STATISTICAL ANALYSIS PLAN

A Study to Evaluate the Pharmacokinetics and Glucodynamics of LY900014 compared to Humalog Following a Single Dose in Patients with T2DM

Statistical Analysis Plan Status: Final
Statistical Analysis Plan Date: 28th September 2017

Study Drug: LY900014

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Covance CRU Study: 1001215-8370487

Clinical Phase I

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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
AUC	Area under the concentration versus time curve
AUC(0-30min)	Area under the concentration versus time curve from time zero to 30 minutes
AUC(0-1 h)	Area under the concentration versus time curve from time zero to 1 hour
AUC(0-2 h)	Area under the concentration versus time curve from time zero to 2 hours
AUC(0-10 h)	Area under the concentration versus time curve from time zero to 10 hours
AUC(3-10 h)	Area under the concentration versus time curve from time 3 to 10 hours
AUC(0-∞)	Area under the concentration versus time curve from time zero to infinity
AUC(0-tlast)	Area under the concentration versus time curve from time zero to the last recorded time
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
CSR	Clinical Study Report
CRU	Clinical Research Unit
CV	Coefficient of variation
DPP	Dipeptidyl peptidase
early 50% tmax	Time to early half-maximal drug concentration
early 50% tRmax	Time to half-maximal GIR before tRmax
EC	Early Clinical
ECG	Electrocardiogram

ED	Early discontinuation
e.g.	For example (Latin: *exempli gratia*)
GD	Glucodynamic
GIR	Glucose infusion rate
G_{tot}	Total amount of glucose infused
Gtot(0-30min)	total amount of glucose infused over 30 minutes
Gtot(0-1h)	total amount of glucose infused over 1 hour
Gtot(0-2h)	total amount of glucose infused over 2 hours
Gtot(3-10h)	total amount of glucose infused from 3 to 10 hours
ICF	Informed consent form
ICH	International Council on Harmonisation
late 50% tmax	Time to late half-maximal drug concentration
late 50% tRmax	Time to half-maximal GIR after tRmax
LS	Least square
LOESS	Locally weighted scatterplot smoothing
MedDRA	Medical Dictionary for Regulatory Activities
NPH	Neutral protamine Hagedorn
OAD	Oral antidiabetic
PK	Pharmacokinetic
R_{max}	Maximum glucose infusion rate
SAP	Statistical Analysis Plan
SC	Subcutaneous
SD	Standard deviation
SGLT	Sodium glucose co-transporter
SMPG	Self monitoring plasma glucose
T2DM	Type 2 diabetes mellitus
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
t_{max}	Time of maximum glucose infusion rate
t_{onset}	Time to onset of insulin action

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 14 July 2017).

This SAP describes the planned analysis of the safety, tolerability and pharmacokinetic (PK) and glucodynamic (GD) 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 patient 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 Council 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 Objective

- To evaluate the PK of insulin lispro following administration of a single 15 U subcutaneous (SC) dose of LY900014 compared to Humalog in patients with type 2 diabetes mellitus (T2DM).

4.2 Secondary Objectives

- To compare the euglycaemic clamp GD of insulin lispro following administration of a single 15 U SC dose of LY900014 or Humalog in patients with T2DM.
- To evaluate the tolerability of LY900014.

4.3 Exploratory Objectives

- Explore the formation of anti-drug antibodies to insulin lispro.
- To assess C-peptide levels following administration of LY900014 and Humalog.

5. STUDY DESIGN

ITRU is a Phase 1, randomised, patient- and investigator-blind, 2-treatment, single-dose, 2-period, 10 hour glycemic clamp, crossover study that evaluates the PK and GD of insulin lispro following administration of a single 15 U SC dose of either LY900014 or Humalog in patients with T2DM. Study ITRU may be conducted at 1 or more sites. Figure 1 illustrates the study design. Patients will be required to attend at the clinical research unit (CRU) on at least 5 occasions as noted in the Study Schedule (see Section 2 of the protocol):

- informed consent
- screening
- inpatient study Periods 1 and 2
- follow-up or early discontinuation

Patients will be required to visit the CRU to sign the informed consent form (ICF). Once the ICF is signed, patients will return to the CRU in a fasted state to participate in the screening procedures. Screening procedures may be completed up to 28 days prior to randomisation.

