint Standard Error
          Limits
Asymptotic (Moses) -4.0000 0.0000 -2.0000      1.2159
Exact          -4.0000 0.0000 -2.0000

```

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Normal

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res_Area	Lambda z	lnCmax	lnAUCT
1	101	65.40000	8.00000	1622.48750	14.31625	1.81632	2046.25114	20.70927	0.04842	4.18052	7.39172
2	102	60.80000	8.00000	1421.13750	12.64878	1.79845	1712.48846	17.01331	0.05480	4.10759	7.25921
3	103	89.90000	8.00000	1765.70500	8.55370	2.26527	1905.63475	7.34295	0.08103	4.49870	7.47631
4	104	77.00000	8.00000	1578.40617	8.71141	1.59174	1717.79161	8.11422	0.07957	4.34381	7.36417
5	105	34.50000	4.00000	629.62000	12.80730	0.70113	737.98538	14.68395	0.05412	3.54096	6.44512
6	106	70.90000	4.00000	1267.15500	8.04806	1.79999	1351.60507	6.24813	0.08613	4.26127	7.14453
7	107	69.10000	8.03333	1439.94250	10.72780	1.79353	1649.92717	12.72691	0.06461	4.23555	7.27236
8	108	55.50000	8.00000	1336.16300	12.46407	1.43729	1629.00185	17.97658	0.05561	4.01638	7.19756

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrCL
1	7.62376	0.59681	-3.02791	8.0	115.00000	163.85000
2	7.44570	0.58692	-2.90407	8.0	102.00000	152.84000
3	7.55257	0.81769	-2.51288	8.0	94.00000	100.45000
4	7.44879	0.46483	-2.53115	8.0	109.00000	124.34000
5	6.60392	-0.35506	-2.91653	1.5	102.00000	155.18000
6	7.20905	0.58778	-2.45194	1.5	116.00000	120.18000
7	7.40849	0.58418	-2.73935	12.0	98.00000	116.39000
8	7.39572	0.36276	-2.88936	8.0	118.00000	147.36000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Severe

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res_Area	Lambda z	lnCmax	lnAUCT
9	013-01	68.30000	8.00000	1748.49750	24.77645	0.51524	2863.39423	38.93619	0.02798	4.22391	7.46651
10	013-02	90.70000	6.00000	2073.23500	19.35086	0.42887	2955.06339	29.84127	0.03582	4.50756	7.63687
11	013-03	71.60000	12.00000	2002.04000	26.20845	1.48157	3518.28125	43.09608	0.02645	4.27110	7.60192
12	013-04	86.90000	12.08333	2299.13583	45.55366	0.65712	5991.68955	61.62792	0.01522	4.46476	7.74029
13	013-05	77.40000	6.00000	1736.29833	23.54602	0.31198	2671.16709	34.99851	0.02944	4.34899	7.45951
14	013-06	93.10000	12.00000	2726.85000	42.77174	0.58419	6704.18507	59.32615	0.01621	4.53367	7.91090
15	013-07	132.00000	12.00000	3378.34583	18.65050	1.24216	4878.47360	30.74994	0.03717	4.88280	8.12514
16	013-08	81.70000	8.00000	2231.73750	25.49687	0.99874	3825.46501	41.66101	0.02719	4.40305	7.71054

Obs	lnAUCinf	lnAe	lnLambda_z	RkTmax	eGFR	CrCL
9	7.95976	-0.66312	-3.57641	8.0	23.00000	29.51000
10	7.99128	-0.84661	-3.32925	3.5	27.00000	26.90000
11	8.16573	0.39310	-3.63259	14.0	26.00000	43.68000
12	8.69813	-0.41989	-4.18540	16.0	28.00000	65.77000
13	7.89027	-1.16481	-3.52547	3.5	16.00000	20.27000
14	8.81049	-0.53754	-4.12239	14.0	26.00000	40.09000
15	8.49259	0.21685	-3.29239	14.0	19.00000	30.22000
16	8.24944	-0.00126	-3.60507	8.0	21.00000	30.33000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 DESCRIPTIVE RESULTS (OVERALL)
 ----- SUMMARY REPORT -----

Parameter	Renal Function Group	n	Min	Mean	Geometric Mean	Median	Max	Standard Deviation	Coefficient of Variation
Cmax	Normal	8	34.50000	65.38750	63.31345	67.25000	89.90000	16.26885	24.881
Cmax	Severe	8	68.30000	87.71250	86.01138	84.30000	132.00000	19.92468	22.716
Tmax	Normal	8	4.00000	7.00417	6.73067	8.00000	8.03333	1.85425	26.473
Tmax	Severe	8	6.00000	9.51042	9.12592	10.00000	12.08333	2.78831	29.318
AUCT	Normal	8	629.62000	1382.57708	1331.24627	1430.54000	1765.70500	344.31954	24.904
AUCT	Severe	8	1736.29833	2274.51750	2222.65966	2152.48625	3378.34583	548.58434	24.119
Thalf	Normal	8	8.04806	11.03467	10.80637	11.59593	14.31625	2.36420	21.425
Thalf	Severe	8	18.65050	28.29432	26.89951	25.13666	45.55366	10.19501	36.032
Ae	Normal	8	0.70113	1.65046	1.57734	1.79599	2.26527	0.45045	27.292
Ae	Severe	8	0.31198	0.77748	0.68529	0.62065	1.48157	0.41738	53.684
AUCinf	Normal	8	737.98538	1593.83568	1534.56427	1681.20781	2046.25114	401.22674	25.174
AUCinf	Severe	8	2671.16709	4175.96490	3952.91869	3671.87313	6704.18507	1522.00659	36.447
Res_Area	Normal	8	6.24813	13.10191	12.03682	13.70543	20.70927	5.40626	41.263
Res_Area	Severe	8	29.84127	42.52964	41.14168	40.29860	61.62792	12.05540	28.346
Lambda_z	Normal	8	0.04842	0.06554	0.06414	0.06011	0.08613	0.01463	22.329
Lambda_z	Severe	8	0.01522	0.02693	0.02577	0.02758	0.03717	0.00796	29.562
lnCmax	Normal	8	3.54096	4.14810		4.20804	4.49870	0.28544	6.881
lnCmax	Severe	8	4.22391	4.45448		4.43391	4.88280	0.20467	4.595
lnAUCT	Normal	8	6.44512	7.19387		7.26579	7.47631	0.32103	4.463
lnAUCT	Severe	8	7.45951	7.70646		7.67370	8.12514	0.22443	2.912
lnAUCinf	Normal	8	6.60392	7.33600		7.42709	7.62376	0.31967	4.358
lnAUCinf	Severe	8	7.89027	8.28221		8.20758	8.81049	0.34912	4.215
lnAe	Normal	8	-0.35506	0.45574		0.58555	0.81769	0.35217	77.275
lnAe	Severe	8	-1.16481	-0.37791		-0.47871	0.39310	0.53952	-142.764
lnLambda_z	Normal	8	-3.02791	-2.74665		-2.81436	-2.45194	0.22075	-8.037
lnLambda_z	Severe	8	-4.18540	-3.65862		-3.59074	-3.29239	0.33020	-9.025
RkTmax	Normal	8	1.50000	6.87500	5.53798	8.00000	12.00000	3.59315	52.264
RkTmax	Severe	8	3.50000	10.12500	8.75190	11.00000	16.00000	5.01960	49.576

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=1 Param=Cmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	125.11180089	
1	1	124.82611966	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	396.99
Residual	FunctionGroup Normal	264.68

Fit Statistics

-2 Res Log Likelihood	124.8
AIC (Smaller is Better)	128.8
AICC (Smaller is Better)	129.9
BIC (Smaller is Better)	130.4

Null Model Likelihood

DF	Chi-Square	Pr > ChiSq
1	0.29	0.5930

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
FunctionGroup	1	14	6.03	0.0278	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	87.7125	7.0444	14	12.45	<.0001		0.1	75.3051	100.12
FunctionGroup	Normal	65.3875	5.7519	14	11.37	<.0001		0.1	55.2566	75.5184

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	22.3250	9.0944	14	2.45	0.0278		0.1	6.3069	38.3431

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=3 Param=AUCT

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	215.44058880	
1	1	213.97391815	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	300945
Residual	FunctionGroup Normal	118556

Fit Statistics

-2 Res Log Likelihood	214.0
AIC (Smaller is Better)	218.0
AICC (Smaller is Better)	219.1
BIC (Smaller is Better)	219.5

Null Model Likelihood

DF	Chi-Square	Pr > ChiSq
1	1.47	0.2259

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	15.17	0.0016

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	2274.52	193.95	14	11.73	<.0001	0.1	1932.90	2616.13
FunctionGroup	Normal	1382.58	121.74	14	11.36	<.0001	0.1	1168.16	1596.99

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	891.94	228.99	14	3.90	0.0016	0.1	488.61	1295.27

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=6 Param=AUCinf

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	240.30367540	
1	1	230.40152400	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	2316504
Residual	FunctionGroup Normal	160983

Fit Statistics

-2 Res Log Likelihood	230.4
AIC (Smaller is Better)	234.4
AICC (Smaller is Better)	235.5
BIC (Smaller is Better)	235.9

Null Model Likelihood

Ratio Test	DF	Chi-Square	Pr > ChiSq
1	9.90	0.0017	

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	21.53	0.0004	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	4175.96	538.11	14	7.76	<.0001	0.1	3228.19	5123.74	
FunctionGroup	Normal	1593.84	141.86	14	11.24	<.0001	0.1	1343.98	1843.69	

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	2582.13	556.49	14	4.64	0.0004	0.1	1601.97	3562.29	

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=9 Param=lnCmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	4.88862737	
1	1	4.12790664	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.04189
Residual	FunctionGroup Normal	0.08148

Fit Statistics

-2 Res Log Likelihood	4.1
AIC (Smaller is Better)	8.1
AICC (Smaller is Better)	9.2
BIC (Smaller is Better)	9.7

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	0.76	0.3831

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	6.09	0.0271	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	4.4545	0.07236	14	61.56	<.0001	0.1	4.3270	4.5819	
FunctionGroup	Normal	4.1481	0.1009	14	41.10	<.0001	0.1	3.9703	4.3258	

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.3064	0.1242	14	2.47	0.0271	0.1	0.08766	0.5251	

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=10 Param=lnAUCT

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	7.94191682	
1	1	7.06343593	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.05037
Residual	FunctionGroup Normal	0.1031

Fit Statistics

-2 Res Log Likelihood	7.1
AIC (Smaller is Better)	11.1
AICC (Smaller is Better)	12.2
BIC (Smaller is Better)	12.6

Null Model Likelihood

Ratio Test	DF	Chi-Square	Pr > ChiSq
1	0.88	0.3486	

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	13.70	0.0024

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	7.7065	0.07935	14	97.12	<.0001	0.1	7.5667	7.8462
FunctionGroup	Normal	7.1939	0.1135	14	63.38	<.0001	0.1	6.9940	7.3938

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.5126	0.1385	14	3.70	0.0024	0.1	0.2687	0.7565

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=11 Param=lnAUCinf

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	13.24438753	
1	1	13.19010744	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.1219
Residual	FunctionGroup Normal	0.1022

Fit Statistics

-2 Res Log Likelihood	13.2
AIC (Smaller is Better)	17.2
AICC (Smaller is Better)	18.3
BIC (Smaller is Better)	18.7

Null Model Likelihood

Ratio Test

DF	Chi-Square	Pr > ChiSq
1	0.05	0.8158

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	31.96	<.0001

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	8.2822	0.1234	14	67.10	<.0001	0.1	8.0648	8.4996
FunctionGroup	Normal	7.3360	0.1130	14	64.91	<.0001	0.1	7.1369	7.5351

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.9462	0.1674	14	5.65	<.0001	0.1	0.6514	1.2410

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=14 Param=RkTmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	85.15072586	
1	1	84.38248056	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	25.1964
Residual	FunctionGroup Normal	12.9107

Fit Statistics

-2 Res Log Likelihood	84.4
AIC (Smaller is Better)	88.4
AICC (Smaller is Better)	89.5
BIC (Smaller is Better)	89.9

Null Model Likelihood

Ratio Test

DF	Chi-Square	Pr > ChiSq
1	0.77	0.3808

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
FunctionGroup	1	14	2.22	0.1586	

Least Squares Means

Effect	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	FunctionGroup		Error							
FunctionGroup	Severe	10.1250	1.7747	14	5.71	<.0001	0.1	6.9992	13.2508	
FunctionGroup	Normal	6.8750	1.2704	14	5.41	<.0001	0.1	4.6375	9.1125	

Differences of Least Squares Means

Effect	Renal	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	FunctionGroup	FunctionGroup		Error							
FunctionGroup	Severe	Normal	3.2500	2.1825	14	1.49	0.1586	0.1	-0.5941	7.0941	

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 Geometric LSmeans
 ----- SUMMARY REPORT -----

Obs	Parameters	Group	GeoLSmeans
1	lnCmax	Severe	86.0114
2	lnCmax	Normal	63.3135
3	lnAUCT	Severe	2222.66
4	lnAUCT	Normal	1331.25
5	lnAUCinf	Severe	3952.92
6	lnAUCinf	Normal	1534.56

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,R)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RATIO ESTIMATE BASED ON ln-TRANSFORMED PARAMETERS
 ----- SUMMARY REPORT -----

Obs	Parameters	Group	vs Group	Ratio (%)	L90	U90
1	lnCmax	Severe	Normal	135.850	109.162	169.063
2	lnAUCT	Severe	Normal	166.961	130.822	213.082
3	lnAUCinf	Severe	Normal	257.592	191.829	345.901

16.1.9.5 Documentation of statistical analysis – SAS® output of (S,S)-M18

Legend:

- AUCinf= $AUC_{(0-\infty)}$
- AUCT= $AUC_{(0-tlast)}$
- V_{Z_F}= V_Z/F
- CL_F= CL/F
- LambdaZ = λ_Z
- lCmax= $\ln(C_{max})$
- lAUCT= $\ln(AUC_{(0-tlast)})$
- lAUCinf= $\ln(AUC_{(0-\infty)})$
- lCLF= $\ln(CL/F)$
- lLambdaZ = $\ln(\lambda_Z)$
- lV_{Z_F}= $\ln(V_Z/F)$
- RkTmax= Rank of T_{max}

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Normal

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res Area	Lambda z	lnCmax	lnAUCT
1	101	11.60000	4.00000	251.07875	11.49043	0.29028	291.46523	13.85636	0.06032	2.45101	5.52577
2	102	11.60000	6.00000	237.11000	9.64792	0.36323	262.55454	9.69115	0.07184	2.45101	5.46852
3	103	30.50000	4.00000	410.77500	6.13046	0.68963	420.79761	2.38181	0.11307	3.41773	6.01805
4	104	17.70000	4.05000	250.40233	6.75169	0.35708	284.88339	12.10357	0.10266	2.87356	5.52307
5	105	10.20000	6.00000	140.57375	8.09317	0.17223	165.52203	15.07248	0.08565	2.32239	4.94573
6	106	26.20000	4.00000	294.73500	6.55312	0.49921	327.35368	9.96435	0.10577	3.26576	5.68608
7	107	16.30000	8.03333	262.55675	10.35958	0.35874	290.19352	9.52357	0.06691	2.79117	5.57047
8	108	15.70000	8.00000	298.52700	7.04445	0.35671	315.40243	5.35045	0.09840	2.75366	5.69886

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrCL
1	5.67492	-1.23692	-2.80803	5.0	115.00000	163.85000
2	5.57046	-1.01271	-2.63325	9.5	102.00000	152.84000
3	6.04215	-0.37160	-2.17978	5.0	94.00000	100.45000
4	5.65208	-1.02980	-2.27631	8.0	109.00000	124.34000
5	5.10910	-1.75895	-2.45753	9.5	102.00000	155.18000
6	5.79104	-0.69474	-2.24645	5.0	116.00000	120.18000
7	5.67055	-1.02517	-2.70442	13.0	98.00000	116.39000
8	5.75385	-1.03082	-2.31875	11.5	118.00000	147.36000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Severe

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res_Area	Lambda z	lnCmax	lnAUCT
9	201	8.63000	8.00000	226.50375	23.37308	0.05148	360.22751	37.12203	0.02966	2.15524	5.42276
10	202	20.30000	4.00000	321.06250	14.67003	0.10180	393.73800	18.45783	0.04725	3.01062	5.77164
11	203	17.90000	12.00000	355.50900	15.98556	0.28436	464.47530	23.46008	0.04336	2.88480	5.87355
12	204	17.00000	12.00000	394.10558	13.57770	0.14649	489.91608	19.55651	0.05105	2.83321	5.97662
13	205	21.40000	3.00000	392.19250	12.93609	0.08889	464.78850	15.61915	0.05358	3.06339	5.97175
14	206	25.80000	3.00000	430.38083	17.84727	0.08234	559.95407	23.13998	0.03884	3.25037	6.06467
15	207	21.10000	4.00000	312.17500	11.80038	0.10227	359.52637	13.17049	0.05874	3.04927	5.74356
16	208	8.61000	12.08333	211.49083	24.81341	0.05965	356.02825	40.59718	0.02793	2.15292	5.35418

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrCL
9	5.88674	-2.96660	-3.51810	11.5	26.00000	40.09000
10	5.97569	-2.28477	-3.05232	5.0	23.00000	29.51000
11	6.14091	-1.25750	-3.13820	14.5	26.00000	43.68000
12	6.19423	-1.92077	-2.97494	14.5	19.00000	30.22000
13	6.14158	-2.42039	-2.92653	1.5	27.00000	26.90000
14	6.32785	-2.49689	-3.24836	1.5	16.00000	20.27000
15	5.88479	-2.28014	-2.83464	5.0	21.00000	30.33000
16	5.87501	-2.81924	-3.57790	16.0	28.00000	65.77000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 DESCRIPTIVE RESULTS (OVERALL)
 ----- SUMMARY REPORT -----

Parameter	Renal Function Group	n	Min	Mean	Geometric Mean	Median	Max	Standard Deviation	Coefficient of Variation
Cmax	Normal	8	10.20000	17.47500	16.29379	16.00000	30.50000	7.29300	41.7339
Cmax	Severe	8	8.61000	17.59250	16.44432	19.10000	25.80000	6.12898	34.8386
Tmax	Normal	8	4.00000	5.51042	5.27522	5.02500	8.03333	1.77359	32.1862
Tmax	Severe	8	3.00000	7.26042	6.13409	6.00000	12.08333	4.24765	58.5042
AUCT	Normal	8	140.57375	268.21982	258.41524	256.81775	410.77500	75.44937	28.1297
AUCT	Severe	8	211.49083	330.42750	321.28929	338.28575	430.38083	79.15310	23.9548
Thalf	Normal	8	6.13046	8.25885	8.05710	7.56881	11.49043	1.99997	24.2160
Thalf	Severe	8	11.80038	16.87544	16.31952	15.32780	24.81341	4.84002	28.6809
Ae	Normal	8	0.17223	0.38589	0.36056	0.35791	0.68963	0.15252	39.5232
Ae	Severe	8	0.05148	0.11466	0.09968	0.09534	0.28436	0.07451	64.9800
AUCinf	Normal	8	165.52203	294.77155	286.58045	290.82938	420.79761	70.95555	24.0714
AUCinf	Severe	8	356.02825	431.08176	425.53613	429.10665	559.95407	75.10840	17.4232
Res_Area	Normal	8	2.38181	9.74297	8.58932	9.82775	15.07248	4.21692	43.2817
Res_Area	Severe	8	13.17049	23.89041	22.28147	21.34824	40.59718	9.90358	41.4542
Lambda_z	Normal	8	0.06032	0.08808	0.08603	0.09202	0.11307	0.01980	22.4815
Lambda_z	Severe	8	0.02793	0.04380	0.04247	0.04531	0.05874	0.01108	25.3046
lnCmax	Normal	8	2.32239	2.79078		2.77241	3.41773	0.39228	14.0563
lnCmax	Severe	8	2.15292	2.79998		2.94771	3.25037	0.41772	14.9186
lnAUCT	Normal	8	4.94573	5.55457		5.54812	6.01805	0.30073	5.4142
lnAUCT	Severe	8	5.35418	5.77234		5.82259	6.06467	0.26052	4.5132
lnAUCinf	Normal	8	5.10910	5.65802		5.67273	6.04215	0.26292	4.6469
lnAUCinf	Severe	8	5.87501	6.05335		6.05830	6.32785	0.17099	2.8247
lnAe	Normal	8	-1.75895	-1.02009		-1.02748	-0.37160	0.39993	-39.2056
lnAe	Severe	8	-2.96660	-2.30579		-2.35258	-1.25750	0.53428	-23.1713
lnLambda_z	Normal	8	-2.80803	-2.45307		-2.38814	-2.17978	0.23553	-9.6015
lnLambda_z	Severe	8	-3.57790	-3.15887		-3.09526	-2.83464	0.27186	-8.6062
RkTmax	Normal	8	5.00000	8.31250	7.78504	8.75000	13.00000	3.11606	37.4864
RkTmax	Severe	8	1.50000	8.68750	6.19740	8.25000	16.00000	6.08826	70.0807

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=9 Param=lnCmax
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.00639	0.00639	0.04 0.8462
Error	14	2.29255	0.16375	
Corrected Total	15	2.29894		

Root MSE	0.40467	R-Square	0.0028
Dependent Mean	2.79538	Adj R-Sq	-0.0685
Coeff Var	14.47620		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	2.82612	0.18557	15.23	<.0001	2.42810 3.22413
eGFR	eGFR	1	-0.00047282	0.00239	-0.20	0.8462	-0.00561 0.00466

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Output Statistics										
Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual	-2	-1	0 1 2	Cook's D
1	2.4510	2.7717	0.1567	-0.3207	0.373	-0.860	*			0.065
2	2.4510	2.7779	0.1345	-0.3269	0.382	-0.856	*			0.046
3	3.4177	2.7817	0.1227	0.6361	0.386	1.649		***		0.138
4	2.8736	2.7746	0.1460	0.0990	0.377	0.262				0.005
5	2.3224	2.7779	0.1345	-0.4555	0.382	-1.193	**			0.088
