Statistical Analysis Plan I6T-MC-AMBE

A Safety, Tolerability, and Pharmacokinetic Study of Injections of LY3074828 Solution Using Investigational 1-mL Pre-filled Syringes and Investigational 1-mL Autoinjector in Healthy Subjects

NCT03886948

Approval Date: 04-Mar-2019

STATISTICAL ANALYSIS PLAN

A Safety, Tolerability, and Pharmacokinetic Study of Injections of LY3074828 Solution Using Investigational 1-mL Pre-filled Syringes and Investigational 1-mL Autoinjector in Healthy Subjects

Statistical Analysis Plan Status: Final
Statistical Analysis Plan Date: 28-February-2019

Study Drug: LY3074828

Sponsor Reference: I6T-MC-AMBE
Covance CRU Study: 1000071-8379029

Clinical Phase I

Approval Date: 04-Mar-2019 GMT

1. TABLE OF CONTENTS

2. ABBREVIATIONS

Abbreviations pertain to the Statistical Analysis Plan (SAP) only (not the tables, figures and listings [TFLs]).

AE	Adverse event
ADA	Anti-drug antibody
AI	Autoinjector
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
AUC	Area under the concentration versus time curve
AUC(0-∞)	Area under the concentration versus time curve from time zero to infinity
AUC(0-t_{last})	Area under the concentration versus time curve from time zero to time t, where t is the last time point with a measurable concentration
%AUC(t_{last}-∞)	Percentage of AUC(0-∞) extrapolated
BQL	Below the lower limit of quantitation
C_{max}	Maximum observed drug concentration
CI	Confidence interval
CL/F	Apparent total body clearance of drug calculated after extra-vascular administration
CRF	Case Report Form
CRU	Clinical Research Unit
CSR	Clinical Study Report
CV	Coefficient of variation
EC	Early Clinical
ECG	Electrocardiogram
e.g.	For example (Latin: *exempli gratia*)
ICH	International Conference on Harmonisation
LLOQ	Lower limit of quantitation
MedDRA	Medical Dictionary for Regulatory Activities
PC	Product complaint
PFS	Pre-filled syringe
PK	Pharmacokinetic

SAP	Statistical Analysis Plan
SC	Subcutaneous
SD	Standard deviation
SOP	Standard Operating Procedure
TBL	Total bilirubin
TFLs	Tables, Figures, and Listings
$t_{1/2}$	Half-life associated with the terminal rate constant (λ_z) in non-compartmental analysis
t_{max}	Time of maximum observed drug concentration
ULN	Upper limit of normal
VAS	Visual analog scale
V_{SS}/F	apparent volume of distribution at steady state after extra-vascular administration
V_z/F	Apparent volume of distribution during the terminal phase after extra-vascular administration
WHO	World Health Organization

3. INTRODUCTION

This SAP has been developed after review of the Clinical Study Protocol (final version dated 17 December 2018).

This SAP describes the planned analysis of the safety, tolerability and pharmacokinetic (PK) data from this study. A detailed description of the planned TFLs to be presented in the clinical study report (CSR) is provided in the accompanying TFL shell document.

The intent of this document is to provide guidance for the statistical and PK analyses of data. In general, the analyses are based on information from the protocol, unless they have been modified by agreement between Eli Lilly and Company and Covance Early Clinical (EC) Biometrics. A limited amount of information concerning this study (e.g., objectives, study design) is given to help the reader's interpretation. This SAP must be signed off prior to first subject administration for this study. When the SAP and TFL shells are agreed upon and finalized, they will serve as the template for this study's CSR.

This SAP supersedes the statistical considerations identified in the protocol; where considerations are substantially different, they will be so identified. If additional analyses are required to supplement the planned analyses described in this SAP, they may be performed and will be identified in the CSR. Any substantial deviations from this SAP will be agreed upon between Eli Lilly and Company and Covance EC Biometrics and identified in the CSR. Any minor deviations from the TFLs may not be documented in the CSR.

This SAP is written with consideration of the recommendations outlined in the International Conference on Harmonisation (ICH) E9 Guideline entitled Guidance for Industry: Statistical Principles for Clinical Trials[1] and the ICH E3 Guideline entitled Guidance for Industry: Structure and Content of Clinical Study Reports[2].

4. STUDY OBJECTIVES

4.1 Primary Objectives

- To evaluate the PK after subcutaneous (SC) administration of 125-mg doses of LY3074828 solution formulation using a 1-mL pre-filled syringe (PFS) and a 1-mL autoinjector (AI) injector in healthy subjects.