Prior to CRU admission on Day -1 of Period 1, patients with T2DM receiving oral antidiabetic (OAD) medication should discontinue their medication according to the following guidance (patients can continue taking metformin throughout the study):

- At most, 2 weeks prior to Day -1 of Period 1, patients should discontinue dipeptidyl peptidase (DPP)-IV inhibitors, sulphonylureas and sodium-glucose co-transporter (SGLT)-2 inhibitors.

Prior to each dosing visit, patients with T2DM on multiple daily insulin injections have to discontinue their basal insulin, according to the following guidance:

- For patients using insulin glargine U300, the last injection should occur no later than 72 hours prior to dosing.
- For patients using insulin detemir or glargine, the last injection of insulin detemir or glargine should occur no later than 48 hours prior to dosing.
- For patients using neutral protamine Hagedorn (NPH) insulin, insulin mixtures or other intermediate-acting insulin, the last injection of NPH insulin or other intermediate-acting insulin should occur no later than 24 hours prior to dosing.
- Any injection of more than 6 U of short-acting insulin should occur between 11 and 6 hours prior to dosing. Any injection should occur no later than 6 hours prior to dosing.

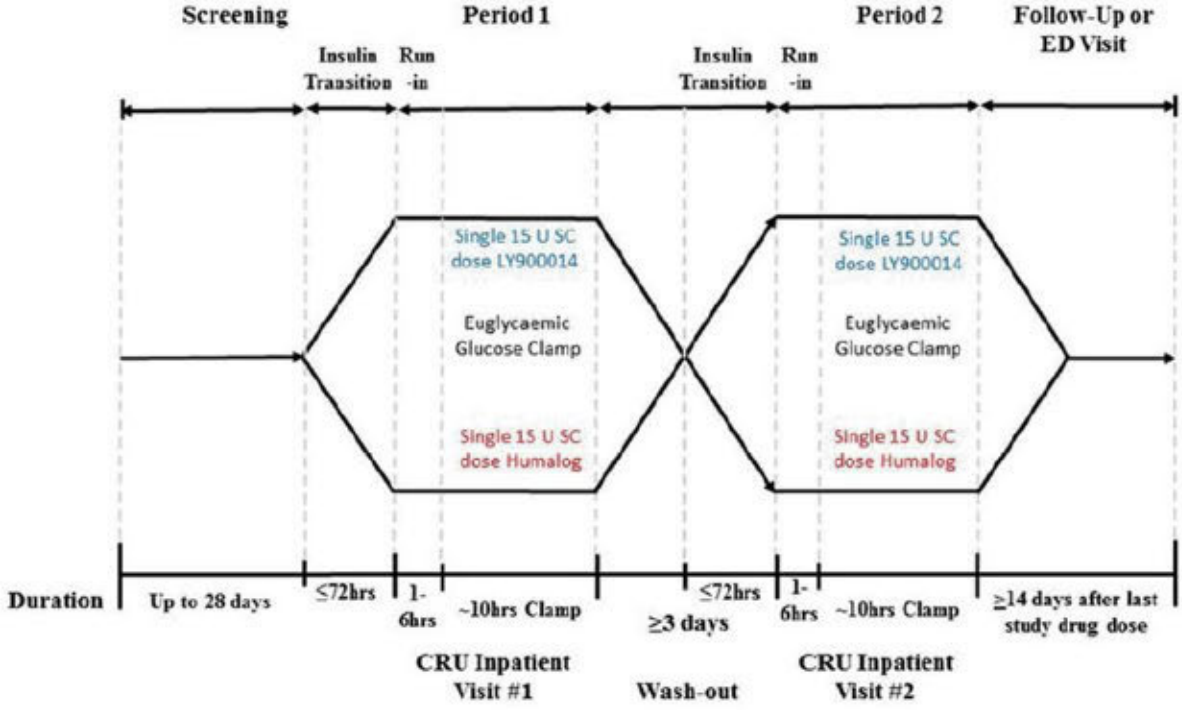
All patients will be instructed to perform at least 4-point daily self-monitoring plasma glucose (SMPG), as well as continue their short-acting insulin during insulin transition period (see Section 6.3.4 of the protocol). A diary will be provided to patients in order for SMPG results and prandial insulin doses to be recorded during the insulin transition period. The patients' diary will serve as a source document.