6	3.2658	2.7713	0.1585	0.4945	0.372	1.328		**		0.160
7	2.7912	2.7798	0.1283	0.0114	0.384	0.0297				0.000
8	2.7537	2.7703	0.1623	-0.0167	0.371	-0.0449				0.000
9	2.1552	2.8138	0.1377	-0.6586	0.381	-1.731	***			0.196
10	3.0106	2.8152	0.1426	0.1954	0.379	0.516		*		0.019
11	2.8848	2.8138	0.1377	0.0710	0.381	0.187				0.002
12	2.8332	2.8171	0.1495	0.0161	0.376	0.0428				0.000
13	3.0634	2.8133	0.1360	0.2500	0.381	0.656		*		0.027
14	3.2504	2.8186	0.1549	0.4318	0.374	1.155		**		0.114
15	3.0493	2.8162	0.1460	0.2331	0.377	0.618		*		0.029
16	2.1529	2.8129	0.1345	-0.6600	0.382	-1.729	***			0.185

Sum of Residuals 0
 Sum of Squared Residuals 2.29255
 Predicted Residual SS (PRESS) 2.95371

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.21173	0.21173	2.73	0.1208
Error	14	1.08615	0.07758		
Corrected Total	15	1.29787			

Root MSE	0.27854	R-Square	0.1631
Dependent Mean	5.66345	Adj R-Sq	0.1034
Coeff Var	4.91812		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	5.84035	0.12773	45.72	<.0001	5.56640 6.11431
eGFR	eGFR	1	-0.00272	0.00165	-1.65	0.1208	-0.00625 0.00081184

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Output Statistics										
Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual	-2	-1	0 1 2	Cook's D
1	5.5258	5.5274	0.1079	-0.001612	0.257	-0.0063				0.000
2	5.4685	5.5628	0.0925	-0.0942	0.263	-0.359				0.008
3	6.0180	5.5845	0.0844	0.4335	0.265	1.633			***	0.135
4	5.5231	5.5437	0.1005	-0.0206	0.260	-0.0795				0.000
5	4.9457	5.5628	0.0925	-0.6170	0.263	-2.349	****			0.342
6	5.6861	5.5247	0.1091	0.1614	0.256	0.630		*		0.036
7	5.5705	5.5736	0.0883	-0.003178	0.264	-0.0120				0.000
8	5.6989	5.5192	0.1117	0.1796	0.255	0.704		*		0.047
9	5.4228	5.7696	0.0947	-0.3468	0.262	-1.324	**			0.115
10	5.7716	5.7778	0.0982	-0.006123	0.261	-0.0235				0.000
11	5.8736	5.7696	0.0947	0.1040	0.262	0.397				0.010
12	5.9766	5.7886	0.1029	0.1880	0.259	0.726		*		0.042
13	5.9718	5.7669	0.0936	0.2049	0.262	0.781		*		0.039
14	6.0647	5.7968	0.1066	0.2679	0.257	1.041		**		0.093
15	5.7436	5.7832	0.1005	-0.0396	0.260	-0.153				0.002
16	5.3542	5.7642	0.0925	-0.4100	0.263	-1.561	***			0.151

Sum of Residuals 0
 Sum of Squared Residuals 1.08615
 Predicted Residual SS (PRESS) 1.38435

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

 Order=11 Param=lnAUCinf
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.63297	0.63297	13.02	0.0029
Error	14	0.68073	0.04862		
Corrected Total	15	1.31370			

Root MSE	0.22051	R-Square	0.4818
Dependent Mean	5.85568	Adj R-Sq	0.4448
Coeff Var	3.76570		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	6.16155	0.10112	60.93	<.0001	5.94466 6.37843
eGFR	eGFR	1	-0.00471	0.00130	-3.61	0.0029	-0.00750 -0.00191

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error	Residual	Std Error	Student						
			Mean Predict		Residual	Residual						
1	5.6749	5.6204	0.0854	0.0545	0.203	0.268						0.006
2	5.5705	5.6816	0.0733	-0.1111	0.208	-0.534	*					0.018
3	6.0422	5.7192	0.0669	0.3229	0.210	1.537			***			0.120
4	5.6521	5.6486	0.0796	0.003441	0.206	0.0167						0.000
5	5.1091	5.6816	0.0733	-0.5725	0.208	-2.753	*****					0.470
6	5.7910	5.6157	0.0864	0.1753	0.203	0.864		*				0.068
7	5.6705	5.7004	0.0699	-0.0299	0.209	-0.143						0.001
8	5.7538	5.6063	0.0884	0.1476	0.202	0.730		*				0.051
9	5.8867	6.0392	0.0750	-0.1525	0.207	-0.735	*					0.035
10	5.9757	6.0533	0.0777	-0.0776	0.206	-0.376						0.010
11	6.1409	6.0392	0.0750	0.1017	0.207	0.490						0.016
12	6.1942	6.0721	0.0815	0.1221	0.205	0.596		*				0.028
13	6.1416	6.0345	0.0741	0.1071	0.208	0.516		*				0.017
14	6.3279	6.0863	0.0844	0.2416	0.204	1.186		**				0.121
15	5.8848	6.0627	0.0796	-0.1779	0.206	-0.865	*					0.056
16	5.8750	6.0298	0.0733	-0.1548	0.208	-0.744	*					0.034

Sum of Residuals 0
 Sum of Squared Residuals 0.68073
 Predicted Residual SS (PRESS) 0.87286

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	6.27816	6.27816	25.46	0.0002
Error	14	3.45176	0.24655		
Corrected Total	15	9.72992			

Root MSE	0.49654	R-Square	0.6452
Dependent Mean	-1.66294	Adj R-Sq	0.6199
Coeff Var	-29.85933		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-2.62622	0.22771	-11.53	<.0001	-3.11460 -2.13784
eGFR	eGFR	1	0.01482	0.00294	5.05	0.0002	0.00852 0.02112

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Output Statistics										
Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual	-2	-1	0 1 2	Cook's D
1	-1.2369	-0.9220	0.1923	-0.3150	0.458	-0.688	*			0.042
2	-1.0127	-1.1146	0.1650	0.1019	0.468	0.218				0.003
3	-0.3716	-1.2332	0.1505	0.8616	0.473	1.821			***	0.168
4	-1.0298	-1.0109	0.1792	-0.0189	0.463	-0.0409				0.000
5	-1.7590	-1.1146	0.1650	-0.6443	0.468	-1.376	**			0.117
6	-0.6947	-0.9071	0.1945	0.2124	0.457	0.465				0.020
7	-1.0252	-1.1739	0.1575	0.1487	0.471	0.316				0.006
8	-1.0308	-0.8775	0.1991	-0.1533	0.455	-0.337				0.011
9	-2.9666	-2.2409	0.1689	-0.7257	0.467	-1.554	***			0.158
10	-2.2848	-2.2854	0.1750	0.000591	0.465	0.00127				0.000
11	-1.2575	-2.2409	0.1689	0.9834	0.467	2.106			****	0.290
12	-1.9208	-2.3446	0.1835	0.4239	0.461	0.919			*	0.067
13	-2.4204	-2.2261	0.1669	-0.1943	0.468	-0.415				0.011
14	-2.4969	-2.3891	0.1900	-0.1078	0.459	-0.235				0.005
15	-2.2801	-2.3150	0.1792	0.0349	0.463	0.0753				0.000
16	-2.8192	-2.2113	0.1650	-0.6080	0.468	-1.298	**			0.105

Sum of Residuals 0
 Sum of Squared Residuals 3.45176
 Predicted Residual SS (PRESS) 4.38311

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.90378	1.90378	26.80	0.0001
Error	14	0.99455	0.07104		
Corrected Total	15	2.89833			

Root MSE	0.26653	R-Square	0.6569
Dependent Mean	-2.80597	Adj R-Sq	0.6323
Coeff Var	-9.49874		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-3.33642	0.12223	-27.30	<.0001	-3.59857 -3.07427
eGFR	eGFR	1	0.00816	0.00158	5.18	0.0001	0.00478 0.01154

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z

Output Statistics										
Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual	-2	-1	0 1 2	Cook's D
1	-2.8080	-2.3979	0.1032	-0.4101	0.246	-1.669	***			0.246
2	-2.6333	-2.5040	0.0886	-0.1292	0.251	-0.514	*			0.016
3	-2.1798	-2.5693	0.0808	0.3895	0.254	1.534		***		0.119
4	-2.2763	-2.4469	0.0962	0.1706	0.249	0.686		*		0.035
5	-2.4575	-2.5040	0.0886	0.0465	0.251	0.185				0.002
6	-2.2465	-2.3898	0.1044	0.1433	0.245	0.584		*		0.031
7	-2.7044	-2.5367	0.0845	-0.1678	0.253	-0.664	*			0.025
8	-2.3188	-2.3734	0.1069	0.0547	0.244	0.224				0.005
9	-3.5181	-3.1242	0.0907	-0.3939	0.251	-1.571	***			0.162
10	-3.0523	-3.1487	0.0939	0.0964	0.249	0.386				0.011
11	-3.1382	-3.1242	0.0907	-0.0140	0.251	-0.0557				0.000
12	-2.9749	-3.1814	0.0985	0.2064	0.248	0.833		*		0.055
13	-2.9265	-3.1161	0.0896	0.1895	0.251	0.755		*		0.036
14	-3.2484	-3.2058	0.1020	-0.0425	0.246	-0.173				0.003
15	-2.8346	-3.1650	0.0962	0.3304	0.249	1.329		**		0.132
16	-3.5779	-3.1079	0.0886	-0.4700	0.251	-1.870	***			0.217

Sum of Residuals 0
 Sum of Squared Residuals 0.99455
 Predicted Residual SS (PRESS) 1.28619

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

 Order=14 Param=RkTmax

 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.28336	0.28336	0.01	0.9140
Error	14	327.71664	23.40833		
Corrected Total	15	328.00000			

Root MSE	4.83822	R-Square	0.0009
Dependent Mean	8.50000	Adj R-Sq	-0.0705
Coeff Var	56.92019		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	8.70465	2.21873	3.92	0.0015	3.94594 13.46335
eGFR	eGFR	1	-0.00315	0.02862	-0.11	0.9140	-0.06452 0.05823

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Output Statistics										
Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual	-2	-1	0 1 2	Cook's D
1	5.0000	8.3426	1.8736	-3.3426	4.461	-0.749	*			0.050
2	9.5000	8.3835	1.6075	1.1165	4.563	0.245				0.004
3	5.0000	8.4087	1.4669	-3.4087	4.610	-0.739	*			0.028
4	8.0000	8.3615	1.7460	-0.3615	4.512	-0.0801				0.000
5	9.5000	8.3835	1.6075	1.1165	4.563	0.245				0.004
6	5.0000	8.3394	1.8955	-3.3394	4.451	-0.750	*			0.051
7	13.0000	8.3961	1.5345	4.6039	4.588	1.003		**		0.056
8	11.5000	8.3331	1.9399	3.1669	4.432	0.715		*		0.049
9	11.5000	8.6228	1.6458	2.8772	4.550	0.632		*		0.026
10	5.0000	8.6322	1.7051	-3.6322	4.528	-0.802	*			0.046
11	14.5000	8.6228	1.6458	5.8772	4.550	1.292		**		0.109
12	14.5000	8.6448	1.7877	5.8552	4.496	1.302		**		0.134
13	1.5000	8.6196	1.6265	-7.1196	4.557	-1.562	***			0.156
14	1.5000	8.6543	1.8518	-7.1543	4.470	-1.601	***			0.220
15	5.0000	8.6385	1.7460	-3.6385	4.512	-0.806	*			0.049
16	16.0000	8.6165	1.6075	7.3835	4.563	1.618		***		0.162

Sum of Residuals 0
 Sum of Squared Residuals 327.71664
 Predicted Residual SS (PRESS) 427.89663

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.19376	0.19376	1.29 0.2754
Error	14	2.10519	0.15037	
Corrected Total	15	2.29894		

Root MSE	0.38778	R-Square	0.0843
Dependent Mean	2.79538	Adj R-Sq	0.0189
Coeff Var	13.87203		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	2.97397	0.18480	16.09	<.0001	2.57762 3.37033
CrCL	CrCL	1	-0.00209	0.00184	-1.14	0.2754	-0.00604 0.00186

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Output Statistics									
Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual	-2 -1 0 1 2	Cook's D	
1	2.4510	2.6316	0.1739	-0.1806	0.347	-0.521	*	0.034	
2	2.4510	2.6546	0.1574	-0.2036	0.354	-0.574	*	0.033	
3	3.4177	2.7641	0.1008	0.6537	0.374	1.746	***	0.110	
4	2.8736	2.7141	0.1205	0.1594	0.369	0.433		0.010	
5	2.3224	2.6497	0.1608	-0.3273	0.353	-0.928	*	0.089	
6	3.2658	2.7228	0.1161	0.5429	0.370	1.467	**	0.106	
7	2.7912	2.7307	0.1124	0.0604	0.371	0.163		0.001	
8	2.7537	2.6660	0.1496	0.0876	0.358	0.245		0.005	
9	2.1552	2.8902	0.1280	-0.7349	0.366	-2.008	****	0.246	
10	3.0106	2.9123	0.1414	0.0983	0.361	0.272		0.006	
11	2.8848	2.8827	0.1238	0.002109	0.368	0.00574		0.000	
12	2.8332	2.9108	0.1405	-0.0776	0.361	-0.215		0.003	
13	3.0634	2.9178	0.1450	0.1456	0.360	0.405		0.013	
14	3.2504	2.9316	0.1543	0.3188	0.356	0.896	*	0.075	
15	3.0493	2.9106	0.1404	0.1387	0.361	0.384		0.011	
16	2.1529	2.8365	0.1035	-0.6836	0.374	-1.829	***	0.128	

Sum of Residuals 0
 Sum of Squared Residuals 2.10519
 Predicted Residual SS (PRESS) 2.60039

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.42771	0.42771	6.88	0.0200
Error	14	0.87017	0.06215		
Corrected Total	15	1.29787			

Root MSE	0.24931	R-Square	0.3295
Dependent Mean	5.66345	Adj R-Sq	0.2817
Coeff Var	4.40206		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	5.92879	0.11881	49.90	<.0001	5.67397 6.18362
CrCL	CrCL	1	-0.00310	0.00118	-2.62	0.0200	-0.00564 -0.00056627

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Output Statistics										
Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual	-2	-1	0 1 2	Cook's D
1	5.5258	5.4201	0.1118	0.1057	0.223	0.474				0.028
2	5.4685	5.4543	0.1012	0.0143	0.228	0.0626				0.000
3	6.0180	5.6169	0.0648	0.4011	0.241	1.666			***	0.101
4	5.5231	5.5427	0.0775	-0.0197	0.237	-0.0830				0.000
5	4.9457	5.4470	0.1034	-0.5013	0.227	-2.210	****			0.507
6	5.6861	5.5557	0.0747	0.1304	0.238	0.548			*	0.015
7	5.5705	5.5674	0.0723	0.003045	0.239	0.0128				0.000
8	5.6989	5.4713	0.0962	0.2276	0.230	0.990			*	0.086
9	5.4228	5.8043	0.0823	-0.3816	0.235	-1.621	***			0.161
10	5.7716	5.8372	0.0909	-0.0655	0.232	-0.282				0.006
11	5.8736	5.7932	0.0796	0.0804	0.236	0.340				0.007
12	5.9766	5.8350	0.0903	0.1417	0.232	0.610			*	0.028
13	5.9718	5.8453	0.0932	0.1265	0.231	0.547			*	0.024
14	6.0647	5.8659	0.0992	0.1988	0.229	0.869			*	0.071
15	5.7436	5.8346	0.0902	-0.0911	0.232	-0.392				0.012
16	5.3542	5.7246	0.0665	-0.3704	0.240	-1.542	***			0.091

Sum of Residuals 0
 Sum of Squared Residuals 0.87017
 Predicted Residual SS (PRESS) 1.13301

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.84028	0.84028	24.85	0.0002
Error	14	0.47341	0.03382		
Corrected Total	15	1.31370			

Root MSE	0.18389	R-Square	0.6396
Dependent Mean	5.85568	Adj R-Sq	0.6139
Coeff Var	3.14036		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	6.22760	0.08763	71.06	<.0001	6.03964 6.41555
CrCL	CrCL	1	-0.00435	0.00087302	-4.98	0.0002	-0.00622 -0.00248

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Obs	Dependent Variable		Output Statistics		Std Error		Student		-2 -1 0 1 2				Cook's D
			Predicted Value	Mean Predict	Residual	Std Error Residual	Residual	Residual					
1	5.6749	5.5145	0.0824	0.1604	0.164	0.976		*					0.120
2	5.5705	5.5625	0.0747	0.008005	0.168	0.0476							0.000
3	6.0422	5.7904	0.0478	0.2517	0.178	1.417		**					0.073
4	5.6521	5.6865	0.0571	-0.0344	0.175	-0.197							0.002
5	5.1091	5.5523	0.0763	-0.4432	0.167	-2.649	*****						0.729
6	5.7910	5.7046	0.0551	0.0865	0.175	0.493							0.012
7	5.6705	5.7211	0.0533	-0.0505	0.176	-0.287							0.004
8	5.7538	5.5863	0.0709	0.1675	0.170	0.988		*					0.085
9	5.8867	6.0531	0.0607	-0.1664	0.174	-0.959		*					0.056
10	5.9757	6.0992	0.0671	-0.1235	0.171	-0.721		*					0.040
11	6.1409	6.0375	0.0587	0.1034	0.174	0.593		*					0.020
12	6.1942	6.0961	0.0666	0.0982	0.171	0.573		*					0.025
13	6.1416	6.1105	0.0688	0.0311	0.171	0.182							0.003
14	6.3279	6.1394	0.0732	0.1885	0.169	1.117		**					0.117
15	5.8848	6.0956	0.0666	-0.2108	0.171	-1.230		**					0.114
16	5.8750	5.9414	0.0491	-0.0664	0.177	-0.374							0.005

Sum of Residuals 0
 Sum of Squared Residuals 0.47341
 Predicted Residual SS (PRESS) 0.64860

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	4.63980	4.63980	12.76 0.0031
Error	14	5.09012	0.36358	
Corrected Total	15	9.72992		

Root MSE	0.60298	R-Square	0.4769
Dependent Mean	-1.66294	Adj R-Sq	0.4395
Coeff Var	-36.25967		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-2.53687	0.28735	-8.83	<.0001	-3.15318 -1.92056
CrCL	CrCL	1	0.01023	0.00286	3.57	0.0031	0.00409 0.01637

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Obs	Dependent Variable		Output Statistics		Std Error		Student		-2 -1 0 1 2				Cook's D
			Predicted Value	Mean Predict	Residual	Std Error Residual	Residual	Residual					
1	-1.2369	-0.8613	0.2703	-0.3756	0.539	-0.697	*						0.061
2	-1.0127	-0.9739	0.2448	-0.0388	0.551	-0.0704							0.000
3	-0.3716	-1.5096	0.1567	1.1381	0.582	1.955		***					0.138
4	-1.0298	-1.2653	0.1874	0.2355	0.573	0.411							0.009
5	-1.7590	-0.9500	0.2501	-0.8090	0.549	-1.474	**						0.226
6	-0.6947	-1.3079	0.1806	0.6131	0.575	1.066		**					0.056
7	-1.0252	-1.3466	0.1748	0.3215	0.577	0.557		*					0.014
8	-1.0308	-1.0299	0.2326	-0.000885	0.556	-0.0016							0.000
9	-2.9666	-2.1269	0.1990	-0.8397	0.569	-1.475	**						0.133
10	-2.2848	-2.2351	0.2199	-0.0497	0.561	-0.0885							0.001
11	-1.2575	-2.0902	0.1924	0.8327	0.571	1.457		**					0.120
12	-1.9208	-2.2278	0.2185	0.3071	0.562	0.546		*					0.023
13	-2.4204	-2.2618	0.2254	-0.1586	0.559	-0.284							0.007
14	-2.4969	-2.3296	0.2399	-0.1673	0.553	-0.302							0.009
15	-2.2801	-2.2267	0.2182	-0.0534	0.562	-0.0951							0.001
16	-2.8192	-1.8643	0.1609	-0.9549	0.581	-1.643	***						0.104

Sum of Residuals 0
 Sum of Squared Residuals 5.09012
 Predicted Residual SS (PRESS) 6.32252

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.30324	1.30324	11.44	0.0045
Error	14	1.59509	0.11394		
Corrected Total	15	2.89833			

Root MSE	0.33754	R-Square	0.4497
Dependent Mean	-2.80597	Adj R-Sq	0.4103
Coeff Var	-12.02945		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-3.26914	0.16086	-20.32	<.0001	-3.61415 -2.92413
CrCL	CrCL	1	0.00542	0.00160	3.38	0.0045	0.00198 0.00886

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z

Output Statistics									
Obs	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual	-2 -1 0 1 2	Cook's D	
1	-2.8080	-2.3811	0.1513	-0.4269	0.302	-1.415	**		0.252
2	-2.6333	-2.4408	0.1370	-0.1925	0.308	-0.624	*		0.038
3	-2.1798	-2.7247	0.0877	0.5449	0.326	1.672		***	0.101
4	-2.2763	-2.5953	0.1049	0.3189	0.321	0.994		*	0.053
5	-2.4575	-2.4281	0.1400	-0.0294	0.307	-0.0958			0.001
6	-2.2465	-2.6178	0.1011	0.3713	0.322	1.153		**	0.065
7	-2.7044	-2.6383	0.0979	-0.0661	0.323	-0.205			0.002
8	-2.3188	-2.4705	0.1302	0.1517	0.311	0.487			0.021
9	-3.5181	-3.0519	0.1114	-0.4662	0.319	-1.463	**		0.131
10	-3.0523	-3.1092	0.1231	0.0569	0.314	0.181			0.003
11	-3.1382	-3.0324	0.1077	-0.1058	0.320	-0.331			0.006
12	-2.9749	-3.1054	0.1223	0.1304	0.315	0.415			0.013
13	-2.9265	-3.1233	0.1262	0.1968	0.313	0.629		*	0.032
14	-3.2484	-3.1593	0.1343	-0.0891	0.310	-0.288			0.008
15	-2.8346	-3.1048	0.1222	0.2701	0.315	0.858		*	0.056
16	-3.5779	-2.9127	0.0901	-0.6652	0.325	-2.045	****		0.160

Sum of Residuals 0
 Sum of Squared Residuals 1.59509
 Predicted Residual SS (PRESS) 1.99707

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=14 Param=RkTmax
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	3.31172	3.31172	0.14	0.7112
Error	14	324.68828	23.19202		
Corrected Total	15	328.00000			

Root MSE	4.81581	R-Square	0.0101
Dependent Mean	8.50000	Adj R-Sq	-0.0606
Coeff Var	56.65658		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	7.76166	2.29503	3.38	0.0045	2.83932 12.68400
CrCL	CrCL	1	0.00864	0.02286	0.38	0.7112	-0.04040 0.05768

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Obs	Output Statistics						-2	-1	0	1	2	Cook's D
	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	5.0000	9.1773	2.1591	-4.1773	4.305	-0.970		*				0.118
2	9.5000	9.0821	1.9552	0.4179	4.401	0.0949						0.001
3	5.0000	8.6295	1.2518	-3.6295	4.650	-0.780		*				0.022
4	8.0000	8.8359	1.4966	-0.8359	4.577	-0.183						0.002
5	9.5000	9.1024	1.9976	0.3976	4.382	0.0907						0.001
6	5.0000	8.8000	1.4421	-3.8000	4.595	-0.827		*				0.034
7	13.0000	8.7672	1.3963	4.2328	4.609	0.918			*			0.039
8	11.5000	9.0348	1.8581	2.4652	4.443	0.555			*			0.027
9	11.5000	8.1080	1.5892	3.3920	4.546	0.746			*			0.034
10	5.0000	8.0166	1.7567	-3.0166	4.484	-0.673		*				0.035
11	14.5000	8.1390	1.5369	6.3610	4.564	1.394			**			0.110
12	14.5000	8.0227	1.7449	6.4773	4.489	1.443			**			0.157
13	1.5000	7.9941	1.8006	-6.4941	4.467	-1.454		**				0.172
14	1.5000	7.9368	1.9160	-6.4368	4.418	-1.457		**				0.200
15	5.0000	8.0237	1.7430	-3.0237	4.489	-0.674		*				0.034
16	16.0000	8.3299	1.2854	7.6701	4.641	1.653			***			0.105

Sum of Residuals 0
 Sum of Squared Residuals 324.68828
 Predicted Residual SS (PRESS) 419.12128