- To assess pain associated with LY3074828 PFS and AI SC administrations in healthy subjects at 3 different injection sites (arm, thigh, and abdomen).

4.2 Secondary Objective

- To assess the safety and tolerability of LY3074828 in healthy subjects.

5. STUDY DESIGN

Study I6T-MC-AMBE (AMBE) is a single-center, randomized, parallel-arm, open-label, Phase 1 single-dose study of LY3074828 solution formulation in healthy subjects. Pharmacokinetics,

safety and tolerability of, and pain associated with, 125-mg SC doses administered using a PFS or AI at 3 different injection sites will be evaluated.

Screening Period (≤28 days): Subjects will be evaluated for study eligibility ≤28 days prior to enrollment.

Residential Period (2 days): A total of approximately 66 subjects who fulfill the eligibility criteria will be randomized to 1 of 6 dosing regimen arms, with 11 subjects randomized to each arm to ensure completion of 10 subjects in each:

- Test 1: 1-mL AI injector containing 125 mg LY3074828 solution to be administered in the arm
- Test 2: 1-mL AI injector containing 125 mg LY3074828 solution to be administered in the thigh
- Test 3: 1-mL AI injector containing 125 mg LY3074828 solution to be administered in the abdomen
- Reference 1: 1-mL PFS containing 125 mg LY3074828 solution to be administered in the arm
- Reference 2: 1-mL PFS containing 125 mg LY3074828 solution to be administered in the thigh
- Reference 3: 1-mL PFS containing 125 mg LY3074828 solution to be administered in the abdomen

Subjects will report to the clinical research unit (CRU) on Day -1 and will remain at the CRU until the scheduled procedures have been completed on Day 2. Study drug will be administered by investigative site staff by SC injection per the randomization scheme in the morning of Day 1 after an overnight fast.

Safety and tolerability will be assessed by clinical laboratory tests, vital sign measurements, 12-lead electrocardiograms (ECGs), recording of AEs and product complaints (PCs), physical examinations/medical assessments, immunogenicity, and injection-site assessments. Pain assessments will be made using an injection-site pain visual analog scale (VAS).

Outpatient Follow-up Period (12 weeks): The follow-up period will include outpatient visits for a total of 12 weeks (Days 4, 8, 11, 15, 22, 29, 43, 57, 71, and 85) following dose administration on Day 1 to assess the PK, safety and tolerability of, and pain associated with LY3074828 PFS and AI administrations. Assessment of pain at the Follow-up visits does not include VAS score.

6. TREATMENTS

The following is a list of the study treatment abbreviations that will be used in the TFLs.

Study Treatment Name	Abbreviation	Treatment order in TFL
125 mg LY3074828 PFS (Arm)	Reference 1	1
125 mg LY3074828 PFS (Thigh)	Reference 2	2
125 mg LY3074828 PFS (Abdomen)	Reference 3	3
125 mg LY3074828 AI (Arm)	Test 1	4
125 mg LY3074828 AI (Thigh)	Test 2	5
125 mg LY3074828 AI (Abdomen)	Test 3	6

Abbreviations: AI = Autoinjector; PFS = pre-filled syringe.

7. SAMPLE SIZE JUSTIFICATION

Approximately 66 subjects will be enrolled with a target of 60 subjects completing the study (10 completers per treatment).

Data from AMAL (2 x 1-mL doses of 125 mg LY3074828) and AMAE (2 x 1-mL PFS doses of 125 mg LY3074828) studies showed that the geometric coefficient of variation (CV) ranged from 55% to 40% for the PK measurements (ie, area under the concentration versus time curve [AUC] from time zero to infinity [AUC(0-∞)], AUC from time zero to time t, where t is the last sample with a measurable concentration [AUC(0-t_{last})], and maximum observed drug concentration [C_{max}]). Thus, the geometric coefficient of variation was assumed to be 55% when calculating precision.

A sample size of 60 subjects will provide a precision (ie, half-width of 90% of confidence interval [CI] with a coverage probability of 90%), in log scale, of approximately 0.48 for the geometric means ratio of reference versus test for AUC(0-∞), AUC(0-t_{last}), and C_{max}. Equivalently, there is a 90% probability that the distance between the lower limit of the 90% CI and the point estimate of the geometric means ratio is not larger than 38%.