After satisfying the study entry criteria, each patient will be randomised to 1 of 2 treatment sequences according to the actual randomisation table provided to the site. Each study period

will be separated by a wash-out period of at least 72 hours. Each patient will participate in 2 inpatient visits; at each visit, the time-concentration and time-action profiles will be evaluated simultaneously during a euglycaemic glucose clamp of approximately 10 hours. The maximum duration allowed for both periods is 5 weeks. Briefly, the aim of the euglycaemic clamp is to maintain euglycaemia after the administration of a dose of insulin by means of variable glucose infusion. The variable glucose infusion maintains or "clamps" glucose to a constant euglycaemic target.

Patients will return to the CRU at least 14 days following last dose of study drug for follow-up or early discontinuation procedures.

Figure 1 illustrates the study design.



Abbreviations: CRU = clinical research unit; ED = early discontinuation; SC = subcutaneous

Figure 1. Illustration of study design

6. TREATMENTS

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

Study Treatment Name	Treatment order in TFL
15 U LY900014 SC	1

15 U Humalog SC	2

7. SAMPLE SIZE JUSTIFICATION

Up to 42 patients may be enrolled to ensure that at least 34 patients complete the study. Thirty-four completing patients will provide approximately 95% power to demonstrate a 40% increase in the insulin lispro area under the concentration versus time curve (AUC) from time zero to 30 minutes (AUC[0-30min]) between LY900014 and Humalog. Testing will be done at alpha-level of 0.05 with a 2-sided 95% confidence interval (CI). The variability was estimated by analysing Lilly internal studies that showed an average log-scale standard deviation (SD) of within-patient difference in AUC(0-30min) of 0.5. Analysis of internal data showed a log-scale standard deviation of within-patient difference in time to early half-maximal drug concentration (early 50% time of maximum observed drug concentration [t_{max}]) of 0.5, which provides approximately 95% power to show a 30% reduction in early 50% t_{max}, testing with alpha-level of 0.05 and a 2-sided CI.

In addition, the study is adequately powered to evaluate the GD parameters. There is approximately 80% power to detect a 20% decrease in both time to onset of insulin action (tonset) and time to half-maximal glucose infusion rate (GIR) before tR_{max} (early 50% tR_{max}) and approximately 85% power to detect at least a 40% increase in total amount of glucose infused (G_{tot}) over 30 minutes (G_{tot}[0-30min]) and G_{tot} over 1 hour (G_{tot}[0-1h]).

8. DEFINITION OF ANALYSIS POPULATIONS

The "Safety" population will consist of all enrolled patients who received at least one dose of study drug.

The primary statistical analyses for PK will be conducted on those patients who receive at least 1 dose of study drug and have measurable insulin lispro concentrations.

The primary statistical analysis for GD will be conducted on those patients who complete at least the first period of treatment.

Supportive analyses will be done on the key parameters for the patients who complete all treatment periods with evaluable data.

All protocol deviations that occur during the study will be considered for their severity/impact and will be taken into consideration when patients 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 SD, median, min, max and N; for log-normal data (e.g. the PK parameters: AUCs and maximum observed drug concentration

[C_{max}]) the geometric mean and geometric coefficient of variation (CV%) will also be presented. For categorical data, frequency count and percentages will be presented. Data listings will be provided for all patients up to the point of withdrawal, with any patients excluded from the relevant population highlighted. Summary statistics and statistical analyses will generally only be performed for patients 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 patients' change from baseline values. Each individual change from baseline will be calculated by subtracting the individual patient's baseline value from the value at the timepoint. The individual patient's change from baseline values will be used to calculate the mean change from baseline using a CCI procedure such as CCI

Data analysis will be performed using C C or greater.