```

----- SUMMARY REPORT -----
Algorithm Pharma
CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18
(Healthy vs Severe)
ANOVA analysis
NON-PARAMETRIC TEST OF FIXED EFFECT for Tmax parameter
----- SUMMARY REPORT -----

```

The NPAR1WAY Procedure

```

Wilcoxon Scores (Rank Sums) for Variable Value
Classified by Variable Group
Group      N      Sum of      Expected Std Dev      Mean
          Scores Under H0 Under H0      Score
1             8      66.50      68.0 9.352362  8.31250
2             8      69.50      68.0 9.352362  8.68750

```

Average scores were used for ties.

Wilcoxon Two-Sample Test

```

Statistic                                     66.5000

Normal Approximation
Z                                             -0.1069
One-Sided Pr < Z                             0.4574
Two-Sided Pr > |Z|                           0.9148

```

```

t Approximation
One-Sided Pr < Z                             0.4581
Two-Sided Pr > |Z|                           0.9163

```

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test

```

Chi-Square      0.0257
DF              1
Pr > Chi-Square  0.8726

```

Hodges-Lehmann Estimation

```

Location Shift (1 - 2)      0.0000
Type      90%      Interval      Asymptotic
          Confidence      Midpoint Standard Error
          Limits
Asymptotic (Moses) -6.0000 2.0000 -2.0000      2.4318
Exact           -6.0000 2.0000 -2.0000

```

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Normal

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res Area	Lambda z	lnCmax	lnAUCT
1	101	11.60000	4.00000	251.07875	11.49043	0.29028	291.46523	13.85636	0.06032	2.45101	5.52577
2	102	11.60000	6.00000	237.11000	9.64792	0.36323	262.55454	9.69115	0.07184	2.45101	5.46852
3	103	30.50000	4.00000	410.77500	6.13046	0.68963	420.79761	2.38181	0.11307	3.41773	6.01805
4	104	17.70000	4.05000	250.40233	6.75169	0.35708	284.88339	12.10357	0.10266	2.87356	5.52307
5	105	10.20000	6.00000	140.57375	8.09317	0.17223	165.52203	15.07248	0.08565	2.32239	4.94573
6	106	26.20000	4.00000	294.73500	6.55312	0.49921	327.35368	9.96435	0.10577	3.26576	5.68608
7	107	16.30000	8.03333	262.55675	10.35958	0.35874	290.19352	9.52357	0.06691	2.79117	5.57047
8	108	15.70000	8.00000	298.52700	7.04445	0.35671	315.40243	5.35045	0.09840	2.75366	5.69886

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrCL
1	5.67492	-1.23692	-2.80803	5.0	115.00000	163.85000
2	5.57046	-1.01271	-2.63325	9.5	102.00000	152.84000
3	6.04215	-0.37160	-2.17978	5.0	94.00000	100.45000
4	5.65208	-1.02980	-2.27631	8.0	109.00000	124.34000
5	5.10910	-1.75895	-2.45753	9.5	102.00000	155.18000
6	5.79104	-0.69474	-2.24645	5.0	116.00000	120.18000
7	5.67055	-1.02517	-2.70442	13.0	98.00000	116.39000
8	5.75385	-1.03082	-2.31875	11.5	118.00000	147.36000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Severe

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res_Area	Lambda z	lnCmax	lnAUCT
9	013-01	20.30000	4.00000	321.06250	14.67003	0.10180	393.73800	18.45783	0.04725	3.01062	5.77164
10	013-02	21.40000	3.00000	392.19250	12.93609	0.08889	464.78850	15.61915	0.05358	3.06339	5.97175
11	013-03	17.90000	12.00000	355.50900	15.98556	0.28436	464.47530	23.46008	0.04336	2.88480	5.87355
12	013-04	8.61000	12.08333	211.49083	24.81341	0.05965	356.02825	40.59718	0.02793	2.15292	5.35418
13	013-05	25.80000	3.00000	430.38083	17.84727	0.08234	559.95407	23.13998	0.03884	3.25037	6.06467
14	013-06	8.63000	8.00000	226.50375	23.37308	0.05148	360.22751	37.12203	0.02966	2.15524	5.42276
15	013-07	17.00000	12.00000	394.10558	13.57770	0.14649	489.91608	19.55651	0.05105	2.83321	5.97662
16	013-08	21.10000	4.00000	312.17500	11.80038	0.10227	359.52637	13.17049	0.05874	3.04927	5.74356

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrCL
9	5.97569	-2.28477	-3.05232	5.0	23.00000	29.51000
10	6.14158	-2.42039	-2.92653	1.5	27.00000	26.90000
11	6.14091	-1.25750	-3.13820	14.5	26.00000	43.68000
12	5.87501	-2.81924	-3.57790	16.0	28.00000	65.77000
13	6.32785	-2.49689	-3.24836	1.5	16.00000	20.27000
14	5.88674	-2.96660	-3.51810	11.5	26.00000	40.09000
15	6.19423	-1.92077	-2.97494	14.5	19.00000	30.22000
16	5.88479	-2.28014	-2.83464	5.0	21.00000	30.33000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 DESCRIPTIVE RESULTS (OVERALL)
 ----- SUMMARY REPORT -----

Parameter	Renal Function Group	n	Min	Mean	Geometric Mean	Median	Max	Standard Deviation	Coefficient of Variation
Cmax	Normal	8	10.20000	17.47500	16.29379	16.00000	30.50000	7.29300	41.7339
Cmax	Severe	8	8.61000	17.59250	16.44432	19.10000	25.80000	6.12898	34.8386
Tmax	Normal	8	4.00000	5.51042	5.27522	5.02500	8.03333	1.77359	32.1862
Tmax	Severe	8	3.00000	7.26042	6.13409	6.00000	12.08333	4.24765	58.5042
AUCT	Normal	8	140.57375	268.21982	258.41524	256.81775	410.77500	75.44937	28.1297
AUCT	Severe	8	211.49083	330.42750	321.28929	338.28575	430.38083	79.15310	23.9548
Thalf	Normal	8	6.13046	8.25885	8.05710	7.56881	11.49043	1.99997	24.2160
Thalf	Severe	8	11.80038	16.87544	16.31952	15.32780	24.81341	4.84002	28.6809
Ae	Normal	8	0.17223	0.38589	0.36056	0.35791	0.68963	0.15252	39.5232
Ae	Severe	8	0.05148	0.11466	0.09968	0.09534	0.28436	0.07451	64.9800
AUCinf	Normal	8	165.52203	294.77155	286.58045	290.82938	420.79761	70.95555	24.0714
AUCinf	Severe	8	356.02825	431.08176	425.53613	429.10665	559.95407	75.10840	17.4232
Res_Area	Normal	8	2.38181	9.74297	8.58932	9.82775	15.07248	4.21692	43.2817
Res_Area	Severe	8	13.17049	23.89041	22.28147	21.34824	40.59718	9.90358	41.4542
Lambda_z	Normal	8	0.06032	0.08808	0.08603	0.09202	0.11307	0.01980	22.4815
Lambda_z	Severe	8	0.02793	0.04380	0.04247	0.04531	0.05874	0.01108	25.3046
lnCmax	Normal	8	2.32239	2.79078		2.77241	3.41773	0.39228	14.0563
lnCmax	Severe	8	2.15292	2.79998		2.94771	3.25037	0.41772	14.9186
lnAUCT	Normal	8	4.94573	5.55457		5.54812	6.01805	0.30073	5.4142
lnAUCT	Severe	8	5.35418	5.77234		5.82259	6.06467	0.26052	4.5132
lnAUCinf	Normal	8	5.10910	5.65802		5.67273	6.04215	0.26292	4.6469
lnAUCinf	Severe	8	5.87501	6.05335		6.05830	6.32785	0.17099	2.8247
lnAe	Normal	8	-1.75895	-1.02009		-1.02748	-0.37160	0.39993	-39.2056
lnAe	Severe	8	-2.96660	-2.30579		-2.35258	-1.25750	0.53428	-23.1713
lnLambda_z	Normal	8	-2.80803	-2.45307		-2.38814	-2.17978	0.23553	-9.6015
lnLambda_z	Severe	8	-3.57790	-3.15887		-3.09526	-2.83464	0.27186	-8.6062
RkTmax	Normal	8	5.00000	8.31250	7.78504	8.75000	13.00000	3.11606	37.4864
RkTmax	Severe	8	1.50000	8.68750	6.19740	8.25000	16.00000	6.08826	70.0807

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=1 Param=Cmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	97.29896280	
1	1	97.08836376	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	37.5644
Residual	FunctionGroup Normal	53.1879

Fit Statistics

-2 Res Log Likelihood	97.1
AIC (Smaller is Better)	101.1
AICC (Smaller is Better)	102.2
BIC (Smaller is Better)	102.6

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	0.21	0.6463

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	0.00	0.9727	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	17.5925	2.1669	14	8.12	<.0001	0.1	13.7759	21.4091	
FunctionGroup	Normal	17.4750	2.5785	14	6.78	<.0001	0.1	12.9335	22.0165	

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.1175	3.3681	14	0.03	0.9727	0.1	-5.8148	6.0498	

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=3 Param=AUCT

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	165.63307285	
1	1	165.61700324	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	6265.21
Residual	FunctionGroup Normal	5692.61

Fit Statistics

-2 Res Log Likelihood	165.6
AIC (Smaller is Better)	169.6
AICC (Smaller is Better)	170.7
BIC (Smaller is Better)	171.2

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	0.02	0.8991

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	2.59	0.1299	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	330.43	27.9848	14	11.81	<.0001	0.1	281.14	379.72	
FunctionGroup	Normal	268.22	26.6754	14	10.05	<.0001	0.1	221.24	315.20	

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	62.2077	38.6617	14	1.61	0.1299	0.1	-5.8876	130.30	

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=6 Param=AUCinf

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	164.04560222	
1	1	164.02296805	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	5641.27
Residual	FunctionGroup Normal	5034.69

Fit Statistics

-2 Res Log Likelihood	164.0
AIC (Smaller is Better)	168.0
AICC (Smaller is Better)	169.1
BIC (Smaller is Better)	169.6

Null Model Likelihood

Ratio Test

DF	Chi-Square	Pr > ChiSq
1	0.02	0.8804

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	13.92	0.0022	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	431.08	26.5548	14	16.23	<.0001	0.1	384.31	477.85
FunctionGroup	Normal	294.77	25.0866	14	11.75	<.0001	0.1	250.59	338.96

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	136.31	36.5307	14	3.73	0.0022	0.1	71.9682	200.65

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=9 Param=lnCmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	18.59459448	
1	1	18.56697737	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.1745
Residual	FunctionGroup Normal	0.1539

Fit Statistics

-2 Res Log Likelihood	18.6
AIC (Smaller is Better)	22.6
AICC (Smaller is Better)	23.7
BIC (Smaller is Better)	24.1

Null Model Likelihood

Ratio Test

DF	Chi-Square	Pr > ChiSq
1	0.03	0.8680

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
FunctionGroup	1	14	0.00	0.9644	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	2.8000	0.1477	14	18.96	<.0001	0.1	2.5399	3.0601	
FunctionGroup	Normal	2.7908	0.1387	14	20.12	<.0001	0.1	2.5465	3.0351	

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.009196	0.2026	14	0.05	0.9644	0.1	-0.3476	0.3660	

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=10 Param=lnAUCT

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	8.38031706	
1	1	8.23655439	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.06787
Residual	FunctionGroup Normal	0.09044

Fit Statistics

-2 Res Log Likelihood	8.2
AIC (Smaller is Better)	12.2
AICC (Smaller is Better)	13.3
BIC (Smaller is Better)	13.8

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	0.14	0.7046

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	2.40	0.1439	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	5.7723	0.09211	14	62.67	<.0001		0.1	5.6101	5.9346
FunctionGroup	Normal	5.5546	0.1063	14	52.24	<.0001		0.1	5.3673	5.7418

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.2178	0.1407	14	1.55	0.1439	0.1	-0.02999	0.4655	

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=11 Param=lnAUCinf

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	1.71804990	
1	1	0.46038460	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.02924
Residual	FunctionGroup Normal	0.06913

Fit Statistics

-2 Res Log Likelihood	0.5
AIC (Smaller is Better)	4.5
AICC (Smaller is Better)	5.6
BIC (Smaller is Better)	6.0

Null Model Likelihood
Ratio Test

DF	Chi-Square	Pr > ChiSq
1	1.26	0.2621

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	12.71	0.0031	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	6.0533	0.06045	14	100.13	<.0001		0.1	5.9469	6.1598
FunctionGroup	Normal	5.6580	0.09296	14	60.87	<.0001		0.1	5.4943	5.8217

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.3953	0.1109	14	3.57	0.0031		0.1	0.2000	0.5906

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=14 Param=RkTmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	88.02052016	
1	1	85.09021011	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	37.0670
Residual	FunctionGroup Normal	9.7098

Fit Statistics

-2 Res Log Likelihood	85.1
AIC (Smaller is Better)	89.1
AICC (Smaller is Better)	90.2
BIC (Smaller is Better)	90.6

Null Model Likelihood

Ratio Test

DF	Chi-Square	Pr > ChiSq
1	2.93	0.0869

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
FunctionGroup	1	14	0.02	0.8790	

Least Squares Means

Effect	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	FunctionGroup		Error							
FunctionGroup	Severe	8.6875	2.1525	14	4.04	0.0012	0.1	4.8962	12.4788	
FunctionGroup	Normal	8.3125	1.1017	14	7.55	<.0001	0.1	6.3721	10.2529	

Differences of Least Squares Means

Effect	Renal	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	FunctionGroup	FunctionGroup		Error							
FunctionGroup	Severe	Normal	0.3750	2.4181	14	0.16	0.8790	0.1	-3.8840	4.6340	

----- SUMMARY REPORT -----
Algorithm Pharma
CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18 - Additional Analysis
(Healthy vs Severe)
ANOVA analysis
Geometric LSmeans
----- SUMMARY REPORT -----

Obs	Parameters	Group	GeoLSmeans
1	lnCmax	Severe	16.4443
2	lnCmax	Normal	16.2938
3	lnAUCT	Severe	321.29
4	lnAUCT	Normal	258.42
5	lnAUCinf	Severe	425.54
6	lnAUCinf	Normal	286.58

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - (S,S)-M18 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RATIO ESTIMATE BASED ON ln-TRANSFORMED PARAMETERS
 ----- SUMMARY REPORT -----

Obs	Parameters	Group	vs Group	Ratio (%)	L90	U90
1	lnCmax	Severe	Normal	100.924	70.635	144.201
2	lnAUCT	Severe	Normal	124.331	97.045	159.288
3	lnAUCinf	Severe	Normal	148.487	122.144	180.513

16.1.9.6 Documentation of statistical analysis – SAS® output of M7

Legend:

- AUCinf= $AUC_{(0-\infty)}$
- AUCT= $AUC_{(0-tlast)}$
- V_{Z_F}= V_Z/F
- CL_F= CL/F
- LambdaZ = λ_Z
- lCmax= $\ln(C_{max})$
- lAUCT= $\ln(AUC_{(0-tlast)})$
- lAUCinf= $\ln(AUC_{(0-\infty)})$
- lCLF= $\ln(CL/F)$
- lLambdaZ = $\ln(\lambda_Z)$
- lV_{Z_F}= $\ln(V_Z/F)$
- RkTmax= Rank of T_{max}

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Normal

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res Area	Lambda z	lnCmax	lnAUCT
1	101	42.00000	2.00000	388.30000	6.86451	0.00079	399.05876	2.69603	0.10098	3.73767	5.96178
2	102	63.80000	2.50000	665.35750	6.44652	0.00198	681.17001	2.32138	0.10752	4.15575	6.50032
3	103	101.00000	1.25000	526.88250	3.01629	0.00249	541.63949	2.72450	0.22980	4.61512	6.26698
4	104	99.80000	2.00000	707.53067	4.37683	0.00249	725.99535	2.54336	0.15837	4.60317	6.56178
5	105	59.20000	1.00000	439.38500	4.65142		453.00695	3.00701	0.14902	4.08092	6.08538
6	106	71.60000	2.00000	440.10750	3.77330	0.00149	446.82229	1.50279	0.18370	4.27110	6.08702
7	107	72.30000	3.00000	767.57700	5.65628	0.00248	779.01561	1.46834	0.12254	4.28082	6.64324
8	108	60.80000	2.50000	581.04250	6.13125	0.00339	591.19310	1.71697	0.11305	4.10759	6.36482

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrLR
1	5.98911	-7.14378	-2.29288	8.5	115.00000	163.85000
2	6.52381	-6.22294	-2.23005	12.5	102.00000	152.84000
3	6.29460	-5.99463	-1.47054	3.0	94.00000	100.45000
4	6.58754	-5.99405	-1.84284	8.5	109.00000	124.34000
5	6.11591		-1.90368	1.5	102.00000	155.18000
6	6.10216	-6.50710	-1.69446	8.5	116.00000	120.18000
7	6.65803	-5.99982	-2.09928	15.0	98.00000	116.39000
8	6.38214	-5.68805	-2.17991	12.5	118.00000	147.36000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Severe

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res Area	Lambda z	lnCmax	lnAUCT
9	201	36.10000	1.00000	480.53000	9.70927	0.00136	517.98321	7.23058	0.07139	3.58629	6.17489
10	202	80.40000	2.00000	581.41500	4.55733	0.00040	599.24800	2.97590	0.15209	4.38701	6.36546
11	203	97.10000	4.00000	1312.96000	9.78691	0.00635	1423.69135	7.77776	0.07082	4.57574	7.18004
12	204	70.20000	2.00000	595.48083	6.36062	0.00531	604.46565	1.48641	0.10897	4.25135	6.38937
13	205	247.00000	1.50000	3662.33500	10.49066	0.00220	4049.76869	9.56681	0.06607	5.50939	8.20586
14	206	157.00000	1.86667	1449.96833	11.33526	0.00541	1569.00249	7.58661	0.06115	5.05625	7.27930
15	207	124.00000	2.00000	826.49500	9.67678	0.00194	863.75748	4.31400	0.07163	4.82028	6.71719
16	208	30.30000	2.56667	373.34958	7.81383	0.00127	390.93106	4.49734	0.08871	3.41115	5.92252

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrLR
9	6.24994	-6.60174	-2.63959	1.5	26.00000	40.09000
10	6.39568	-7.83410	-1.88325	8.5	23.00000	29.51000
11	7.26101	-5.05902	-2.64756	16.0	26.00000	43.68000
12	6.40434	-5.23737	-2.21664	8.5	19.00000	30.22000
13	8.30642	-6.11803	-2.71700	4.0	27.00000	26.90000
14	7.35820	-5.21913	-2.79443	5.0	16.00000	20.27000
15	6.76129	-6.24641	-2.63624	8.5	21.00000	30.33000
16	5.96853	-6.66858	-2.42241	14.0	28.00000	65.77000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 DESCRIPTIVE RESULTS (OVERALL)
 ----- SUMMARY REPORT -----

Parameter	Renal Function Group	n	Min	Mean	Geometric Mean	Median	Max	Standard Deviation	Coefficient of Variation
Cmax	Normal	8	42.00000	71.31250	68.82161	67.70000	101.00000	20.23727	28.3783
Cmax	Severe	8	30.30000	105.26250	85.59976	88.75000	247.00000	71.14809	67.5911
Tmax	Normal	8	1.00000	2.03125	1.92365	2.00000	3.00000	0.66059	32.5215
Tmax	Severe	8	1.00000	2.11667	1.97338	2.00000	4.00000	0.88479	41.8012
AUCT	Normal	8	388.30000	564.52283	549.44841	553.96250	767.57700	139.24936	24.6667
AUCT	Severe	8	373.34958	1160.31672	879.47766	710.98792	3662.33500	1083.27048	93.3599
Thalf	Normal	8	3.01629	5.11455	4.94162	5.15385	6.86451	1.36926	26.7718
Thalf	Severe	8	4.55733	8.71633	8.39912	9.69302	11.33526	2.29044	26.2775
Ae	Normal	7	0.00079	0.00216	0.00199	0.00248	0.00339	0.00083	38.6537
Ae	Severe	8	0.00040	0.00303	0.00219	0.00207	0.00635	0.00229	75.4936
AUCinf	Normal	8	399.05876	577.23770	562.09079	566.41629	779.01561	141.06547	24.4380
AUCinf	Severe	8	390.93106	1252.35599	932.78585	734.11156	4049.76869	1209.12103	96.5477
Res_Area	Normal	8	1.46834	2.24755	2.17132	2.43237	3.00701	0.60258	26.8105
Res_Area	Severe	8	1.48641	5.67943	4.93235	5.86396	9.56681	2.77000	48.7726
Lambda_z	Normal	8	0.10098	0.14562	0.14027	0.13578	0.22980	0.04432	30.4331
Lambda_z	Severe	8	0.06115	0.08636	0.08253	0.07151	0.15209	0.03063	35.4702
lnCmax	Normal	8	3.73767	4.23152		4.21342	4.61512	0.28709	6.7845
lnCmax	Severe	8	3.41115	4.44968		4.48138	5.50939	0.70826	15.9170
lnAUCT	Normal	8	5.96178	6.30891		6.31590	6.64324	0.24984	3.9601
lnAUCT	Severe	8	5.92252	6.77933		6.55328	8.20586	0.74376	10.9709
lnAUCinf	Normal	8	5.98911	6.33166		6.33837	6.65803	0.24767	3.9117
lnAUCinf	Severe	8	5.96853	6.83818		6.58282	8.30642	0.76505	11.1880
lnAe	Normal	7	-7.14378	-6.22148		-5.99982	-5.68805	0.47768	-7.6780
lnAe	Severe	8	-7.83410	-6.12305		-6.18222	-5.05902	0.94138	-15.3743
lnLambda_z	Normal	8	-2.29288	-1.96421		-2.00148	-1.47054	0.28744	-14.6337
lnLambda_z	Severe	8	-2.79443	-2.49464		-2.63792	-1.88325	0.30707	-12.3094
RkTmax	Normal	8	1.50000	8.75000	7.10269	8.50000	15.00000	4.67516	53.4304
RkTmax	Severe	8	1.50000	8.25000	6.71357	8.50000	16.00000	4.89168	59.2931

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=9 Param=lnCmax