Subjects who are randomized but not administered treatment, or subjects (maximum of 2 subjects per dose regimen arm) that are administered treatment but do not have PK and anti-drug antibody (ADA) samples collected up to and including Day 57, may be replaced to ensure that approximately 10 subjects from each treatment arm may complete the study.

8. DEFINITION OF ANALYSIS POPULATIONS

The “Safety” population will consist of all subjects who received at least one dose of LY3074828 and have at least one postdose safety assessment.

The “Pharmacokinetic” population will consist of all subjects who received at least one dose of LY3074828 and have evaluable PK data.

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

9. STATISTICAL METHODOLOGY

9.1 General

Data listings will be provided for all data that is databased. Summary statistics and statistical analysis will only be presented for data where detailed in this SAP. For continuous data, summary statistics will include the arithmetic mean, arithmetic standard deviation (SD), median, min, max and N; for log-normal data (e.g. the PK parameters: AUCs and C_{max}) the geometric mean and geometric CV% will also be presented. For categorical data, frequency count and percentages will be presented. Data listings will be provided for all subjects up to the point of withdrawal, with any subjects excluded from the relevant population highlighted. Summary statistics and statistical analyses will generally only be performed for subjects included in the relevant analysis population. For the calculation of summary statistics and statistical analysis, unrounded data will be used.

Mean change from baseline is the mean of all individual subjects' change from baseline values. Each individual change from baseline will be calculated by subtracting the individual subject's baseline value from the value at the timepoint. The individual subject's change from baseline values will be used to calculate the mean change from baseline using a SAS procedure such as Proc Univariate.

Data analysis will be performed using SAS® Version 9.4 or greater.

9.2 Demographics and Subject Disposition

Subject disposition will be listed. The demographic variables age, sex, race, ethnicity, country of enrolment, site ID, body weight, height and body mass index will be summarized and listed.

All other demographic variables will be listed only.

9.3 Pharmacokinetic Assessment

9.3.1 Pharmacokinetic Analysis

The PK parameter estimates will be determined using non-compartmental procedures in validated software program (Phoenix WinNonlin Version 8.1 or later).

Serum concentrations of LY3074828 will be used to determine the following PK parameters, when possible:

Parameter	Units	Definition
AUC(0-t_{last})	day*µg/mL	area under the concentration versus time curve from time zero to time t, where t is the last time point with a measurable concentration
AUC(0-∞)	day*µg/mL	area under the concentration versus time curve from time zero to infinity
%AUC(t_{last}-∞)	%	percentage of AUC(0-∞) extrapolated
C_{max}	µg/mL	maximum observed drug concentration
t_{max}	day	time of maximum observed drug concentration
$t_{1/2}$	day	half-life associated with the terminal rate constant (λz) in non-compartmental analysis
CL/F	L/day	apparent total body clearance of drug calculated after extra-vascular administration
V_Z/F	L	apparent volume of distribution during the terminal phase after extra-vascular administration
V_{SS}/F	L	apparent volume of distribution at steady state after extra-vascular administration

Additional PK parameters may be calculated, as appropriate. The software and version used for the final analyses will be specified in the clinical study report. Any exceptions or special handling of data will be clearly documented within the final study report.

Formatting of tables, figures and abbreviations will follow the Eli Lilly Global PK/PD/TS Tool: NON-COMPARTMENTAL PHARMACOKINETIC STYLE GUIDE. The version of the tool effective at the time of PK analysis will be followed.

General PK Parameter Rules

- Actual sampling times will be used in the final analyses of individual PK parameters, except for non-bolus pre-dose sampling times which will be set to zero.
- C_{max} and t_{max} will be reported from observed values. If C_{max} occurs at more than one time point, t_{max} will be assigned to the first occurrence of C_{max}.
- AUC parameters will be calculated using a combination of the linear and logarithmic trapezoidal methods (linear-log trapezoidal rule). The linear trapezoidal method will be applied up to t_{max} and then the logarithmic trapezoidal method will be used after t_{max}. The minimum requirement for the calculation of AUC will be the inclusion of at least three consecutive concentrations above the lower limit of quantitation (LLOQ), with at least one of these concentrations following C_{max}.
- AUC(0-∞) values where the percentage of the total area extrapolated is more than 20% will be flagged. Any AUC(0-∞) value excluded from summary statistics will be noted in the footnote of the summary table.