9.2 Demographics and Patient Disposition

Patient disposition will be listed. The demographic variables age, sex, race, ethnicity, country of enrolment, body weight, height, body mass index, duration of diabetes, screening HbA1c and fasting blood glucose will be summarized and listed.

9.3 Pharmacokinetic Assessment

9.3.1 Pharmacokinetic Parameter Estimation

Patients who receive at least 1 dose of study drug and have measurable insulin lispro concentrations will be included in the PK analysis dataset.

PK analyses will be conducted using standard noncompartmental methods of analysis using CCI on a computer that meets or exceeds the minimum system requirements for these programs. The version of any software used for the analysis will be documented, and the program will meet the Lilly requirements of software validation. It is possible that other validated equivalent PK software programs may be used if appropriate, warranted and approved by global PK management.

Free serum insulin lispro concentrations will be used to calculate several PK parameters, including early 50% t_{max}, time to late half-maximal drug concentration (late 50% t_{max}), C_{max}, t_{max}, half-life ($t_{1/2}$), AUC from time zero to the last recorded time [AUC(0-tlast)], AUC(0-30min), AUC from time zero to 1 hour [AUC(0-1h)], AUC from time zero to 10 hours [AUC(0-10h)], AUC from time 3 to 10 hours (AUC[3-10h]) and AUC from time zero to infinity [AUC(0-∞)]. In addition, the apparent total body clearance of drug calculated after extra-vascular administration (CL/F), and volume of distribution after extra-vascular administration (Vz/F) also will be determined. Other parameters may be calculated as deemed appropriate. Additional partial AUCs may be computed as necessary, such as AUC from time zero to 2 hours [AUC(0-2h)].

The insulin lispro PK parameters for assessing faster insulin lispro absorption are the early 50% tmax and AUC(0-30min).

The insulin lispro PK parameters for assessing reduction in the late insulin lispro exposure are the late 50% t_{max} and AUC(3-10h).

Although attempts will be made to adhere to the scheduled collection times (Section 2 of the protocol), it is recognised that situations arise that may compromise the scheduled times. Parameters will be individually calculated for each patient based on actual collection times and presented by summary statistics.

9.3.2 Pharmacokinetic Statistical Inference

Log-transformed PK parameters for insulin lispro will be evaluated to estimate least-squares (LS) geometric means, ratios of geometric means between LY900014 and Humalog, and their corresponding 95% CIs using the mixed-effects model that includes treatment, sequence and period as fixed effects and patient within sequence as a random effect.

Example CCI code:

```
proc mixed data=pk;
class patient period treatment sequence ;
model logpk = treatment period sequence / ddfm=kr;
random patient(sequence);
lsmeans treatment;
run;
```

The same model without log transformation will be used for the analysis of the PK time parameters (early 50% t_{max}, late 50% t_{max}, t_{max} and $t_{1/2}$). LS means, treatment differences in LS means and the corresponding 95% CIs for the treatment differences will be estimated from the model. The treatment ratios and 95% CIs for the ratios will be calculated using Fieller's theorem.

Statistical significance will be achieved when the p-value for a test is less than 0.05.

The analyses described above will also be performed on the population of patients who completed and had evaluable PK data for both study periods.

9.4 Glucodynamic Assessment

9.4.1 Glucodynamic Parameter Estimation

GD assessments will be determined from the glucose clamp procedure, where the GIR over time will be used as a measure of insulin effect. GD analyses will be conducted on those patients who complete at least 1 clamp procedure.