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.27548	0.27548	0.96	0.3430
Error	14	4.00323	0.28595		
Corrected Total	15	4.27871			

Root MSE 0.53474 R-Square 0.0644
 Dependent Mean 4.34060 Adj R-Sq -0.0024
 Coeff Var 12.31946

Parameter Estimates

Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	4.54238	0.24522	18.52	<.0001	4.01643 5.06833
eGFR	eGFR	1	-0.00310	0.00316	-0.98	0.3430	-0.00989 0.00368

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Obs	Output Statistics							-2	-1	0	1	2	Cook's D
	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual							
1	3.7377	4.1854	0.2071	-0.4477	0.493	-0.908		*					0.073
2	4.1558	4.2257	0.1777	-0.0700	0.504	-0.139							0.001
3	4.6151	4.2506	0.1621	0.3645	0.510	0.715				*			0.026
4	4.6032	4.2040	0.1930	0.3992	0.499	0.800				*			0.048
5	4.0809	4.2257	0.1777	-0.1448	0.504	-0.287							0.005
6	4.2711	4.1823	0.2095	0.0888	0.492	0.181							0.003
7	4.2808	4.2382	0.1696	0.0427	0.507	0.0841							0.000
8	4.1076	4.1761	0.2144	-0.0685	0.490	-0.140							0.002
9	3.5863	4.4617	0.1819	-0.8754	0.503	-1.741		***					0.198
10	4.3870	4.4710	0.1885	-0.0840	0.500	-0.168							0.002
11	4.5757	4.4617	0.1819	0.1141	0.503	0.227							0.003
12	4.2513	4.4834	0.1976	-0.2321	0.497	-0.467							0.017
13	5.5094	4.4586	0.1798	1.0508	0.504	2.087				****			0.277
14	5.0562	4.4927	0.2047	0.5635	0.494	1.141				**			0.112
15	4.8203	4.4772	0.1930	0.3431	0.499	0.688				*			0.035
16	3.4111	4.4555	0.1777	-1.0443	0.504	-2.071		****					0.266

Sum of Residuals 0
 Sum of Squared Residuals 4.00323
 Predicted Residual SS (PRESS) 5.15290

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=10 Param=lnAUCT
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.94179	0.94179	3.10	0.1001
Error	14	4.25252	0.30375		
Corrected Total	15	5.19431			

Root MSE 0.55114 R-Square 0.1813
 Dependent Mean 6.54412 Adj R-Sq 0.1228
 Coeff Var 8.42185

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	6.91721	0.25274	27.37	<.0001	6.37513 7.45929
eGFR	eGFR	1	-0.00574	0.00326	-1.76	0.1001	-0.01273 0.00125

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Obs	Dependent Variable	Predicted Value	Output Statistics					-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual							
1	5.9618	6.2571	0.2134	-0.2954	0.508	-0.581		*					0.030
2	6.5003	6.3317	0.1831	0.1686	0.520	0.324							0.007
3	6.2670	6.3777	0.1671	-0.1107	0.525	-0.211							0.002
4	6.5618	6.2916	0.1989	0.2702	0.514	0.526			*				0.021
5	6.0854	6.3317	0.1831	-0.2464	0.520	-0.474							0.014
6	6.0870	6.2514	0.2159	-0.1644	0.507	-0.324							0.010
7	6.6432	6.3547	0.1748	0.2885	0.523	0.552			*				0.017
8	6.3648	6.2399	0.2210	0.1249	0.505	0.247							0.006
9	6.1749	6.7680	0.1875	-0.5931	0.518	-1.144		**					0.086
10	6.3655	6.7852	0.1942	-0.4197	0.516	-0.814		*					0.047
11	7.1800	6.7680	0.1875	0.4121	0.518	0.795			*				0.041
12	6.3894	6.8082	0.2036	-0.4188	0.512	-0.818			*				0.053
13	8.2059	6.7622	0.1853	1.4436	0.519	2.781			*****				0.493
14	7.2793	6.8254	0.2109	0.4539	0.509	0.891			*				0.068
15	6.7172	6.7967	0.1989	-0.0795	0.514	-0.155							0.002
16	5.9225	6.7565	0.1831	-0.8340	0.520	-1.604		***					0.160

Sum of Residuals 0
 Sum of Squared Residuals 4.25252
 Predicted Residual SS (PRESS) 5.45834

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	1.08329	1.08329	3.39 0.0867
Error	14	4.46949	0.31925	
Corrected Total	15	5.55278		

Root MSE	0.56502	R-Square	0.1951
Dependent Mean	6.58492	Adj R-Sq	0.1376
Coeff Var	8.58054		

Parameter Estimates						
Variable	Label	DF	Parameter Estimate	Standard Error	t Value Pr > t	95% Confidence Limits
Intercept	Intercept	1	6.98506	0.25911	26.96 <.0001	6.42932 7.54079
eGFR	eGFR	1	-0.00616	0.00334	-1.84 0.0867	-0.01332 0.00101

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error	Residual	Std Error	Student						
			Mean Predict		Residual	Residual						
1	5.9891	6.2771	0.2188	-0.2880	0.521	-0.553		*				0.027
2	6.5238	6.3571	0.1877	0.1667	0.533	0.313						0.006
3	6.2946	6.4064	0.1713	-0.1118	0.538	-0.208						0.002
4	6.5875	6.3141	0.2039	0.2735	0.527	0.519			*			0.020
5	6.1159	6.3571	0.1877	-0.2412	0.533	-0.453						0.013
6	6.1022	6.2710	0.2214	-0.1688	0.520	-0.325						0.010
7	6.6580	6.3818	0.1792	0.2763	0.536	0.516			*			0.015
8	6.3821	6.2587	0.2265	0.1235	0.518	0.239						0.005
9	6.2499	6.8250	0.1922	-0.5751	0.531	-1.082		**				0.077
10	6.3957	6.8435	0.1991	-0.4478	0.529	-0.847		*				0.051
11	7.2610	6.8250	0.1922	0.4360	0.531	0.821			*			0.044
12	6.4043	6.8681	0.2088	-0.4637	0.525	-0.883		*				0.062
13	8.3064	6.8188	0.1899	1.4876	0.532	2.795			*****			0.498
14	7.3582	6.8866	0.2163	0.4716	0.522	0.904			*			0.070
15	6.7613	6.8558	0.2039	-0.0945	0.527	-0.179						0.002
16	5.9685	6.8127	0.1877	-0.8442	0.533	-1.584		***				0.156

Sum of Residuals 0
 Sum of Squared Residuals 4.46949
 Predicted Residual SS (PRESS) 5.73936

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Number of Observations Read 16
 Number of Observations Used 15
 Number of Observations with Missing Values 1

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.09243	0.09243	0.16 0.6958
Error	13	7.51617	0.57817	
Corrected Total	14	7.60860		

Root MSE 0.76037 R-Square 0.0121
 Dependent Mean -6.16898 Adj R-Sq -0.0638
 Coeff Var -12.32574

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-6.05355	0.34913	-17.34	<.0001	-6.80780 -5.29930
eGFR	eGFR	1	-0.00185	0.00462	-0.40	0.6958	-0.01182 0.00813

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	-7.1438	-6.2658	0.3118	-0.8779	0.694	-1.266	**					0.162
2	-6.2229	-6.2418	0.2679	0.0189	0.712	0.0266						0.000
3	-5.9946	-6.2271	0.2442	0.2324	0.720	0.323						0.006
4	-5.9941	-6.2548	0.2908	0.2607	0.703	0.371						0.012
5		-6.2418	0.2679									
6	-6.5071	-6.2677	0.3154	-0.2394	0.692	-0.346						0.012
7	-5.9998	-6.2345	0.2556	0.2346	0.716	0.328						0.007
8	-5.6880	-6.2714	0.3227	0.5833	0.689	0.847		*				0.079
9	-6.6017	-6.1015	0.2588	-0.5002	0.715	-0.700	*					0.032
10	-7.8341	-6.0960	0.2681	-1.7381	0.712	-2.443	****					0.423
11	-5.0590	-6.1015	0.2588	1.0425	0.715	1.458		**				0.139
12	-5.2374	-6.0886	0.2810	0.8512	0.707	1.205		**				0.115
13	-6.1180	-6.1034	0.2558	-0.0146	0.716	-0.0204						0.000
14	-5.2191	-6.0831	0.2910	0.8640	0.702	1.230		**				0.130
15	-6.2464	-6.0923	0.2744	-0.1541	0.709	-0.217						0.004
16	-6.6686	-6.1052	0.2529	-0.5633	0.717	-0.786	*					0.038

Sum of Residuals 0
 Sum of Squared Residuals 7.51617
 Predicted Residual SS (PRESS) 10.01373

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.01701	1.01701	10.57	0.0058
Error	14	1.34683	0.09620		
Corrected Total	15	2.36384			

Root MSE	0.31016	R-Square	0.4302
Dependent Mean	-2.22942	Adj R-Sq	0.3895
Coeff Var	-13.91234		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-2.61713	0.14224	-18.40	<.0001	-2.92219 -2.31206
eGFR	eGFR	1	0.00596	0.00183	3.25	0.0058	0.00203 0.00990

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z

Obs	Output Statistics							-2	-1	0	1	2	Cook's D
	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual							
1	-2.2929	-1.9312	0.1201	-0.3617	0.286	-1.265		**					0.141
2	-2.2301	-2.0087	0.1031	-0.2213	0.293	-0.757		*					0.036
3	-1.4705	-2.0564	0.0940	0.5859	0.296	1.982			***				0.199
4	-1.8428	-1.9670	0.1119	0.1241	0.289	0.429							0.014
5	-1.9037	-2.0087	0.1031	0.1050	0.293	0.359							0.008
6	-1.6945	-1.9252	0.1215	0.2308	0.285	0.809			*				0.059
7	-2.0993	-2.0326	0.0984	-0.0667	0.294	-0.227							0.003
8	-2.1799	-1.9133	0.1244	-0.2666	0.284	-0.938		*					0.084
9	-2.6396	-2.4620	0.1055	-0.1775	0.292	-0.609		*					0.024
10	-1.8833	-2.4799	0.1093	0.5967	0.290	2.056			****				0.300
11	-2.6476	-2.4620	0.1055	-0.1855	0.292	-0.636		*					0.026
12	-2.2166	-2.5038	0.1146	0.2872	0.288	0.996			*				0.078
13	-2.7170	-2.4561	0.1043	-0.2609	0.292	-0.893		*					0.051
14	-2.7944	-2.5217	0.1187	-0.2727	0.287	-0.952		*					0.078
15	-2.6362	-2.4919	0.1119	-0.1444	0.289	-0.499							0.019
16	-2.4224	-2.4501	0.1031	0.0277	0.293	0.0947							0.001

Sum of Residuals 0
 Sum of Squared Residuals 1.34683
 Predicted Residual SS (PRESS) 1.75057

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

 Order=14 Param=RkTmax

 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	2.65515	2.65515	0.12	0.7378
Error	14	318.84485	22.77463		
Corrected Total	15	321.50000			

Root MSE	4.77228	R-Square	0.0083
Dependent Mean	8.50000	Adj R-Sq	-0.0626
Coeff Var	56.14444		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	7.87356	2.18849	3.60	0.0029	3.17971 12.56741
eGFR	eGFR	1	0.00964	0.02823	0.34	0.7378	-0.05090 0.07018

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	8.5000	8.9819	1.8480	-0.4819	4.400	-0.110						0.001
2	12.5000	8.8566	1.5856	3.6434	4.501	0.809			*			0.041
3	3.0000	8.7795	1.4469	-5.7795	4.548	-1.271		**				0.082
4	8.5000	8.9241	1.7222	-0.4241	4.451	-0.0953						0.001
5	1.5000	8.8566	1.5856	-7.3566	4.501	-1.634		***				0.166
6	8.5000	8.9915	1.8697	-0.4915	4.391	-0.112						0.001
7	15.0000	8.8180	1.5136	6.1820	4.526	1.366			**			0.104
8	12.5000	9.0108	1.9135	3.4892	4.372	0.798			*			0.061
9	1.5000	8.1241	1.6233	-6.6241	4.488	-1.476		**				0.143
10	8.5000	8.0952	1.6819	0.4048	4.466	0.0906						0.001
11	16.0000	8.1241	1.6233	7.8759	4.488	1.755			***			0.202
12	8.5000	8.0567	1.7633	0.4433	4.435	0.1000						0.001
13	4.0000	8.1338	1.6043	-4.1338	4.495	-0.920		*				0.054
14	5.0000	8.0278	1.8266	-3.0278	4.409	-0.687		*				0.040
15	8.5000	8.0759	1.7222	0.4241	4.451	0.0953						0.001
16	14.0000	8.1434	1.5856	5.8566	4.501	1.301			**			0.105

Sum of Residuals 0
 Sum of Squared Residuals 318.84485
 Predicted Residual SS (PRESS) 404.88659

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.71970	0.71970	2.83 0.1146
Error	14	3.55901	0.25421	
Corrected Total	15	4.27871		

Root MSE	0.50420	R-Square	0.1682
Dependent Mean	4.34060	Adj R-Sq	0.1088
Coeff Var	11.61584		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	4.68479	0.24028	19.50	<.0001	4.16944 5.20015
CrLR	CrLR	1	-0.00403	0.00239	-1.68	0.1146	-0.00916 0.00111

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	3.7377	4.0249	0.2260	-0.2872	0.451	-0.637	*					0.051
2	4.1558	4.0692	0.2047	0.0865	0.461	0.188						0.003
3	4.6151	4.2802	0.1311	0.3349	0.487	0.688			*			0.017
4	4.6032	4.1840	0.1567	0.4192	0.479	0.875			*			0.041
5	4.0809	4.0598	0.2091	0.0211	0.459	0.0460						0.000
6	4.2711	4.2008	0.1510	0.0703	0.481	0.146						0.001
7	4.2808	4.2160	0.1462	0.0648	0.483	0.134						0.001
8	4.1076	4.0913	0.1945	0.0163	0.465	0.0350						0.000
9	3.5863	4.5233	0.1664	-0.9370	0.476	-1.969	***					0.237
10	4.3870	4.5659	0.1839	-0.1789	0.469	-0.381						0.011
11	4.5757	4.5089	0.1609	0.0669	0.478	0.140						0.001
12	4.2513	4.5631	0.1827	-0.3117	0.470	-0.663	*					0.033
13	5.5094	4.5765	0.1885	0.9329	0.468	1.995			***			0.323
14	5.0562	4.6032	0.2006	0.4531	0.463	0.979			*			0.090
15	4.8203	4.5626	0.1825	0.2576	0.470	0.548			*			0.023
16	3.4111	4.4199	0.1346	-1.0088	0.486	-2.076	****					0.165

Sum of Residuals 0
 Sum of Squared Residuals 3.55901
 Predicted Residual SS (PRESS) 4.51243

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.31743	1.31743	4.76	0.0467
Error	14	3.87688	0.27692		
Corrected Total	15	5.19431			

Root MSE	0.52623	R-Square	0.2536
Dependent Mean	6.54412	Adj R-Sq	0.2003
Coeff Var	8.04129		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	7.00981	0.25078	27.95	<.0001	6.47193 7.54768
CrLR	CrLR	1	-0.00545	0.00250	-2.18	0.0467	-0.01081 -0.0009085

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error	Residual	Std Error	Student						
			Mean Predict		Residual	Residual						
1	5.9618	6.1170	0.2359	-0.1552	0.470	-0.330						0.014
2	6.5003	6.1770	0.2136	0.3234	0.481	0.672			*			0.045
3	6.2670	6.4624	0.1368	-0.1955	0.508	-0.385						0.005
4	6.5618	6.3323	0.1635	0.2295	0.500	0.459						0.011
5	6.0854	6.1642	0.2183	-0.0788	0.479	-0.165						0.003
6	6.0870	6.3549	0.1576	-0.2679	0.502	-0.534		*				0.014
7	6.6432	6.3756	0.1526	0.2677	0.504	0.531			*			0.013
8	6.3648	6.2068	0.2030	0.1580	0.485	0.325						0.009
9	6.1749	6.7913	0.1737	-0.6165	0.497	-1.241		**				0.094
10	6.3655	6.8490	0.1920	-0.4835	0.490	-0.987		*				0.075
11	7.1800	6.7718	0.1679	0.4083	0.499	0.819			*			0.038
12	6.3894	6.8451	0.1907	-0.4558	0.490	-0.929		*				0.065
13	8.2059	6.8632	0.1968	1.3426	0.488	2.751			*****			0.615
14	7.2793	6.8994	0.2094	0.3799	0.483	0.787			*			0.058
15	6.7172	6.8445	0.1905	-0.1273	0.491	-0.260						0.005
16	5.9225	6.6514	0.1405	-0.7289	0.507	-1.437		**				0.079

Sum of Residuals 0
 Sum of Squared Residuals 3.87688
 Predicted Residual SS (PRESS) 5.06049

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.47846	1.47846	5.08	0.0408
Error	14	4.07432	0.29102		
Corrected Total	15	5.55278			

Root MSE	0.53947	R-Square	0.2663
Dependent Mean	6.58492	Adj R-Sq	0.2138
Coeff Var	8.19243		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	7.07824	0.25709	27.53	<.0001	6.52685 7.62964
CrLR	CrLR	1	-0.00577	0.00256	-2.25	0.0408	-0.01127 -0.00027954

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error	Residual	Std Error	Student						
		Mean	Predict	Residual	Residual	Residual						
1	5.9891	6.1324	0.2419	-0.1433	0.482	-0.297						0.011
2	6.5238	6.1960	0.2190	0.3278	0.493	0.665			*			0.044
3	6.2946	6.4984	0.1402	-0.2038	0.521	-0.391						0.006
4	6.5875	6.3605	0.1676	0.2271	0.513	0.443						0.010
5	6.1159	6.1825	0.2238	-0.0665	0.491	-0.136						0.002
6	6.1022	6.3845	0.1615	-0.2823	0.515	-0.549		*				0.015
7	6.6580	6.4064	0.1564	0.2517	0.516	0.487						0.011
8	6.3821	6.2276	0.2081	0.1545	0.498	0.311						0.008
9	6.2499	6.8468	0.1780	-0.5969	0.509	-1.172		**				0.084
10	6.3957	6.9079	0.1968	-0.5122	0.502	-1.020		**				0.080
11	7.2610	6.8261	0.1722	0.4349	0.511	0.851		*				0.041
12	6.4043	6.9038	0.1955	-0.4995	0.503	-0.993		*				0.075
13	8.3064	6.9230	0.2017	1.3835	0.500	2.765			*****			0.621
14	7.3582	6.9612	0.2146	0.3970	0.495	0.802		*				0.060
15	6.7613	6.9032	0.1953	-0.1419	0.503	-0.282						0.006
16	5.9685	6.6986	0.1440	-0.7301	0.520	-1.404		**				0.076

Sum of Residuals 0
 Sum of Squared Residuals 4.07432
 Predicted Residual SS (PRESS) 5.32456

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Number of Observations Read 16
 Number of Observations Used 15
 Number of Observations with Missing Values 1

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.17671	0.17671	0.31	0.5877
Error	13	7.43189	0.57168		
Corrected Total	14	7.60860			

Root MSE 0.75610 R-Square 0.0232
 Dependent Mean -6.16898 Adj R-Sq -0.0519
 Coeff Var -12.25644

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-5.99737	0.36523	-16.42	<.0001	-6.78640 -5.20833
CrLR	CrLR	1	-0.00212	0.00382	-0.56	0.5877	-0.01038 0.00613

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	-7.1438	-6.3453	0.3724	-0.7985	0.658	-1.213	**					0.236
2	-6.2229	-6.3219	0.3374	0.0990	0.677	0.146						0.003
3	-5.9946	-6.2107	0.2091	0.2161	0.727	0.297						0.004
4	-5.9941	-6.2614	0.2564	0.2674	0.711	0.376						0.009
5		-6.3269	0.3447									
6	-6.5071	-6.2526	0.2464	-0.2545	0.715	-0.356						0.008
7	-5.9998	-6.2445	0.2379	0.2447	0.718	0.341						0.006
8	-5.6880	-6.3103	0.3205	0.6223	0.685	0.909		*				0.090
9	-6.6017	-6.0825	0.2496	-0.5192	0.714	-0.728	*					0.032
10	-7.8341	-6.0600	0.2766	-1.7741	0.704	-2.521	*****					0.491
11	-5.0590	-6.0901	0.2413	1.0311	0.717	1.439		**				0.117
12	-5.2374	-6.0615	0.2747	0.8242	0.704	1.170		**				0.104
13	-6.1180	-6.0545	0.2838	-0.0635	0.701	-0.0907						0.001
14	-5.2191	-6.0404	0.3026	0.8213	0.693	1.185		**				0.134
15	-6.2464	-6.0618	0.2744	-0.1846	0.705	-0.262						0.005
16	-6.6686	-6.1370	0.2035	-0.5315	0.728	-0.730	*					0.021

Sum of Residuals 0
 Sum of Squared Residuals 7.43189
 Predicted Residual SS (PRESS) 10.09273

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.70917	0.70917	6.00 0.0281
Error	14	1.65468	0.11819	
Corrected Total	15	2.36384		

Root MSE	0.34379	R-Square	0.3000
Dependent Mean	-2.22942	Adj R-Sq	0.2500
Coeff Var	-15.42056		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-2.57109	0.16384	-15.69	<.0001	-2.92248 -2.21969
CrLR	CrLR	1	0.00400	0.00163	2.45	0.0281	0.00049737 0.00750

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	-2.2929	-1.9160	0.1541	-0.3769	0.307	-1.226	**					0.189
2	-2.2301	-1.9600	0.1396	-0.2700	0.314	-0.859	*					0.073
3	-1.4705	-2.1695	0.0894	0.6990	0.332	2.105			****			0.161
4	-1.8428	-2.0740	0.1068	0.2311	0.327	0.707		*				0.027
5	-1.9037	-1.9507	0.1426	0.0470	0.313	0.150						0.002
6	-1.6945	-2.0906	0.1029	0.3962	0.328	1.208			**			0.072
7	-2.0993	-2.1058	0.0997	0.006487	0.329	0.0197						0.000
8	-2.1799	-1.9819	0.1326	-0.1980	0.317	-0.624	*					0.034
9	-2.6396	-2.4108	0.1134	-0.2288	0.325	-0.705	*					0.030
10	-1.8833	-2.4531	0.1254	0.5699	0.320	1.780			***			0.243
11	-2.6476	-2.3965	0.1097	-0.2511	0.326	-0.771	*					0.034
12	-2.2166	-2.4503	0.1246	0.2336	0.320	0.729		*				0.040
13	-2.7170	-2.4635	0.1285	-0.2535	0.319	-0.795	*					0.051
14	-2.7944	-2.4901	0.1368	-0.3044	0.315	-0.965	*					0.088
15	-2.6362	-2.4498	0.1244	-0.1864	0.320	-0.582	*					0.026
16	-2.4224	-2.3081	0.0918	-0.1143	0.331	-0.345						0.005

Sum of Residuals 0
 Sum of Squared Residuals 1.65468
 Predicted Residual SS (PRESS) 2.12830

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	6.45865	6.45865	0.29	0.6005
Error	14	315.04135	22.50295		
Corrected Total	15	321.50000			

Root MSE	4.74373	R-Square	0.0201
Dependent Mean	8.50000	Adj R-Sq	-0.0499
Coeff Var	55.80856		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	7.46890	2.26067	3.30	0.0052	2.62024 12.31757
CrLR	CrLR	1	0.01207	0.02252	0.54	0.6005	-0.03624 0.06037

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	8.5000	9.4458	2.1268	-0.9458	4.240	-0.223						0.006
2	12.5000	9.3130	1.9259	3.1870	4.335	0.735			*			0.053
3	3.0000	8.6809	1.2330	-5.6809	4.581	-1.240		**				0.056
4	8.5000	8.9691	1.4742	-0.4691	4.509	-0.104						0.001
5	1.5000	9.3412	1.9677	-7.8412	4.316	-1.817		***				0.343
6	8.5000	8.9189	1.4205	-0.4189	4.526	-0.0926						0.000
7	15.0000	8.8732	1.3754	6.1268	4.540	1.350			**			0.084
8	12.5000	9.2468	1.8302	3.2532	4.376	0.743			*			0.048
9	1.5000	7.9526	1.5654	-6.4526	4.478	-1.441		**				0.127
10	8.5000	7.8249	1.7304	0.6751	4.417	0.153						0.002
11	16.0000	7.9959	1.5139	8.0041	4.496	1.780			***			0.180
12	8.5000	7.8335	1.7188	0.6665	4.421	0.151						0.002
13	4.0000	7.7935	1.7736	-3.7935	4.400	-0.862		*				0.060
14	5.0000	7.7135	1.8873	-2.7135	4.352	-0.623		*				0.037
15	8.5000	7.8348	1.7170	0.6652	4.422	0.150						0.002
16	14.0000	8.2624	1.2661	5.7376	4.572	1.255			**			0.060

Sum of Residuals 0
 Sum of Squared Residuals 315.04135
 Predicted Residual SS (PRESS) 404.24623