- Half-life ($t_{½}$) will be calculated, when appropriate, based on the apparent terminal log-linear portion of the concentration-time curve. The start of the terminal elimination phase for each subject will be defined by visual inspection and generally will be the first point at which there is no systematic deviation from the log-linear decline in serum concentrations. Half-life will only be calculated when a reliable estimate for this parameter can be obtained comprising of at least 3 data points. If $t_{½}$ is estimated over a time window of less than 2 half-lives, the values will be flagged in the data listings. Any $t_{½}$ value excluded from summary statistics will be documented in the footnote of the summary table.

- A uniform weighting scheme will be used in the regression analysis of the terminal log-linear portion of the concentration-time curve.

- The parameters based on observed C_{last} will be reported.

Individual PK Parameter Rules

- Only quantifiable concentrations will be used to calculate PK parameters with the exception of special handling of certain concentrations reported below the lower limit of quantitation (BQL). Serum concentrations reported as BQL will be set to a value of zero when all of the following conditions are met:

    - The compound is non-endogenous.

    - The samples are from the initial dose period for a subject or from a subsequent dose period following a suitable wash-out period.

    - The time points occur before the first quantifiable concentration.

- All other BQL concentrations that do not meet the above criteria will be set to missing.

- Also, where two or more consecutive concentrations are BQL towards the end of a profile, the profile will be deemed to have terminated and therefore any further quantifiable concentrations will be set to missing for the calculation of the PK parameters unless it is considered to be a true characteristic of the profile of the drug.

Individual Concentration vs. Time Profiles

- Individual concentrations will be plotted utilizing actual sampling times.

- The terminal point selections will be indicated on a semi-logarithmic plot.

Average Concentration vs. Time Profiles

- The average concentration profiles will be graphed using scheduled (nominal) sampling times.

- The average concentration profiles will be graphed using arithmetic average concentrations.

- The pre-dose average concentration for single-dose data from non-endogenous compounds will be set to zero. Otherwise, only quantifiable concentrations will be used to calculate average concentrations.

- Concentrations at a sampling time exceeding the sampling time window specified in the protocol, or ± 10%, will be excluded from the average concentration profiles.

- Concentrations excluded from the mean calculation will be documented in the final study report.

- A concentration average will be plotted for a given sampling time only if 2/3 of the individual data at the time point have quantifiable measurements that are within the sampling time window specified in the protocol or ± 10%. An average concentration estimated with less than 2/3 but more than 3 data points may be displayed on the mean concentration plot if determined to be appropriate and will be documented within the final study report.

Treatment of Outliers during Pharmacokinetic Analysis

Application of this procedure to all PK analyses is not a requirement. Rather, this procedure provides justification for exclusion of data when scientifically appropriate. This procedure describes the methodology for identifying an individual value as an outlier for potential exclusion, but does not require that the value be excluded from analysis. The following methodology will not be used to exclude complete profiles from analysis.

Data within an Individual Profile

A value within an individual profile may be excluded from analysis if any of the following criteria are met:

- For PK profiles during single dosing of non-endogenous compounds, the concentration in a pre-dose sample is quantifiable.

- For any questionable datum that does not satisfy the above criteria, the profile will be evaluated and results reported with and without the suspected datum.

Data between Individual Profiles

1. If $n<6$, then the dataset is too small to conduct a reliable range test. Data will be analyzed with and without the atypical value, and both sets of results will be reported.

2. If $n\geq6$, then an objective outlier test will be used to compare the atypical value to other values included in that calculation:

    a. Transform all values in the calculation to the logarithmic domain.

b. Find the most extreme value from the arithmetic mean of the log transformed values and exclude that value from the dataset.

c. Calculate the lower and upper bounds of the range defined by the arithmetic mean ±3*SD of the remaining log-transformed values.

d. If the extreme value is within the range of arithmetic mean ±3*SD, then it is not an outlier and will be retained in the dataset.

e. If the extreme value is outside the range of arithmetic mean ±3*SD, then it is an outlier and will be excluded from analysis.

If the remaining dataset contains another atypical datum suspected to be an outlier and $n \geq 6$ following the exclusion, then repeat step 2 above. This evaluation may be repeated as many times as necessary, excluding only one suspected outlier in each iteration, until all data remaining in the dataset fall within the range of arithmetic mean ±3*SD of the log-transformed values.

Reporting of Excluded Values

Individual values excluded as outliers will be documented in the final report. Approval of the final report will connote approval of the exclusion.