A locally weighted scatterplot smoothing (LOESS) function will be applied to all individual GIR versus time profiles in each treatment group and/or period using S-PLUS software (version 8.2). The fitted data for each patient will be used to calculate the following GD parameters: Tonset, maximum GIR (R_{max}), time to R_{max} (tR_{max}), time to half-maximal GIR before tR_{max} (early 50% tR_{max}), time to half-maximal GIR after tR_{max} (late 50% tR_{max}), total amount of glucose infused over the duration of the clamp (G_{tot}), total amount of glucose infused over 30 minutes (G_{tot}[0-30min]), and total amount of glucose infused over 1 hour (G_{tot}[0-1h]). Additional partial

glucose AUCs, such as total amount of glucose infused over 2 hours (G_{tot}[0-2h]), and total amount of glucose infused from 3 hours to 10 hours (G_{tot}[3-10h]) may be computed, as necessary. The values of these GD parameters will be summarised by treatment and/or period through descriptive statistics. Mean LOESS fits of GIR versus time profiles will be generated. The primary GD parameters for earlier PD onset are early 50% tR_{max}, G_{tot}(0-30min), G_{tot}(0-1h), and T_{onset}.

9.4.2 Glucodynamic Statistical Inference

The GD statistical model will be the same as the model used for the analysis of the PK parameters. The following variables will be log transformed prior to analysis: R_{max}, G_{tot}, G_{tot}(0-30min), and G_{tot}(0-1h). Additional partial glucose AUCs, such as G_{tot} over 2 hours (G_{tot}[0-2h]), and G_{tot} from 3 hours to 10 hours G_{tot}[3-10h) may be analyzed as necessary. For GD parameters that have at least 1 patient with a value equal to zero, a value equal to the smallest non-zero observed GD value for that parameter divided by 2 will be added to all values, and the analysis of the log-transformed data will be performed.

The same model without log transformation will be used for the analysis of the GD time parameters (t_{onset}, tR_{max}, early 50% tR_{max}, late 50% tR_{max}). LS means, treatment differences in LS means and the corresponding 95% CIs for the treatment differences will be estimated from the model. bThe p-value for the difference between LS means will be used to determine statistical significance. The treatment ratios and 95% CIs for the ratios will be calculated using Fieller's theorem.

Statistical significance will be achieved when the p-value for a test is less than 0.05.

The analyses described above will also be performed on the population of patients who completed and had evaluable GD data for both study periods.

9.5 Safety and Tolerability Assessments

9.5.1 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 patient 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 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 patients experiencing an AE and the percentage of patients experiencing an AE) of treatment-emergent AEs will be summarized by treatment, Medical Dictionary for Regulatory Activities (MedDRA) version 20.0 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 tabulated.

9.5.2 Concomitant medication

Concomitant medication will be coded using the WHO drug dictionary (Version March 2017). Concomitant medication will be listed.

9.5.3 Clinical laboratory parameters

All clinical chemistry, hematology and urinalysis data will be listed. 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 patient data listings.

9.5.4 Vital signs

Vital signs data will be listed for individual patients. Vital signs data will be summarized by treatment together with changes from baseline, where baseline is defined as Day 1 predose of each period.

9.5.5 Electrocardiogram (ECG)

The ECG data will not be databased in this study.

9.5.6 Blood Glucose Monitoring and Hypoglycemia

Hypoglycemic events will be appropriately recorded in the CRF. In the case of a hypoglycemic event, the actual blood glucose value, if measured, will be recorded in the CRF, together with any treatments administered. Each category of hypoglycemic events (defined below) will be listed and summarized by treatment.

Hypoglycemia is defined as follows:

- **Documented Glucose Alert Level (Level 1)**, Plasma Glucose (PG) ≤70 mg/dL (3.9 mmol/L):
    - **Symptomatic hypoglycemia**: an event during which typical symptoms of hypoglycemia are accompanied by PG ≤70 mg/dL (3.9 mmol/L)
    - **Asymptomatic hypoglycemia**: an event not accompanied by typical symptoms of hypoglycemia but with PG ≤70 mg/dL (3.9 mmol/L)
    - **Unspecified hypoglycemia**: an event during which PG ≤70 mg/dL (3.9 mmol/L) but no information relative to symptoms of hypoglycemia was recorded
- **Documented Clinically Significant Hypoglycaemia (Level 2)** PG <54 mg/dL (3.0 mmol/L):