```

----- SUMMARY REPORT -----
Algorithm Pharma
CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7
(Healthy vs Severe)
ANOVA analysis
NON-PARAMETRIC TEST OF FIXED EFFECT for Tmax parameter
----- SUMMARY REPORT -----

```

The NPAR1WAY Procedure

```

Wilcoxon Scores (Rank Sums) for Variable Value
Classified by Variable Group
Group      N      Sum of      Expected Std Dev      Mean
          Scores Under H0 Under H0      Score
1           8       70.0       68.0 9.259230      8.750
2           8       66.0       68.0 9.259230      8.250

```

Average scores were used for ties.

Wilcoxon Two-Sample Test

```

Statistic                                70.0000

Normal Approximation
Z                                          0.1620
One-Sided Pr > Z                        0.4357
Two-Sided Pr > |Z|                      0.8713

```

```

t Approximation
One-Sided Pr > Z                        0.4367
Two-Sided Pr > |Z|                      0.8735

```

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test

```

Chi-Square      0.0467
DF              1
Pr > Chi-Square  0.8290

```

Hodges-Lehmann Estimation

```

Location Shift (1 - 2)      0.0000
Type      90%      Interval      Asymptotic
          Confidence      Midpoint Standard Error
          Limits
Asymptotic (Moses) -0.7500 0.5000 -0.1250      0.3800
Exact          -0.7500 0.5000 -0.1250

```

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Normal

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res Area	Lambda z	lnCmax	lnAUCT
1	101	42.00000	2.00000	388.30000	6.86451	0.00079	399.05876	2.69603	0.10098	3.73767	5.96178
2	102	63.80000	2.50000	665.35750	6.44652	0.00198	681.17001	2.32138	0.10752	4.15575	6.50032
3	103	101.00000	1.25000	526.88250	3.01629	0.00249	541.63949	2.72450	0.22980	4.61512	6.26698
4	104	99.80000	2.00000	707.53067	4.37683	0.00249	725.99535	2.54336	0.15837	4.60317	6.56178
5	105	59.20000	1.00000	439.38500	4.65142		453.00695	3.00701	0.14902	4.08092	6.08538
6	106	71.60000	2.00000	440.10750	3.77330	0.00149	446.82229	1.50279	0.18370	4.27110	6.08702
7	107	72.30000	3.00000	767.57700	5.65628	0.00248	779.01561	1.46834	0.12254	4.28082	6.64324
8	108	60.80000	2.50000	581.04250	6.13125	0.00339	591.19310	1.71697	0.11305	4.10759	6.36482

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrLR
1	5.98911	-7.14378	-2.29288	8.5	115.00000	163.85000
2	6.52381	-6.22294	-2.23005	12.5	102.00000	152.84000
3	6.29460	-5.99463	-1.47054	3.0	94.00000	100.45000
4	6.58754	-5.99405	-1.84284	8.5	109.00000	124.34000
5	6.11591		-1.90368	1.5	102.00000	155.18000
6	6.10216	-6.50710	-1.69446	8.5	116.00000	120.18000
7	6.65803	-5.99982	-2.09928	15.0	98.00000	116.39000
8	6.38214	-5.68805	-2.17991	12.5	118.00000	147.36000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Severe

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res Area	Lambda z	lnCmax	lnAUCT
9	013-01	80.40000	2.00000	581.41500	4.55733	0.00040	599.24800	2.97590	0.15209	4.38701	6.36546
10	013-02	247.00000	1.50000	3662.33500	10.49066	0.00220	4049.76869	9.56681	0.06607	5.50939	8.20586
11	013-03	97.10000	4.00000	1312.96000	9.78691	0.00635	1423.69135	7.77776	0.07082	4.57574	7.18004
12	013-04	30.30000	2.56667	373.34958	7.81383	0.00127	390.93106	4.49734	0.08871	3.41115	5.92252
13	013-05	157.00000	1.86667	1449.96833	11.33526	0.00541	1569.00249	7.58661	0.06115	5.05625	7.27930
14	013-06	36.10000	1.00000	480.53000	9.70927	0.00136	517.98321	7.23058	0.07139	3.58629	6.17489
15	013-07	70.20000	2.00000	595.48083	6.36062	0.00531	604.46565	1.48641	0.10897	4.25135	6.38937
16	013-08	124.00000	2.00000	826.49500	9.67678	0.00194	863.75748	4.31400	0.07163	4.82028	6.71719

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrLR
9	6.39568	-7.83410	-1.88325	8.5	23.00000	29.51000
10	8.30642	-6.11803	-2.71700	4.0	27.00000	26.90000
11	7.26101	-5.05902	-2.64756	16.0	26.00000	43.68000
12	5.96853	-6.66858	-2.42241	14.0	28.00000	65.77000
13	7.35820	-5.21913	-2.79443	5.0	16.00000	20.27000
14	6.24994	-6.60174	-2.63959	1.5	26.00000	40.09000
15	6.40434	-5.23737	-2.21664	8.5	19.00000	30.22000
16	6.76129	-6.24641	-2.63624	8.5	21.00000	30.33000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 DESCRIPTIVE RESULTS (OVERALL)
 ----- SUMMARY REPORT -----

Parameter	Renal Function Group	n	Min	Mean	Geometric Mean	Median	Max	Standard Deviation	Coefficient of Variation
Cmax	Normal	8	42.00000	71.31250	68.82161	67.70000	101.00000	20.23727	28.3783
Cmax	Severe	8	30.30000	105.26250	85.59976	88.75000	247.00000	71.14809	67.5911
Tmax	Normal	8	1.00000	2.03125	1.92365	2.00000	3.00000	0.66059	32.5215
Tmax	Severe	8	1.00000	2.11667	1.97338	2.00000	4.00000	0.88479	41.8012
AUCT	Normal	8	388.30000	564.52283	549.44841	553.96250	767.57700	139.24936	24.6667
AUCT	Severe	8	373.34958	1160.31672	879.47766	710.98792	3662.33500	1083.27048	93.3599
Thalf	Normal	8	3.01629	5.11455	4.94162	5.15385	6.86451	1.36926	26.7718
Thalf	Severe	8	4.55733	8.71633	8.39912	9.69302	11.33526	2.29044	26.2775
Ae	Normal	7	0.00079	0.00216	0.00199	0.00248	0.00339	0.00083	38.6537
Ae	Severe	8	0.00040	0.00303	0.00219	0.00207	0.00635	0.00229	75.4936
AUCinf	Normal	8	399.05876	577.23770	562.09079	566.41629	779.01561	141.06547	24.4380
AUCinf	Severe	8	390.93106	1252.35599	932.78585	734.11156	4049.76869	1209.12103	96.5477
Res_Area	Normal	8	1.46834	2.24755	2.17132	2.43237	3.00701	0.60258	26.8105
Res_Area	Severe	8	1.48641	5.67943	4.93235	5.86396	9.56681	2.77000	48.7726
Lambda_z	Normal	8	0.10098	0.14562	0.14027	0.13578	0.22980	0.04432	30.4331
Lambda_z	Severe	8	0.06115	0.08636	0.08253	0.07151	0.15209	0.03063	35.4702
lnCmax	Normal	8	3.73767	4.23152		4.21342	4.61512	0.28709	6.7845
lnCmax	Severe	8	3.41115	4.44968		4.48138	5.50939	0.70826	15.9170
lnAUCT	Normal	8	5.96178	6.30891		6.31590	6.64324	0.24984	3.9601
lnAUCT	Severe	8	5.92252	6.77933		6.55328	8.20586	0.74376	10.9709
lnAUCinf	Normal	8	5.98911	6.33166		6.33837	6.65803	0.24767	3.9117
lnAUCinf	Severe	8	5.96853	6.83818		6.58282	8.30642	0.76505	11.1880
lnAe	Normal	7	-7.14378	-6.22148		-5.99982	-5.68805	0.47768	-7.6780
lnAe	Severe	8	-7.83410	-6.12305		-6.18222	-5.05902	0.94138	-15.3743
lnLambda_z	Normal	8	-2.29288	-1.96421		-2.00148	-1.47054	0.28744	-14.6337
lnLambda_z	Severe	8	-2.79443	-2.49464		-2.63792	-1.88325	0.30707	-12.3094
RkTmax	Normal	8	1.50000	8.75000	7.10269	8.50000	15.00000	4.67516	53.4304
RkTmax	Severe	8	1.50000	8.25000	6.71357	8.50000	16.00000	4.89168	59.2931

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=1 Param=Cmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	154.68766592	
1	1	145.70121256	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	5062.05
Residual	FunctionGroup Normal	409.55

Fit Statistics

-2 Res Log Likelihood	145.7
AIC (Smaller is Better)	149.7
AICC (Smaller is Better)	150.8
BIC (Smaller is Better)	151.2

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	8.99	0.0027

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	1.69	0.2152	

Least Squares Means

Effect	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	Function		Error							
	Group									
FunctionGroup	Severe	105.26	25.1546	14	4.18	0.0009	0.1	60.9574	149.57	
FunctionGroup	Normal	71.3125	7.1550	14	9.97	<.0001	0.1	58.7104	83.9146	

Differences of Least Squares Means

Effect	Renal	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	Function	Function		Error							
	Group	Group									
FunctionGroup	Severe	Normal	33.9500	26.1524	14	1.30	0.2152	0.1	-12.1125	80.0125	

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=3 Param=AUCT

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	230.07126462	
1	1	210.82524991	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	1173475
Residual	FunctionGroup Normal	19390

Fit Statistics

-2 Res Log Likelihood	210.8
AIC (Smaller is Better)	214.8
AICC (Smaller is Better)	215.9
BIC (Smaller is Better)	216.4

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	19.25	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	2.38	0.1451

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	1160.32	382.99	14	3.03	0.0090	0.1	485.75	1834.89
FunctionGroup	Normal	564.52	49.2321	14	11.47	<.0001	0.1	477.81	651.24

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	595.79	386.15	14	1.54	0.1451	0.1	-84.3277	1275.92

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=6 Param=AUCinf

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	233.10854613	
1	1	212.54538495	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	1461974
Residual	FunctionGroup Normal	19899

Fit Statistics

-2 Res Log Likelihood	212.5
AIC (Smaller is Better)	216.5
AICC (Smaller is Better)	217.6
BIC (Smaller is Better)	218.1

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	20.56	<.0001

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	2.46	0.1391	

Least Squares Means

Effect	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	Function		Error							
	Group									
FunctionGroup	Severe	1252.36	427.49	14	2.93	0.0110	0.1	499.42	2005.30	
FunctionGroup	Normal	577.24	49.8742	14	11.57	<.0001	0.1	489.39	665.08	

Differences of Least Squares Means

Effect	Renal	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	Function	Function		Error							
	Group	Group									
FunctionGroup	Severe	Normal	675.12	430.39	14	1.57	0.1391	0.1	-82.9291	1433.17	

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=9 Param=lnCmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	26.65625828	
1	1	21.58833865	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.5016
Residual	FunctionGroup Normal	0.08242

Fit Statistics

-2 Res Log Likelihood	21.6
AIC (Smaller is Better)	25.6
AICC (Smaller is Better)	26.7
BIC (Smaller is Better)	27.1

Null Model Likelihood

DF	Chi-Square	Pr > ChiSq
1	5.07	0.0244

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	0.65	0.4329

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	4.4497	0.2504	14	17.77	<.0001	0.1	4.0086	4.8907
FunctionGroup	Normal	4.2315	0.1015	14	41.69	<.0001	0.1	4.0527	4.4103

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.2182	0.2702	14	0.81	0.4329	0.1	-0.2577	0.6941

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=10 Param=lnAUCT

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	27.39274070	
1	1	20.32759078	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.5532
Residual	FunctionGroup Normal	0.06242

Fit Statistics

-2 Res Log Likelihood	20.3
AIC (Smaller is Better)	24.3
AICC (Smaller is Better)	25.4
BIC (Smaller is Better)	25.9

Null Model Likelihood

DF	Chi-Square	Pr > ChiSq
1	7.07	0.0079

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	2.88	0.1120

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	6.7793	0.2630	14	25.78	<.0001	0.1	6.3162	7.2425
FunctionGroup	Normal	6.3089	0.08833	14	71.42	<.0001	0.1	6.1533	6.4645

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.4704	0.2774	14	1.70	0.1120	0.1	-0.01817	0.9590

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=11 Param=lnAUCinf

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	28.08183081	
1	1	20.60090093	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.5853
Residual	FunctionGroup Normal	0.06134

Fit Statistics

-2 Res Log Likelihood	20.6
AIC (Smaller is Better)	24.6
AICC (Smaller is Better)	25.7
BIC (Smaller is Better)	26.1

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	7.48	0.0062

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	3.17	0.0965	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	6.8382	0.2705	14	25.28	<.0001	0.1	6.3618	7.3146	
FunctionGroup	Normal	6.3317	0.08757	14	72.31	<.0001	0.1	6.1774	6.4859	

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.5065	0.2843	14	1.78	0.0965	0.1	0.005757	1.0073	

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=14 Param=RkTmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	87.72071127	
1	1	87.70636883	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	23.9286
Residual	FunctionGroup Normal	21.8571

Fit Statistics

-2 Res Log Likelihood	87.7
AIC (Smaller is Better)	91.7
AICC (Smaller is Better)	92.8
BIC (Smaller is Better)	93.3

Null Model Likelihood

Ratio Test

DF	Chi-Square	Pr > ChiSq
1	0.01	0.9047

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	0.04	0.8375

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	8.2500	1.7295	14	4.77	0.0003	0.1	5.2039	11.2961
FunctionGroup	Normal	8.7500	1.6529	14	5.29	0.0001	0.1	5.8387	11.6613

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	-0.5000	2.3923	14	-0.21	0.8375	0.1	-4.7136	3.7136

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 Geometric LSmeans
 ----- SUMMARY REPORT -----

Obs	Parameters	Group	GeoLSmeans
1	lnCmax	Severe	85.5998
