Statistical Analysis Plan – Part 1

A randomised, double-blind, multi centre, placebo-controlled dose escalation study in healthy subjects investigating the safety, tolerability and pharmacokinetic properties of TD139, a galectin-3 inhibitor, followed by an expansion cohort treating subjects with idiopathic pulmonary brosis (IPF)

Clinical Phase I

Sponsor Protocol Identification: GB-HV-01
Simbec Protocol Identification: RD 676/25641

Prepared by: [redacted] – Statistician I

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2. INTRODUCTION

This statistical analysis plan (SAP) is based on part 1 of the clinical trial protocol (sponsored by Galecto Biotech AB) prepared by Simbec Research Limited dated the 16th December 2014, final version 4.0. This document provides details of the planned statistical methodology for the analysis and presentation of the study data.

3. STUDY OBJECTIVES

3.1 Primary Objective

The primary objective of this study was to evaluate the safety and tolerability of single ascending doses of TD139 in healthy male subjects.

3.2 Secondary Objective

The secondary objective of this study was to evaluate the pharmacokinetics (PK) and pharmacodynamics (PD) of TD139 when administered as a single dose to healthy male subjects.

4. STUDY DESIGN

Part 1 was a randomised, double-blind, single centre, placebo-controlled, single ascending dose (SAD), phase I study designed to assess the safety, tolerability, PK and PD of TD139 in up to 36 healthy male subjects.

Part 1 of the study took place in healthy male volunteers and consisted of up to 6 cohorts of 6 subjects. Within each cohort, 4 subjects received a single dose of TD139 and 2 subjects received a single dose of placebo. Each cohort included a dose leader group of 2 volunteers (1 TD139 and 1 placebo) which were dosed on the day before the rest of the cohort, followed by the remaining 4 subjects who were dosed approximately 24 hours later. The remaining 4 subjects were randomised such that one further volunteer received placebo.

The lowest dose (0.15 mg) of TD139 was evaluated first. Dose administration in the subsequent cohorts proceeded after blinded safety and PK data for 3 days after dose administration from a minimum of 5 subjects in the preceding cohort were reviewed by the Sponsor and Chief Investigator and were found to be satisfactory. The planned and actual maximum dose of TD139 was 50 mg.

Pre-study assessments were carried out in the 28 day period before dosing in order to assess the volunteers for suitability to take part in the study.

Each cohort of subjects underwent 1 Study Period and each cohort was separated by a data review period. Each Study Period was approximately 15 days in duration and subjects were dosed and monitored on a combined inpatient and outpatient basis.

Volunteers were admitted to the Clinical Centre in the morning of Day -1 where final confirmation of eligibility was made after baseline assessments were performed.

Two subjects (dose leaders) received either a single dose of TD139 or placebo via DPI (1 treatment/volunteer) following an overnight fast on the day before the remaining subjects in the cohort. The remaining 4 subjects of each cohort were dosed approximately 24 hours later. These 4 subjects were randomised such that one further volunteer received placebo.

Each subject stayed at the Clinical Centre until 24 h post-dose (morning of Day 2) when they were discharged providing the scheduled assessments had been completed and there were no ongoing safety concerns. Subjects returned to the Clinical Centre on an outpatient basis on Day 3 for PK/safety and then Day 8 and 14 for assessments.

Post-study assessments will be carried out 12 - 16 days after the last day of the Study Period.

5. TREATMENT DESCRIPTION

Up to 6 cohorts of 6 subjects were randomly assigned to receive either a single oral dose of TD139 or a single dose of placebo. Within each cohort, 4 subjects received TD139 and 2 subjects received placebo.

The 6 ascending doses to be studied were:

- Cohort 1: 0.15mg TD139 or matching placebo
- Cohort 2: 1.5mg TD139 or matching placebo
- Cohort 3: 3mg TD139 or matching placebo
- Cohort 4: 10mg TD139 or matching placebo
- Cohort 5: 20mg TD139 or matching placebo
- Cohort 6: 50mg TD139 or matching placebo

6. SAMPLE SIZE

No formal sample size calculation has been performed. The number of subjects is considered sufficient to meet the safety objectives of **Part 1** of the study.