9.3.2 Pharmacokinetic Statistical Methodology

The AUC(0-∞), AUC(0-t_{last}), and C_{max} will be log-transformed and analyzed using a linear fixed-effects model. The model will include device and injection site as fixed effects. The differences between the AI (Test) and PFS (Reference) will be back-transformed to present the ratios of geometric least squares means and the corresponding 90% CI.

Example SAS code:

```
proc mixed data=datain alpha=0.1;
   class device inj_site;
   model log_pk = device inj_site / ddfm=kr alpha=0.1;
   lsmeans device / pdiff cl alpha=0.1;
   ods output lsmeans=lsmeans;
   ods output diffs=diffs;
run;
```

The t_{max} of LY3074828 between AI and PFS administrations will be analyzed using a Wilcoxon rank sum test. Estimates of the median difference, 90% CIs, and p-values from the Wilcoxon rank sum test will be calculated.

In addition, the following comparisons will also be made:

- AI versus PFS separately at each injection site (injection site will be removed from the model above)

- Arm versus abdomen and thigh versus abdomen separately for each device (device will be removed from the model above)

Additional PK analyses may be conducted if deemed appropriate.

9.4 Safety and Tolerability Assessments

9.4.1 Adverse events

Where changes in severity are recorded in the Case Report Form (CRF), each separate severity of the adverse event (AE) will be reported in the listings, only the most severe will be used in the summary tables. A pre-existing condition is defined as an AE that starts before the subject has provided written informed consent and is ongoing at consent. A non-treatment emergent AE is defined as an AE which starts after informed consent but prior to dosing. A treatment-emergent AE is defined as an AE which occurs postdose or which is present prior to dosing and becomes more severe postdose.

All AEs and PCs will be listed. Treatment-emergent AEs will be summarized by treatment, severity and relationship to the study drug. The frequency (the number of AEs, the number of subjects experiencing an AE and the percentage of subjects experiencing an AE) of treatment-emergent AEs will be summarized by treatment, Medical Dictionary for Regulatory Activities (MedDRA) version 21.1 system organ class and preferred term. The summary and frequency AE tables will be presented for all causalities and those considered related to the study drug. Any serious AEs will be listed.

9.4.2 Concomitant medication

Concomitant medication will be coded using the WHO drug dictionary (Version March 2018). Concomitant medication will be listed.

9.4.3 Clinical laboratory parameters

All clinical chemistry and hematology data will be summarized by parameter and treatment, and listed. Urinalysis data will be listed. Changes from baseline, Day -1, will also be presented. Additionally clinical chemistry, hematology and urinalysis data outside the reference ranges will be listed.

Values for any clinical chemistry, hematology and urinalysis values outside the reference ranges will be flagged on the individual subject data listings.

9.4.4 Vital signs

Vital signs data will be summarized by treatment together with changes from baseline, where baseline is defined as Day 1 predose. Figures of mean vital signs and mean changes from baseline will be presented by treatment.

Furthermore, values for individual subjects will be listed.

9.4.5 Electrocardiogram (ECG)

ECGs will be performed for safety monitoring purposes and will not be presented. Any clinically relevant findings will be reported as an AE.

9.4.6 Injection-Site Pain

Intensity of pain data will be quantified using a 100-mm validated VAS. The data will be listed and summarized by treatment and time point. In addition, the scores will be categorized into mild (0- to 30-mm), moderate (31- to 70-mm), and severe (71- to 100-mm), and presented in frequency tables by treatment and timepoint. Furthermore, scatter plots of the 1 minute, 5 minute, and 15-minute VAS scores will be presented by treatment and time point.

A linear fixed-effects model will be used to analyze the 1- and 5-minute post-injection pain VAS scores separately. The model will include device and injection site as fixed effects. The least squares means and differences between the AI (Test) and PFS (Reference) will be presented along with the corresponding 90% CI for the difference.

If the assumptions of this model appear to be violated, a non-parametric method may be used.

The distribution of the data will be explored prior to analysis to determine whether data transformation is required. It is possible that the pain scores will be 0, so if the distribution of the data implies that a log-transformation is required then the score may be updated to log(VAS+1) to allow for the inclusion of the 0 values in the analysis. If the assumptions of this model appear violated, a non-parametric method may be used.

The above analyses will also be repeated for each injection site separately.

SAS code similar to Section 9.3.2 will be used for this model.