2	lnCmax	Normal	68.8216
3	lnAUCT	Severe	879.48
4	lnAUCT	Normal	549.45
5	lnAUCinf	Severe	932.79
6	lnAUCinf	Normal	562.09

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M7 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RATIO ESTIMATE BASED ON ln-TRANSFORMED PARAMETERS
 ----- SUMMARY REPORT -----

Obs	Parameters	Group	vs Group	Ratio (%)	L90	U90
1	lnCmax	Severe	Normal	124.379	77.280	200.183
2	lnAUCT	Severe	Normal	160.066	98.199	260.907
3	lnAUCinf	Severe	Normal	165.949	100.577	273.811

16.1.9.7 Documentation of statistical analysis – SAS® output of M3

Legend:

- AUCinf= $AUC_{(0-\infty)}$
- AUCT= $AUC_{(0-tlast)}$
- Vz_F= V_z/F
- CL_F= CL/F
- LambdaZ = λ_z
- lCmax= $\ln(C_{max})$
- lAUCT= $\ln(AUC_{(0-tlast)})$
- lAUCinf= $\ln(AUC_{(0-\infty)})$
- lCLF= $\ln(CL/F)$
- lLambdaZ = $\ln(\lambda_z)$
- lVz_F= $\ln(V_z/F)$
- RkTmax= Rank of T_{max}

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Normal

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res Area	Lambda z	lnCmax	lnAUCT
1	101	14.00000	1.75000	45.30750	1.75421	1.34999	48.38157	6.35381	0.39513	2.63906	3.81347
2	102	11.40000	2.00000	53.04500	2.87180	0.96915	57.14841	7.18026	0.24136	2.43361	3.97114
3	103	14.70000	1.00000	33.71875	1.50087	0.69261	36.46914	7.54168	0.46183	2.68785	3.51805
4	104	16.80000	1.58333	60.92925	3.29157	1.02231	66.09954	7.82198	0.21058	2.82138	4.10971
5	105	24.30000	1.00000	71.99000	1.91495	2.54294	77.28180	6.84741	0.36197	3.19048	4.27653
6	106	13.80000	2.00000	45.91250	1.81268	0.87162	49.50813	7.26270	0.38239	2.62467	3.82674
7	107	11.90000	2.50000	62.35925	2.72587	1.10029	66.96819	6.88229	0.25428	2.47654	4.13291
8	108	10.70000	1.75000	42.65250	2.55262	0.90420	50.04505	14.77180	0.27154	2.37024	3.75309

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrLR
1	3.87912	0.30010	-0.92853	8.5	115.00000	163.85000
2	4.04565	-0.03133	-1.42145	12.0	102.00000	152.84000
3	3.59647	-0.36729	-0.77256	3.5	94.00000	100.45000
4	4.19116	0.02206	-1.55788	7.0	109.00000	124.34000
5	4.34746	0.93332	-1.01621	3.5	102.00000	155.18000
6	3.90214	-0.13740	-0.96132	12.0	116.00000	120.18000
7	4.20422	0.09557	-1.36930	14.5	98.00000	116.39000
8	3.91292	-0.10071	-1.30363	8.5	118.00000	147.36000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Severe

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res Area	Lambda z	lnCmax	lnAUCT
9	201	13.80000	1.00000	82.06500	5.00063	0.17496	91.27968	10.09500	0.13861	2.62467	4.40751
10	202	17.30000	2.00000	71.44500	2.83059	0.19433	76.21265	6.25572	0.24488	2.85071	4.26893
11	203	15.90000	2.50000	105.23750	5.32130	0.41027	121.19195	13.16462	0.13026	2.76632	4.65622
12	204	40.00000	1.81667	195.71667	3.39472	0.56391	203.01562	3.59527	0.20418	3.68888	5.27667
13	205	28.60000	1.50000	120.06250	3.96358	0.32675	126.79522	5.30992	0.17488	3.35341	4.78801
14	206	19.50000	0.75000	70.00292	3.40484	0.08056	75.62775	7.43752	0.20358	2.97041	4.24854
15	207	21.20000	1.00000	102.14750	3.48605	0.35844	107.28247	4.78640	0.19883	3.05400	4.62642
16	208	5.57000	2.56667	23.83792	2.33870	0.12406	27.53273	13.41972	0.29638	1.71740	3.17128

Obs	lnAUCinf	lnAe	lnLambda_z	RkTmax	eGFR	CrLR
9	4.51393	-1.74318	-1.97608	3.5	26.00000	40.09000
10	4.33353	-1.63820	-1.40700	12.0	23.00000	29.51000
11	4.79738	-0.89094	-2.03823	14.5	26.00000	43.68000
12	5.31328	-0.57287	-1.58873	10.0	19.00000	30.22000
13	4.84257	-1.11858	-1.74366	6.0	27.00000	26.90000
14	4.32582	-2.51873	-1.59171	1.0	16.00000	20.27000
15	4.67547	-1.02600	-1.61528	3.5	21.00000	30.33000
16	3.31538	-2.08697	-1.21611	16.0	28.00000	65.77000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 DESCRIPTIVE RESULTS (OVERALL)
 ----- SUMMARY REPORT -----

Parameter	Renal Function Group	n	Min	Mean	Geometric Mean	Median	Max	Standard Deviation	Coefficient of Variation
Cmax	Normal	8	10.70000	14.70000	14.23179	13.90000	24.30000	4.35234	29.608
Cmax	Severe	8	5.57000	20.23375	17.78266	18.40000	40.00000	10.32319	51.020
Tmax	Normal	8	1.00000	1.69792	1.62445	1.75000	2.50000	0.50970	30.019
Tmax	Severe	8	0.75000	1.64167	1.50434	1.65833	2.56667	0.69591	42.390
AUCT	Normal	8	33.71875	51.98934	50.66348	49.47875	71.99000	12.48521	24.015
AUCT	Severe	8	23.83792	96.31438	83.96890	92.10625	195.71667	49.74951	51.653
Thalf	Normal	8	1.50087	2.30307	2.22520	2.23379	3.29157	0.64115	27.839
Thalf	Severe	8	2.33870	3.71755	3.59875	3.44544	5.32130	1.01576	27.323
Ae	Normal	8	0.69261	1.18164	1.09340	0.99573	2.54294	0.58197	49.252
Ae	Severe	8	0.08056	0.27916	0.23470	0.26054	0.56391	0.16404	58.763
AUCinf	Normal	8	36.46914	56.48773	55.14091	53.59673	77.28180	13.04790	23.099
AUCinf	Severe	8	27.53273	103.61726	91.34732	99.28108	203.01562	51.01128	49.230
Res_Area	Normal	8	6.35381	8.08274	7.79325	7.22148	14.77180	2.73985	33.898
Res_Area	Severe	8	3.59527	8.00802	7.24393	6.84662	13.41972	3.79397	47.377
Lambda_z	Normal	8	0.21058	0.32239	0.31150	0.31675	0.46183	0.08959	27.791
Lambda_z	Severe	8	0.13026	0.19895	0.19261	0.20121	0.29638	0.05423	27.260
lnCmax	Normal	8	2.37024	2.65548		2.63186	3.19048	0.26148	9.847
lnCmax	Severe	8	1.71740	2.87822		2.91056	3.68888	0.57909	20.120
lnAUCT	Normal	8	3.51805	3.92521		3.89894	4.27653	0.24504	6.243
lnAUCT	Severe	8	3.17128	4.43045		4.51696	5.27667	0.60693	13.699
lnAUCinf	Normal	8	3.59647	4.00989		3.97929	4.34746	0.23751	5.923
lnAUCinf	Severe	8	3.31538	4.51467		4.59470	5.31328	0.58038	12.855
lnAe	Normal	8	-0.36729	0.08929		-0.00464	0.93332	0.39131	438.252
lnAe	Severe	8	-2.51873	-1.44943		-1.37839	-0.57287	0.65909	-45.472
lnLambda_z	Normal	8	-1.55788	-1.16636		-1.15992	-0.77256	0.28148	-24.133
lnLambda_z	Severe	8	-2.03823	-1.64710		-1.60350	-1.21611	0.27293	-16.570
RkTmax	Normal	8	3.50000	8.68750	7.74418	8.50000	14.50000	4.00836	46.139
RkTmax	Severe	8	1.00000	8.31250	6.14992	8.00000	16.00000	5.59296	67.284

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=9 Param=lnCmax
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.26616	0.26616	1.35	0.2646
Error	14	2.75837	0.19703		
Corrected Total	15	3.02453			

Root MSE 0.44388 R-Square 0.0880
 Dependent Mean 2.76685 Adj R-Sq 0.0229
 Coeff Var 16.04265

Parameter Estimates

Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	2.96519	0.20355	14.57	<.0001	2.52861 3.40177
eGFR	eGFR	1	-0.00305	0.00263	-1.16	0.2646	-0.00868 0.00258

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
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 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	2.6391	2.6143	0.1719	0.0248	0.409	0.0605						0.000
2	2.4336	2.6539	0.1475	-0.2203	0.419	-0.526	*					0.017
3	2.6878	2.6784	0.1346	0.009487	0.423	0.0224						0.000
4	2.8214	2.6326	0.1602	0.1888	0.414	0.456						0.016
5	3.1905	2.6539	0.1475	0.5365	0.419	1.282			**			0.102
6	2.6247	2.6112	0.1739	0.0134	0.408	0.0329						0.000
7	2.4765	2.6662	0.1408	-0.1896	0.421	-0.450						0.011
8	2.3702	2.6051	0.1780	-0.2349	0.407	-0.578	*					0.032
9	2.6247	2.8859	0.1510	-0.2612	0.417	-0.626	*					0.026
10	2.8507	2.8950	0.1564	-0.0443	0.415	-0.107						0.001
11	2.7663	2.8859	0.1510	-0.1195	0.417	-0.286						0.005
12	3.6889	2.9072	0.1640	0.7817	0.412	1.895			***			0.284
13	3.3534	2.8828	0.1492	0.4706	0.418	1.126			**			0.081
14	2.9704	2.9164	0.1699	0.0540	0.410	0.132						0.001
15	3.0540	2.9011	0.1602	0.1529	0.414	0.369						0.010
16	1.7174	2.8798	0.1475	-1.1624	0.419	-2.776	*****					0.478

Sum of Residuals 0
 Sum of Squared Residuals 2.75837
 Predicted Residual SS (PRESS) 3.54732

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.10064	1.10064	5.28	0.0375
Error	14	2.91927	0.20852		
Corrected Total	15	4.01991			

Root MSE	0.45664	R-Square	0.2738
Dependent Mean	4.17783	Adj R-Sq	0.2219
Coeff Var	10.93006		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	4.58116	0.20941	21.88	<.0001	4.13202 5.03029
eGFR	eGFR	1	-0.00621	0.00270	-2.30	0.0375	-0.01200 -0.00041238

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
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 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	3.8135	3.8676	0.1768	-0.0541	0.421	-0.128						0.001
2	3.9711	3.9482	0.1517	0.0229	0.431	0.0532						0.000
3	3.5181	3.9979	0.1384	-0.4798	0.435	-1.103	**					0.062
4	4.1097	3.9048	0.1648	0.2049	0.426	0.481						0.017
5	4.2765	3.9482	0.1517	0.3283	0.431	0.762		*				0.036
6	3.8267	3.8614	0.1789	-0.0346	0.420	-0.0824						0.001
7	4.1329	3.9731	0.1448	0.1599	0.433	0.369						0.008
8	3.7531	3.8490	0.1831	-0.0959	0.418	-0.229						0.005
9	4.4075	4.4198	0.1553	-0.0123	0.429	-0.0287						0.000
10	4.2689	4.4384	0.1609	-0.1695	0.427	-0.397						0.011
11	4.6562	4.4198	0.1553	0.2364	0.429	0.551		*				0.020
12	5.2767	4.4633	0.1687	0.8134	0.424	1.917		***				0.290
13	4.7880	4.4136	0.1535	0.3744	0.430	0.871		*				0.048
14	4.2485	4.4819	0.1748	-0.2333	0.422	-0.553	*					0.026
15	4.6264	4.4508	0.1648	0.1756	0.426	0.412						0.013
16	3.1713	4.4074	0.1517	-1.2361	0.431	-2.870	*****					0.511

Sum of Residuals 0
 Sum of Squared Residuals 2.91927
 Predicted Residual SS (PRESS) 3.74286

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.07856	1.07856	5.61	0.0328
Error	14	2.69339	0.19238		
Corrected Total	15	3.77195			

Root MSE	0.43862	R-Square	0.2859
Dependent Mean	4.26228	Adj R-Sq	0.2349
Coeff Var	10.29067		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	4.66154	0.20114	23.18	<.0001	4.23013 5.09295
eGFR	eGFR	1	-0.00614	0.00259	-2.37	0.0328	-0.01171 -0.00057843

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error	Mean Predict	Residual	Std Error						
					Residual	Student Residual						
1	3.8791	3.9552	0.1699	-0.0760	0.404	-0.188						0.003
2	4.0457	4.0350	0.1457	0.0106	0.414	0.0257						0.000
3	3.5965	4.0841	0.1330	-0.4877	0.418	-1.167	**					0.069
4	4.1912	3.9920	0.1583	0.1992	0.409	0.487						0.018
5	4.3475	4.0350	0.1457	0.3125	0.414	0.755		*				0.035
6	3.9021	3.9490	0.1718	-0.0469	0.404	-0.116						0.001
7	4.2042	4.0596	0.1391	0.1446	0.416	0.348						0.007
8	3.9129	3.9367	0.1759	-0.0238	0.402	-0.0592						0.000
9	4.5139	4.5018	0.1492	0.0121	0.412	0.0293						0.000
10	4.3335	4.5203	0.1546	-0.1867	0.410	-0.455						0.015
11	4.7974	4.5018	0.1492	0.2955	0.412	0.717		*				0.034
12	5.3133	4.5448	0.1621	0.7684	0.408	1.885			***			0.281
13	4.8426	4.4957	0.1475	0.3469	0.413	0.840		*				0.045
14	4.3258	4.5633	0.1679	-0.2374	0.405	-0.586	*					0.029
15	4.6755	4.5326	0.1583	0.1429	0.409	0.349						0.009
16	3.3154	4.4896	0.1457	-1.1742	0.414	-2.838	*****					0.500

Sum of Residuals 0
 Sum of Squared Residuals 2.69339
 Predicted Residual SS (PRESS) 3.45084

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	9.30262	9.30262	30.42 <.0001
Error	14	4.28074	0.30577	
Corrected Total	15	13.58335		

Root MSE	0.55296	R-Square	0.6849
Dependent Mean	-0.68007	Adj R-Sq	0.6623
Coeff Var	-81.30945		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-1.85264	0.25358	-7.31	<.0001	-2.39652 -1.30877
eGFR	eGFR	1	0.01804	0.00327	5.52	<.0001	0.01102 0.02505

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error	Mean Predict	Residual	Std Error						
					Residual	Student Residual						
1	0.3001	0.2219	0.2141	0.0782	0.510	0.153						0.002
2	-0.0313	-0.0126	0.1837	-0.0187	0.522	-0.0359						0.000
3	-0.3673	-0.1569	0.1676	-0.2104	0.527	-0.399						0.008
4	0.0221	0.1137	0.1995	-0.0916	0.516	-0.178						0.002
5	0.9333	-0.0126	0.1837	0.9459	0.522	1.814			***			0.204
6	-0.1374	0.2399	0.2166	-0.3773	0.509	-0.742		*				0.050
7	0.0956	-0.0848	0.1754	0.1803	0.524	0.344						0.007
8	-0.1007	0.2760	0.2217	-0.3767	0.507	-0.744		*				0.053
9	-1.7432	-1.3836	0.1881	-0.3596	0.520	-0.691		*				0.031
10	-1.6382	-1.4377	0.1949	-0.2005	0.517	-0.387						0.011
11	-0.8909	-1.3836	0.1881	0.4927	0.520	0.947			*			0.059
12	-0.5729	-1.5099	0.2043	0.9370	0.514	1.824			***			0.263
13	-1.1186	-1.3656	0.1859	0.2470	0.521	0.474						0.014
14	-2.5187	-1.5640	0.2116	-0.9547	0.511	-1.869		***				0.300
15	-1.0260	-1.4738	0.1995	0.4478	0.516	0.868			*			0.056
16	-2.0870	-1.3475	0.1837	-0.7394	0.522	-1.418		**				0.125

Sum of Residuals 0
 Sum of Squared Residuals 4.28074
 Predicted Residual SS (PRESS) 5.63517

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	0.87526	0.87526	10.89	0.0053
Error	14	1.12522	0.08037		
Corrected Total	15	2.00048			

Root MSE	0.28350	R-Square	0.4375
Dependent Mean	-1.40673	Adj R-Sq	0.3973
Coeff Var	-20.15320		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-1.76640	0.13001	-13.59	<.0001	-2.04524 -1.48756
eGFR	eGFR	1	0.00553	0.00168	3.30	0.0053	0.00194 0.00913

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	-0.9285	-1.1301	0.1098	0.2015	0.261	0.771			*			0.052
2	-1.4215	-1.2020	0.0942	-0.2195	0.267	-0.821		*				0.042
3	-0.7726	-1.2463	0.0860	0.4737	0.270	1.753			***			0.156