- **Symptomatic hypoglycemia**: an event during which typical symptoms of hypoglycemia are accompanied by PG <54 mg/dL (3.0 mmol/L)
- **Asymptomatic hypoglycemia**: an event not accompanied by typical symptoms of hypoglycemia but with PG <54 mg/dL (3.0 mmol/L)
- **Unspecified hypoglycemia**: an event during which PG <54 mg/dL (3.0 mmol/L) but no information relative to symptoms of hypoglycemia was recorded

- **Severe hypoglycemia (Level 3)**: an event requiring assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions. During these episodes, the patient has an altered mental status and cannot assist in their care, is semiconscious or unconscious, or experienced coma with or without seizures and may require parenteral therapy. Plasma glucose measurements may not be available during such an event, but neurological recovery attributable to the restoration of blood glucose concentration to normal is considered sufficient evidence that the event was induced by a low PG concentration (PG ≤70 mg/dL [3.9 mmol/L])
  - **Severe hypoglycemia requiring medical attention**: a severe hypoglycemic event when patients require therapy by HCPs (EMTs, emergency room personnel, etc)

Other Hypoglycemia:

- **Nocturnal hypoglycemia**: any hypoglycemic event (documented symptomatic, asymptomatic, probable symptomatic, or severe hypoglycemia) that occurs between bedtime and waking
- **Relative hypoglycemia**: an event during which typical symptoms of hypoglycemia, which do not require the assistance of another person, are accompanied by PG >70 mg/dL (3.9 mmol/L), but these levels may be quickly approaching the 70 mg/dL (3.9 mmol/L) threshold
- **Overall (or total) hypoglycemia**: This optional category combines all cases of hypoglycemia. If an event of hypoglycemia falls into multiple subcategories, the event is counted only once in this category
- **Probable symptomatic hypoglycemia**: An event during which symptoms of hypoglycemia are not accompanied by a PG measurement but that was presumably caused by a blood glucose concentration ≤70 mg/dL (3.9 mmol/L).

9.5.7 Injection Site Assessment

Injection site assessment data will be listed for individual patients and will be summarized in frequency tables by treatment.

9.5.8 Visual Analog Scale (VAS) Pain Assessment

Intensity of pain data at the injection site as soon as practicably possible after the injection, and at multiple postdose timepoints, as reported by the patient and measured according to the 0- to 100-mm visual analog scale will be listed and summarized by treatment.

The time 0 (immediately after dosing) data will be analyzed,using the Wilcoxon signed-rank test. The difference in medians between LY900014 and Humalog and the 95% CIs for the difference will be presented.

VAS data will also be summarized based on the following categories of score: 0, 1-10, 11-20, 21-30, 31-40, etc up to the maximum category by treatment and timepoint and also the categories <=10 mm, <=20 mm and <=45 mm. The table will show number and percent of patients with observations in each category.

9.5.9 Immunogenicity

Immunogenicity data will be listed. The number of patients who have not-detected anti-insulin lispro antibody at pre-dose (for period 1) and detected anti-insulin lispro antibody at post-dose (measured in period 2) will be summarized for combined treatments. The number of patients who have detected anti-insulin lispro antibody at pre-dose for period 1 and 57% increase from the pre-dose (for period 1) to post-dose (measured in period 2) will also be summarized in a similar way.

9.5.10 C-peptide

Mean and individual C-peptide concentration versus time plots with both treatments will be presented. In addition, individual plots overlaying the C-peptide concentration versus time will be presented.

9.5.11 Other assessments

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

9.5.12 Safety and Tolerability Statistical Methodology

No inferential statistical analyses are planned.

10. INTERIM ANALYSES

No interim statistical analyses are planned.

11. CHANGES FROM THE PROTOCOL SPECIFIED STATISTICAL ANALYSES

The VAS statistical analysis was updated to a non-parametric analysis due to issues observed in ITSC.

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 patients 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."

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