9.4.7 Injection-Site Reactions

Injection-site reactions will be evaluated through the collection of pain assessments and specific site assessments for local tolerability, which will evaluate erythema, induration, pruritus, and edema. Data from injection-site evaluations (including pain), which are recorded as a result of specific questionnaires, will not be reported as AEs. However, injection site reactions may be reported as AEs if:

a) Spontaneously reported by a subject.
b) At the discretion of the principal investigator.

Injection-site reaction data will be listed and reactions reported as AEs will be summarized by treatment in frequency tables.

Any bruising or bleeding from the injection site will also be listed.

9.4.8 Injection Duration

The duration of the injection (measured in seconds) will be summarized by treatment and listed.

9.4.9 Immunogenicity

Immunogenicity data will be listed and frequency tables will be presented. The frequency of treatment-emergent ADAs will also be calculated. Treatment-emergent ADAs are those that are induced or boosted by exposure to study drug, with a 4-fold increase in titer compared to baseline if ADAs were detected at baseline or a titer 2-fold greater than the minimum required dilution (1:10) if no ADAs were detected at baseline.

If a neutralization assay is performed, the frequency of neutralizing antibodies will be determined. The relationship between the presence (or absence) of antibodies and clinical parameters (AEs) will be assessed. Likewise, the relationship between the presence of antibodies and the PK parameters or concentrations of LY3074828 may be assessed if deemed appropriate.

9.4.10 Hepatic Monitoring

If a study subject experiences elevated alanine aminotransferase (ALT) ≥3× upper limit of normal (ULN), alkaline phosphatase (ALP) ≥2× ULN, or elevated total bilirubin (TBL) ≥2× ULN, liver tests should be repeated within 3 to 5 days including ALT, aspartate aminotransferase, ALP, TBL, direct bilirubin, gamma-glutamyl transferase, and creatine phosphokinase to confirm the abnormality and to determine if it is increasing or decreasing. Monitoring should continue until levels normalize and/or are returning to approximate baseline levels.

Additional safety data may be collected if required, as defined in the protocol. Where applicable, the following will be presented.

The subjects' liver disease history and associated person liver disease history data will be listed. Any concomitant medication of acetaminophen/paracetamol will be listed. Results from a magnetic resonance elastography scan and biopsy assessment will be listed, if performed.

Hepatic risk factor assessment data will be listed. Liver related signs and symptoms data will be summarized by treatment and listed. Alcohol and recreational drug use data will also be listed.

All hepatic chemistry, hematology, coagulation, and serology data will be listed. Values outside the reference ranges will be flagged on the individual subject data listings.

9.4.11 Other assessments

All other safety assessments not detailed in this section will be listed but not summarized or statistically analysed.

10. INTERIM ANALYSES

No formal interim analysis will be conducted. However, data may be accessed and analyzed while the trial is ongoing, but no changes to the study design are planned. An assessment committee will not be formed.

Available safety data will be reviewed at approximately Day 30 of the last cohort dosed in order to review emerging safety and tolerability data.

11. CHANGES FROM THE PROTOCOL SPECIFIED STATISTICAL ANALYSES

There were no changes from the protocol specified statistical analyses.

12. REFERENCES

1. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Harmonized Tripartite Guideline, Statistical Principles for Clinical Trials (E9), 5 February 1998.

2. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Harmonized Tripartite Guideline, Structure and Content of Clinical Study Reports (E3), 30 November 1995.

13. DATA PRESENTATION

13.1 Derived Parameters

Individual derived parameters (e.g. PK parameters) and appropriate summary statistics will be reported to three significant figures. 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. Median values should be treated as an observed parameter and reported to the same number of decimal places as minimum and maximum values.

13.2 Missing Data

Missing data will not be displayed in listings.

13.3 Insufficient Data for Presentation

Some of the TFLs may not have sufficient numbers of subjects or data for presentation. If this occurs, the blank TFL shell will be presented with a message printed in the centre of the table, such as, “No serious adverse events occurred for this study.”

Leo Document ID = 3e3784ea-070a-42f6-aaa2-02560cd023fe

Approver: PPD
Approval Date & Time: 01-Mar-2019 09:32:04 GMT
Signature meaning: Approved

Approver: PPD
Approval Date & Time: 01-Mar-2019 09:52:34 GMT
Signature meaning: Approved

Approver: PPD
Approval Date & Time: 01-Mar-2019 13:30:37 GMT
Signature meaning: Approved

Approver: PPD
Approval Date & Time: 04-Mar-2019 21:02:20 GMT
Signature meaning: Approved