4	-1.5579	-1.1633	0.1023	-0.3946	0.264	-1.493		**				0.167
5	-1.0162	-1.2020	0.0942	0.1858	0.267	0.695			*			0.030
6	-0.9613	-1.1245	0.1111	0.1632	0.261	0.626			*			0.035
7	-1.3693	-1.2241	0.0899	-0.1452	0.269	-0.540		*				0.016
8	-1.3036	-1.1135	0.1137	-0.1902	0.260	-0.732		*				0.051
9	-1.9761	-1.6225	0.0964	-0.3535	0.267	-1.326		**				0.115
10	-1.4070	-1.6391	0.0999	0.2321	0.265	0.875			*			0.054
11	-2.0382	-1.6225	0.0964	-0.4157	0.267	-1.559		***				0.159
12	-1.5887	-1.6613	0.1048	0.0725	0.263	0.275						0.006
13	-1.7437	-1.6170	0.0953	-0.1267	0.267	-0.474						0.014
14	-1.5917	-1.6779	0.1085	0.0862	0.262	0.329						0.009
15	-1.6153	-1.6502	0.1023	0.0349	0.264	0.132						0.001
16	-1.2161	-1.6115	0.0942	0.3954	0.267	1.479			**			0.136

Sum of Residuals 0
 Sum of Squared Residuals 1.12522
 Predicted Residual SS (PRESS) 1.44105

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=14 Param=RkTmax
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	2.36479	2.36479	0.10	0.7560
Error	14	329.63521	23.54537		
Corrected Total	15	332.00000			

Root MSE	4.85236	R-Square	0.0071
Dependent Mean	8.50000	Adj R-Sq	-0.0638
Coeff Var	57.08656		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	7.90880	2.22522	3.55	0.0032	3.13619 12.68141
eGFR	eGFR	1	0.00910	0.02870	0.32	0.7560	-0.05246 0.07065

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of eGFR at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Obs	Output Statistics						-2	-1	0	1	2	Cook's D
	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	8.5000	8.9548	1.8790	-0.4548	4.474	-0.102						0.001
2	12.0000	8.8365	1.6122	3.1635	4.577	0.691			*			0.030
3	3.5000	8.7638	1.4712	-5.2638	4.624	-1.138		**				0.066
4	7.0000	8.9002	1.7511	-1.9002	4.525	-0.420						0.013
5	3.5000	8.8365	1.6122	-5.3365	4.577	-1.166		**				0.084
6	12.0000	8.9639	1.9010	3.0361	4.464	0.680			*			0.042
7	14.5000	8.8001	1.5390	5.6999	4.602	1.239			**			0.086
8	8.5000	8.9821	1.9456	-0.4821	4.445	-0.108						0.001
9	3.5000	8.1453	1.6506	-4.6453	4.563	-1.018		**				0.068
10	12.0000	8.1180	1.7101	3.8820	4.541	0.855			*			0.052
11	14.5000	8.1453	1.6506	6.3547	4.563	1.393			**			0.127
12	10.0000	8.0816	1.7929	1.9184	4.509	0.425						0.014
13	6.0000	8.1544	1.6312	-2.1544	4.570	-0.471						0.014
14	1.0000	8.0543	1.8572	-7.0543	4.483	-1.574		***				0.213
15	3.5000	8.0998	1.7511	-4.5998	4.525	-1.016		**				0.077
16	16.0000	8.1635	1.6122	7.8365	4.577	1.712			***			0.182

Sum of Residuals 0
 Sum of Squared Residuals 329.63521
 Predicted Residual SS (PRESS) 424.24351

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.39512	0.39512	2.10 0.1690
Error	14	2.62941	0.18781	
Corrected Total	15	3.02453		

Root MSE	0.43338	R-Square	0.1306
Dependent Mean	2.76685	Adj R-Sq	0.0685
Coeff Var	15.66315		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	3.02188	0.20653	14.63	<.0001	2.57892 3.46485
CrLR	CrLR	1	-0.00298	0.00206	-1.45	0.1690	-0.00740 0.00143

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=9 Param=lnCmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	2.6391	2.5329	0.1943	0.1061	0.387	0.274						0.009
2	2.4336	2.5658	0.1759	-0.1322	0.396	-0.334						0.011
3	2.6878	2.7221	0.1126	-0.0343	0.418	-0.0819						0.000
4	2.8214	2.6508	0.1347	0.1706	0.412	0.414						0.009
5	3.1905	2.5588	0.1798	0.6317	0.394	1.602			***			0.267
6	2.6247	2.6632	0.1298	-0.0386	0.413	-0.0933						0.000
7	2.4765	2.6745	0.1257	-0.1980	0.415	-0.477						0.010
8	2.3702	2.5821	0.1672	-0.2119	0.400	-0.530	*					0.025
9	2.6247	2.9022	0.1430	-0.2776	0.409	-0.679	*					0.028
10	2.8507	2.9338	0.1581	-0.0831	0.404	-0.206						0.003
11	2.7663	2.8915	0.1383	-0.1252	0.411	-0.305						0.005
12	3.6889	2.9317	0.1570	0.7572	0.404	1.875			***			0.265
13	3.3534	2.9416	0.1620	0.4118	0.402	1.025			**			0.085
14	2.9704	2.9614	0.1724	0.009022	0.398	0.0227						0.000
15	3.0540	2.9314	0.1569	0.1226	0.404	0.304						0.007
16	1.7174	2.8256	0.1157	-1.1082	0.418	-2.653	*****					0.270

Sum of Residuals 0
 Sum of Squared Residuals 2.62941
 Predicted Residual SS (PRESS) 3.33060

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	1.18686	1.18686	5.87 0.0296
Error	14	2.83305	0.20236	
Corrected Total	15	4.01991		

Root MSE	0.44984	R-Square	0.2952
Dependent Mean	4.17783	Adj R-Sq	0.2449
Coeff Var	10.76744		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	4.61983	0.21438	21.55	<.0001	4.16004 5.07963
CrLR	CrLR	1	-0.00517	0.00214	-2.42	0.0296	-0.00975 -0.00059159

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=10 Param=lnAUCT

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	3.8135	3.7724	0.2017	0.0411	0.402	0.102						0.001
2	3.9711	3.8293	0.1826	0.1418	0.411	0.345						0.012
3	3.5181	4.1003	0.1169	-0.5822	0.434	-1.340	**					0.065
4	4.1097	3.9767	0.1398	0.1330	0.428	0.311						0.005
5	4.2765	3.8172	0.1866	0.4593	0.409	1.122		**				0.131
6	3.8267	3.9983	0.1347	-0.1715	0.429	-0.400						0.008
7	4.1329	4.0179	0.1304	0.1151	0.431	0.267						0.003
8	3.7531	3.8577	0.1736	-0.1046	0.415	-0.252						0.006
9	4.4075	4.4125	0.1484	-0.004972	0.425	-0.0117						0.000
10	4.2689	4.4672	0.1641	-0.1983	0.419	-0.473						0.017
11	4.6562	4.3939	0.1436	0.2623	0.426	0.615		*				0.021
12	5.2767	4.4635	0.1630	0.8131	0.419	1.939		***				0.284
13	4.7880	4.4807	0.1682	0.3073	0.417	0.737		*				0.044
14	4.2485	4.5150	0.1790	-0.2665	0.413	-0.646		*				0.039
15	4.6264	4.4630	0.1628	0.1635	0.419	0.390						0.011
16	3.1713	4.2797	0.1201	-1.1084	0.434	-2.557	*****					0.251

Sum of Residuals 0
 Sum of Squared Residuals 2.83305
 Predicted Residual SS (PRESS) 3.51836

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1.14550	1.14550	6.11	0.0269
Error	14	2.62645	0.18760		
Corrected Total	15	3.77195			

Root MSE	0.43313	R-Square	0.3037
Dependent Mean	4.26228	Adj R-Sq	0.2540
Coeff Var	10.16199		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	4.69652	0.20641	22.75	<.0001	4.25380 5.13923
CrLR	CrLR	1	-0.00508	0.00206	-2.47	0.0269	-0.00949 -0.00067084

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=11 Param=lnAUCinf

Obs	Dependent Variable	Predicted Value	Output Statistics				-2-1	0	1	2	Cook's D
			Std Error	Residual	Std Error	Student					
		Mean Predict			Residual	Residual					
1	3.8791	3.8640	0.1942	0.0152	0.387	0.0391					0.000
2	4.0457	3.9199	0.1758	0.1257	0.396	0.318					0.010
3	3.5965	4.1861	0.1126	-0.5896	0.418	-1.410	**				0.072
4	4.1912	4.0647	0.1346	0.1264	0.412	0.307					0.005
5	4.3475	3.9080	0.1797	0.4394	0.394	1.115		**			0.129
6	3.9021	4.0859	0.1297	-0.1837	0.413	-0.445					0.010
7	4.2042	4.1051	0.1256	0.0991	0.415	0.239					0.003
8	3.9129	3.9478	0.1671	-0.0348	0.400	-0.0872					0.001
9	4.5139	4.4928	0.1429	0.0211	0.409	0.0516					0.000
10	4.3335	4.5466	0.1580	-0.2130	0.403	-0.528	*				0.021
11	4.7974	4.4746	0.1382	0.3228	0.410	0.786		*			0.035
12	5.3133	4.5430	0.1569	0.7703	0.404	1.908			***		0.275
13	4.8426	4.5598	0.1619	0.2827	0.402	0.704			*		0.040
14	4.3258	4.5935	0.1723	-0.2677	0.397	-0.674	*				0.043
15	4.6755	4.5424	0.1568	0.1331	0.404	0.330					0.008
16	3.3154	4.3623	0.1156	-1.0470	0.417	-2.508	*****				0.241

Sum of Residuals 0
 Sum of Squared Residuals 2.62645
 Predicted Residual SS (PRESS) 3.25807

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	9.25376	9.25376	29.92 <.0001
Error	14	4.32960	0.30926	
Corrected Total	15	13.58335		

Root MSE	0.55611	R-Square	0.6813
Dependent Mean	-0.68007	Adj R-Sq	0.6585
Coeff Var	-81.77213		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-1.91428	0.26502	-7.22	<.0001	-2.48269 -1.34587
CrLR	CrLR	1	0.01444	0.00264	5.47	<.0001	0.00878 0.02010

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=12 Param=lnAe

Obs	Output Statistics						-2	-1	0	1	2	Cook's D
	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	0.3001	0.4520	0.2493	-0.1519	0.497	-0.306						0.012
2	-0.0313	0.2930	0.2258	-0.3244	0.508	-0.638	*					0.040
3	-0.3673	-0.4636	0.1446	0.0963	0.537	0.179						0.001
4	0.0221	-0.1186	0.1728	0.1406	0.529	0.266						0.004
5	0.9333	0.3268	0.2307	0.6065	0.506	1.199			**			0.149
6	-0.1374	-0.1786	0.1665	0.0412	0.531	0.0777						0.000
7	0.0956	-0.2334	0.1612	0.3290	0.532	0.618			*			0.018
8	-0.1007	0.2139	0.2146	-0.3146	0.513	-0.613	*					0.033
9	-1.7432	-1.3353	0.1835	-0.4079	0.525	-0.777	*					0.037
10	-1.6382	-1.4881	0.2029	-0.1501	0.518	-0.290						0.006
11	-0.8909	-1.2835	0.1775	0.3925	0.527	0.745			*			0.031
12	-0.5729	-1.4778	0.2015	0.9050	0.518	1.746			***			0.230
13	-1.1186	-1.5258	0.2079	0.4072	0.516	0.790			*			0.051
14	-2.5187	-1.6215	0.2212	-0.8972	0.510	-1.759	***					0.291
15	-1.0260	-1.4763	0.2013	0.4503	0.518	0.869			*			0.057
16	-2.0870	-0.9644	0.1484	-1.1225	0.536	-2.095	****					0.168

Sum of Residuals 0
 Sum of Squared Residuals 4.32960
 Predicted Residual SS (PRESS) 5.63135

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z
 Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance				
Source	DF	Sum of Squares	Mean Square	F Value Pr > F
Model	1	0.83237	0.83237	9.98 0.0070
Error	14	1.16811	0.08344	
Corrected Total	15	2.00048		

Root MSE	0.28885	R-Square	0.4161
Dependent Mean	-1.40673	Adj R-Sq	0.3744
Coeff Var	-20.53370		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	-1.77689	0.13766	-12.91	<.0001	-2.07213 -1.48164
CrLR	CrLR	1	0.00433	0.00137	3.16	0.0070	0.00139 0.00727

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value
 Order=13 Param=lnLambda_z

Obs	Output Statistics							-2	-1	0	1	2	Cook's D
	Dependent Variable	Predicted Value	Std Error Mean Predict	Residual	Std Error Residual	Student Residual							
1	-0.9285	-1.0672	0.1295	0.1387	0.258	0.537			*				0.036
2	-1.4215	-1.1149	0.1173	-0.3066	0.264	-1.161		**					0.133
3	-0.7726	-1.3418	0.0751	0.5692	0.279	2.041			****				0.151
4	-1.5579	-1.2383	0.0898	-0.3195	0.275	-1.164		**					0.072
5	-1.0162	-1.1047	0.1198	0.0885	0.263	0.337							0.012
6	-0.9613	-1.2563	0.0865	0.2950	0.276	1.070			**				0.056
7	-1.3693	-1.2728	0.0837	-0.0965	0.276	-0.349							0.006
8	-1.3036	-1.1386	0.1114	-0.1650	0.266	-0.619		*					0.034
9	-1.9761	-1.6032	0.0953	-0.3728	0.273	-1.367		**					0.114
10	-1.4070	-1.6491	0.1054	0.2421	0.269	0.900			*				0.062
11	-2.0382	-1.5877	0.0922	-0.4505	0.274	-1.646		***					0.154
12	-1.5887	-1.6460	0.1047	0.0573	0.269	0.213							0.003
13	-1.7437	-1.6604	0.1080	-0.0833	0.268	-0.311							0.008
14	-1.5917	-1.6891	0.1149	0.0974	0.265	0.367							0.013
15	-1.6153	-1.6455	0.1045	0.0302	0.269	0.112							0.001
16	-1.2161	-1.4920	0.0771	0.2759	0.278	0.991			*				0.038

Sum of Residuals 0
 Sum of Squared Residuals 1.16811
 Predicted Residual SS (PRESS) 1.44904

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Number of Observations Read 16
 Number of Observations Used 16

Analysis of Variance					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	6.13782	6.13782	0.26	0.6156
Error	14	325.86218	23.27587		
Corrected Total	15	332.00000			

Root MSE	4.82451	R-Square	0.0185
Dependent Mean	8.50000	Adj R-Sq	-0.0516
Coeff Var	56.75891		

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > t	95% Confidence Limits
Intercept	Intercept	1	7.49484	2.29917	3.26	0.0057	2.56361 12.42607
CrLR	CrLR	1	0.01176	0.02290	0.51	0.6156	-0.03736 0.06089

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
 (Healthy vs Severe)
 ANOVA analysis
 Regression Analysis of Cockcroft-Gault Estimate of the Creatinine Clearance at Baseline
 ----- SUMMARY REPORT -----

The REG Procedure
 Model: MODEL1
 Dependent Variable: Value

Order=14 Param=RkTmax

Obs	Dependent Variable	Predicted Value	Output Statistics				-2	-1	0	1	2	Cook's D
			Std Error Mean Predict	Residual	Std Error Residual	Student Residual						
1	8.5000	9.4220	2.1630	-0.9220	4.312	-0.214						0.006
2	12.0000	9.2925	1.9587	2.7075	4.409	0.614			*			0.037
3	3.5000	8.6763	1.2540	-5.1763	4.659	-1.111		**				0.045
4	7.0000	8.9573	1.4993	-1.9573	4.586	-0.427						0.010
5	3.5000	9.3200	2.0012	-5.8200	4.390	-1.326		**				0.183
6	12.0000	8.9084	1.4447	3.0916	4.603	0.672			*			0.022
7	14.5000	8.8638	1.3988	5.6362	4.617	1.221			**			0.068
8	8.5000	9.2281	1.8614	-0.7281	4.451	-0.164						0.002
9	3.5000	7.9664	1.5920	-4.4664	4.554	-0.981		*				0.059
10	12.0000	7.8419	1.7598	4.1581	4.492	0.926			*			0.066
11	14.5000	8.0086	1.5396	6.4914	4.572	1.420			**			0.114
12	10.0000	7.8503	1.7480	2.1497	4.497	0.478						0.017
13	6.0000	7.8112	1.8038	-1.8112	4.475	-0.405						0.013
14	1.0000	7.7333	1.9194	-6.7333	4.426	-1.521		***				0.218
15	3.5000	7.8516	1.7462	-4.3516	4.497	-0.968		*				0.071
16	16.0000	8.2684	1.2877	7.7316	4.649	1.663			***			0.106

Sum of Residuals 0
 Sum of Squared Residuals 325.86218
 Predicted Residual SS (PRESS) 416.18300

```

----- SUMMARY REPORT -----
Algorithm Pharma
CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3
(Healthy vs Severe)
ANOVA analysis
NON-PARAMETRIC TEST OF FIXED EFFECT for Tmax parameter
----- SUMMARY REPORT -----

```

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable Value
Classified by Variable Group

Group	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
1	8	69.50	68.0	9.409215	8.68750
2	8	66.50	68.0	9.409215	8.31250

Average scores were used for ties.

Wilcoxon Two-Sample Test

Statistic 69.5000

Normal Approximation

Z	0.1063
One-Sided Pr > Z	0.4577
Two-Sided Pr > Z	0.9154

t Approximation

One-Sided Pr > Z	0.4584
Two-Sided Pr > Z	0.9168

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test

Chi-Square	0.0254
DF	1
Pr > Chi-Square	0.8733

Hodges-Lehmann Estimation

Location Shift (1 - 2) 0.0000

Type	90% Confidence Limits	Interval Midpoint	Asymptotic Standard Error
Asymptotic (Moses)	-0.5667 0.7500	0.0917	0.4002
Exact	-0.5000 0.7500	0.1250	

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Normal

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res Area	Lambda z	lnCmax	lnAUCT
1	101	14.00000	1.75000	45.30750	1.75421	1.34999	48.38157	6.35381	0.39513	2.63906	3.81347
2	102	11.40000	2.00000	53.04500	2.87180	0.96915	57.14841	7.18026	0.24136	2.43361	3.97114
3	103	14.70000	1.00000	33.71875	1.50087	0.69261	36.46914	7.54168	0.46183	2.68785	3.51805
4	104	16.80000	1.58333	60.92925	3.29157	1.02231	66.09954	7.82198	0.21058	2.82138	4.10971
5	105	24.30000	1.00000	71.99000	1.91495	2.54294	77.28180	6.84741	0.36197	3.19048	4.27653
6	106	13.80000	2.00000	45.91250	1.81268	0.87162	49.50813	7.26270	0.38239	2.62467	3.82674
7	107	11.90000	2.50000	62.35925	2.72587	1.10029	66.96819	6.88229	0.25428	2.47654	4.13291
8	108	10.70000	1.75000	42.65250	2.55262	0.90420	50.04505	14.77180	0.27154	2.37024	3.75309

Obs	lnAUCinf	lnAe	lnLambda z	RkTmax	eGFR	CrLR
1	3.87912	0.30010	-0.92853	8.5	115.00000	163.85000
2	4.04565	-0.03133	-1.42145	12.0	102.00000	152.84000
3	3.59647	-0.36729	-0.77256	3.5	94.00000	100.45000
4	4.19116	0.02206	-1.55788	7.0	109.00000	124.34000
5	4.34746	0.93332	-1.01621	3.5	102.00000	155.18000
6	3.90214	-0.13740	-0.96132	12.0	116.00000	120.18000
7	4.20422	0.09557	-1.36930	14.5	98.00000	116.39000
8	3.91292	-0.10071	-1.30363	8.5	118.00000	147.36000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RAW DATA
 ----- SUMMARY REPORT -----

Renal Function Group=Severe

Obs	Subject	Cmax	Tmax	AUCT	Thalf	Ae	AUCinf	Res Area	Lambda z	lnCmax	lnAUCT
9	013-01	17.30000	2.00000	71.44500	2.83059	0.19433	76.21265	6.25572	0.24488	2.85071	4.26893
10	013-02	28.60000	1.50000	120.06250	3.96358	0.32675	126.79522	5.30992	0.17488	3.35341	4.78801
11	013-03	15.90000	2.50000	105.23750	5.32130	0.41027	121.19195	13.16462	0.13026	2.76632	4.65622
12	013-04	5.57000	2.56667	23.83792	2.33870	0.12406	27.53273	13.41972	0.29638	1.71740	3.17128
13	013-05	19.50000	0.75000	70.00292	3.40484	0.08056	75.62775	7.43752	0.20358	2.97041	4.24854
14	013-06	13.80000	1.00000	82.06500	5.00063	0.17496	91.27968	10.09500	0.13861	2.62467	4.40751
15	013-07	40.00000	1.81667	195.71667	3.39472	0.56391	203.01562	3.59527	0.20418	3.68888	5.27667
16	013-08	21.20000	1.00000	102.14750	3.48605	0.35844	107.28247	4.78640	0.19883	3.05400	4.62642

Obs	lnAUCinf	lnAe	lnLambda_z	RkTmax	eGFR	CrLR
9	4.33353	-1.63820	-1.40700	12.0	23.00000	29.51000
10	4.84257	-1.11858	-1.74366	6.0	27.00000	26.90000
11	4.79738	-0.89094	-2.03823	14.5	26.00000	43.68000
12	3.31538	-2.08697	-1.21611	16.0	28.00000	65.77000
13	4.32582	-2.51873	-1.59171	1.0	16.00000	20.27000
14	4.51393	-1.74318	-1.97608	3.5	26.00000	40.09000
15	5.31328	-0.57287	-1.58873	10.0	19.00000	30.22000
16	4.67547	-1.02600	-1.61528	3.5	21.00000	30.33000

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 DESCRIPTIVE RESULTS (OVERALL)
 ----- SUMMARY REPORT -----

Parameter	Renal Function Group	n	Min	Mean	Geometric Mean	Median	Max	Standard Deviation	Coefficient of Variation
Cmax	Normal	8	10.70000	14.70000	14.23179	13.90000	24.30000	4.35234	29.608
Cmax	Severe	8	5.57000	20.23375	17.78266	18.40000	40.00000	10.32319	51.020
Tmax	Normal	8	1.00000	1.69792	1.62445	1.75000	2.50000	0.50970	30.019
Tmax	Severe	8	0.75000	1.64167	1.50434	1.65833	2.56667	0.69591	42.390
AUCT	Normal	8	33.71875	51.98934	50.66348	49.47875	71.99000	12.48521	24.015
AUCT	Severe	8	23.83792	96.31438	83.96890	92.10625	195.71667	49.74951	51.653
Thalf	Normal	8	1.50087	2.30307	2.22520	2.23379	3.29157	0.64115	27.839
Thalf	Severe	8	2.33870	3.71755	3.59875	3.44544	5.32130	1.01576	27.323
Ae	Normal	8	0.69261	1.18164	1.09340	0.99573	2.54294	0.58197	49.252
Ae	Severe	8	0.08056	0.27916	0.23470	0.26054	0.56391	0.16404	58.763
AUCinf	Normal	8	36.46914	56.48773	55.14091	53.59673	77.28180	13.04790	23.099
AUCinf	Severe	8	27.53273	103.61726	91.34732	99.28108	203.01562	51.01128	49.230
Res_Area	Normal	8	6.35381	8.08274	7.79325	7.22148	14.77180	2.73985	33.898
Res_Area	Severe	8	3.59527	8.00802	7.24393	6.84662	13.41972	3.79397	47.377
Lambda_z	Normal	8	0.21058	0.32239	0.31150	0.31675	0.46183	0.08959	27.791
Lambda_z	Severe	8	0.13026	0.19895	0.19261	0.20121	0.29638	0.05423	27.260
lnCmax	Normal	8	2.37024	2.65548		2.63186	3.19048	0.26148	9.847
lnCmax	Severe	8	1.71740	2.87822		2.91056	3.68888	0.57909	20.120
lnAUCT	Normal	8	3.51805	3.92521		3.89894	4.27653	0.24504	6.243
lnAUCT	Severe	8	3.17128	4.43045		4.51696	5.27667	0.60693	13.699
lnAUCinf	Normal	8	3.59647	4.00989		3.97929	4.34746	0.23751	5.923
lnAUCinf	Severe	8	3.31538	4.51467		4.59470	5.31328	0.58038	12.855
lnAe	Normal	8	-0.36729	0.08929		-0.00464	0.93332	0.39131	438.252
lnAe	Severe	8	-2.51873	-1.44943		-1.37839	-0.57287	0.65909	-45.472
lnLambda_z	Normal	8	-1.55788	-1.16636		-1.15992	-0.77256	0.28148	-24.133
lnLambda_z	Severe	8	-2.03823	-1.64710		-1.60350	-1.21611	0.27293	-16.570
RkTmax	Normal	8	3.50000	8.68750	7.74418	8.50000	14.50000	4.00836	46.139
RkTmax	Severe	8	1.00000	8.31250	6.14992	8.00000	16.00000	5.59296	67.284

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=1 Param=Cmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	101.83862169	
1	1	97.16065024	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	106.57
Residual	FunctionGroup Normal	18.9429

Fit Statistics

-2 Res Log Likelihood	97.2
AIC (Smaller is Better)	101.2
AICC (Smaller is Better)	102.3
BIC (Smaller is Better)	102.7

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	4.68	0.0306

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	1.95	0.1841	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	20.2338	3.6498	14	5.54	<.0001	0.1	13.8053	26.6622	
FunctionGroup	Normal	14.7000	1.5388	14	9.55	<.0001	0.1	11.9897	17.4103	

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	5.5338	3.9609	14	1.40	0.1841	0.1	-1.4427	12.5102	

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=3 Param=AUCT

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	144.43620945	
1	1	133.93080097	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	2475.01
Residual	FunctionGroup Normal	155.88

Fit Statistics

-2 Res Log Likelihood	133.9
AIC (Smaller is Better)	137.9
AICC (Smaller is Better)	139.0
BIC (Smaller is Better)	139.5

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	10.51	0.0012

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	5.97	0.0284	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	96.3144	17.5891	14	5.48	<.0001	0.1	65.3345	127.29	
FunctionGroup	Normal	51.9893	4.4142	14	11.78	<.0001	0.1	44.2146	59.7641	

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	44.3250	18.1345	14	2.44	0.0284	0.1	12.3845	76.2656	

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=6 Param=AUCinf

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	145.16965227	
1	1	134.89859671	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	2602.15
Residual	FunctionGroup Normal	170.25

Fit Statistics

-2 Res Log Likelihood	134.9
AIC (Smaller is Better)	138.9
AICC (Smaller is Better)	140.0
BIC (Smaller is Better)	140.4

Null Model Likelihood

DF	Chi-Square	Pr > ChiSq
1	10.27	0.0014

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
FunctionGroup	1	14	6.41	0.0240

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	103.62	18.0352	14	5.75	<.0001	0.1	71.8517	135.38
FunctionGroup	Normal	56.4877	4.6131	14	12.24	<.0001	0.1	48.3626	64.6129

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	47.1295	18.6158	14	2.53	0.0240	0.1	14.3413	79.9178

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=9 Param=lnCmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	21.48676106	
1	1	17.46171905	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.3354
Residual	FunctionGroup Normal	0.06837

Fit Statistics

-2 Res Log Likelihood	17.5
AIC (Smaller is Better)	21.5
AICC (Smaller is Better)	22.6
BIC (Smaller is Better)	23.0

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	4.03	0.0448

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	0.98	0.3382	

Least Squares Means

Effect	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	Function		Error							
	Group									
FunctionGroup	Severe	2.8782	0.2047	14	14.06	<.0001	0.1	2.5176	3.2388	
FunctionGroup	Normal	2.6555	0.09245	14	28.72	<.0001	0.1	2.4926	2.8183	

Differences of Least Squares Means

Effect	Renal	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	Function	Function		Error							
	Group	Group									
FunctionGroup	Severe	Normal	0.2227	0.2246	14	0.99	0.3382	0.1	-0.1729	0.6184	

----- SUMMARY REPORT -----
 Algorithm: Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis

----- SUMMARY REPORT -----

The Mixed Procedure

Order=10 Param=lnAUCT

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	22.31749113	
1	1	17.20945966	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.3684
Residual	FunctionGroup Normal	0.06004

Fit Statistics

-2 Res Log Likelihood	17.2
AIC (Smaller is Better)	21.2
AICC (Smaller is Better)	22.3
BIC (Smaller is Better)	22.8

Null Model Likelihood

Ratio Test		
DF	Chi-Square	Pr > ChiSq
1	5.11	0.0238

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	4.77	0.0465	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	4.4304	0.2146	14	20.65	<.0001	0.1	4.0525	4.8084	
FunctionGroup	Normal	3.9252	0.08663	14	45.31	<.0001	0.1	3.7726	4.0778	

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.5052	0.2314	14	2.18	0.0465	0.1	0.09766	0.9128	

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=11 Param=lnAUCinf

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	21.11877396	
1	1	16.14663386	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	0.3368
Residual	FunctionGroup Normal	0.05641

Fit Statistics

-2 Res Log Likelihood	16.1
AIC (Smaller is Better)	20.1
AICC (Smaller is Better)	21.2
BIC (Smaller is Better)	21.7

Null Model Likelihood
Ratio Test

DF	Chi-Square	Pr > ChiSq
1	4.97	0.0258

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
	DF	DF			
FunctionGroup	1	14	5.18	0.0390	

Least Squares Means

Effect	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	4.5147	0.2052	14	22.00	<.0001	0.1	4.1533	4.8761	
FunctionGroup	Normal	4.0099	0.08397	14	47.75	<.0001	0.1	3.8620	4.1578	

Differences of Least Squares Means

Effect	Renal Function Group	Renal Function Group	Estimate	Standard Error	DF	t	Value	Pr > t	Alpha	Lower	Upper
FunctionGroup	Severe	Normal	0.5048	0.2217	14	2.28	0.0390	0.1	0.1143	0.8953	

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 ----- SUMMARY REPORT -----

The Mixed Procedure

Order=14 Param=RkTmax

Model Information

Data Set	WORK.KINDATA
Dependent Variable	Value
Covariance Structure	Variance Components
Group Effect	FunctionGroup
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
FunctionGroup	2	Severe Normal

Dimensions

Covariance Parameters	2
Columns in X	3
Columns in Z	0
Subjects	16
Max Obs per Subject	1

Number of Observations

Number of Observations Read	16
Number of Observations Used	16
Number of Observations Not Used	0

Iteration History

Iteration Evaluations -2 Res Log Like Criterion			
0	1	88.19050897	
1	1	87.42765094	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	FunctionGroup Severe	31.2813
Residual	FunctionGroup Normal	16.0670

Fit Statistics

-2 Res Log Likelihood	87.4
AIC (Smaller is Better)	91.4
AICC (Smaller is Better)	92.5
BIC (Smaller is Better)	93.0

Null Model Likelihood

Ratio Test

DF	Chi-Square	Pr > ChiSq
1	0.76	0.3824

Type 3 Tests of Fixed Effects

Effect	Num	Den	F	Value	Pr > F
FunctionGroup	1	14	0.02	0.8797	

Least Squares Means

Effect	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	Function Group		Error							
FunctionGroup	Severe	8.3125	1.9774	14	4.20	0.0009	0.1	4.8297	11.7953	
FunctionGroup	Normal	8.6875	1.4172	14	6.13	<.0001	0.1	6.1914	11.1836	

Differences of Least Squares Means

Effect	Renal	Renal	Estimate	Standard	DF	t	Value	Pr > t	Alpha	Lower	Upper
	Function Group	Function Group		Error							
FunctionGroup	Severe	Normal	-0.3750	2.4328	14	-0.15	0.8797	0.1	-4.6599	3.9099	

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 Geometric LSmeans
 ----- SUMMARY REPORT -----

Obs	Parameters	Group	GeoLSmeans
1	lnCmax	Severe	17.7827
2	lnCmax	Normal	14.2318
3	lnAUCT	Severe	83.9689
4	lnAUCT	Normal	50.6635
5	lnAUCinf	Severe	91.3473
6	lnAUCinf	Normal	55.1409

----- SUMMARY REPORT -----
 Algorithm Pharma
 CUD-P4-001: Effect of Renal Impairment on Pharmacokinetics of Lasmiditan - M3 - Additional Analysis
 (Healthy vs Severe)
 ANOVA analysis
 RATIO ESTIMATE BASED ON ln-TRANSFORMED PARAMETERS
 ----- SUMMARY REPORT -----

Obs	Parameters	Group	vs Group	Ratio (%)	L90	U90
1	lnCmax	Severe	Normal	124.950	84.120	185.599
2	lnAUCT	Severe	Normal	165.739	110.258	249.135
3	lnAUCinf	Severe	Normal	165.662	112.106	244.802