7. POPULATIONS

7.1 Safety Population (Safety)

All randomised subjects who received at least one dose of placebo or TD139 will be included in the safety analysis.

7.2 Pharmacokinetic Population (PK)

All randomised subjects who received all doses of TD139, had sufficient plasma concentration by time profiles and who did not violate the protocol in such a way that might invalidate or bias the results (major protocol violators) will be included in the pharmacokinetic analysis.

7.2.1 Major protocol violators

Protocol violations are defined as deviations from the procedures outlined in the protocol. Major protocol violations will include the following:

1. Violations of inclusion or exclusion criteria which are considered clinically significant and which may influence interpretation of study results.

2. Use of concomitant medication that may influence the results of the study.

3. Non-compliance to study medication.

4. Deviation from study specific instructions.

7.3 Pharmacodynamic Population (PD)

All randomised subjects who received all doses of placebo or TD139 and who did not violate the protocol in such a way that might invalidate or bias the results (major protocol violators) will be included in the pharmacodynamic analysis.

8. STUDY END-POINTS

8.1 Pharmacokinetic

The non-compartmental pharmacokinetic end-points for this study are:

- C_{max} Maximum plasma concentration
- t_{max} The time to maximum observed concentration sampled during a dosing interval
- λ_z Elimination rate constant
- $t_{1/2}$ Terminal half-life
- AUC_{0-t} Area under the plasma concentration-time curve (AUC) from the time of dosing to the time of the last observed concentration
- AUC_{0-inf} The area under the curve (AUC) extrapolated to infinity from dosing time, based on the last observed concentration
- CL/F Plasma clearance, calculated as Dose / AUC_{0-inf}
- $AUC_{\%\ extrapolated}$ Residual area.

8.2 Safety

The safety end-points for this study are:

- Vital signs
- 12-lead ECG
- Laboratory safety data
- Adverse events

9. MISSING DATA

No methods to account for missing safety data will be used.

In the instance of missing pharmacokinetic blood samples, the trapezoidal rule will be employed between the samples immediately before and after the missing sample for the AUC calculations.

10. PHARMACOKINETIC ANALYSIS

10.1 Plasma Concentration Data and Derivation of Pharmacokinetic Parameters

The pharmacokinetic parameters of TD139 in plasma will be determined from the individual concentration versus time data using WinNonlin Phoenix 32. For the calculation of derived pharmacokinetic parameters, concentrations below the limit of quantification (BLQ) will be assigned a value of zero. In case of a deviation from the theoretical time, the actual time of the blood sample will be used in the calculation of the derived pharmacokinetic parameters.

Derived pharmacokinetic parameters of TD139 in plasma will be listed and summarised for each treatment. The descriptive statistics presented will be N, n, arithmetic mean, arithmetic standard deviation (SD), coefficient of variation (CV%), minimum, median, maximum and geometric mean (with the exception of t_{max}). The results for t_{max} will be reverted back to the nominal time.

Mean and individual plasma concentration-time curves of TD139 in plasma will be presented for each dose on both linear and semi-logarithmic scales.

10.2 Statistical Analysis of Pharmacokinetic Data

Statistical analysis will be performed using SAS® version 9.1.3 or higher.

10.2.1 Dose-Proportionality/Independence

Dose proportionality will be assessed by performing a regression analysis of the log-transformed C_{max}, AUC_{0-t} and AUC_{0-inf} values versus the log-transformed dose using the power model with a fixed effect for dose and a random effect for subject. For each parameter a point estimate and 95% confidence interval will be calculated for the slope of the regression line.

The power model is defined as:

$$\log_e(C_{max}, AUC_{0-t}, AUC_{0-inf}) = \alpha + \beta \log_e(\text{Dose}) + \varepsilon,$$

where α is the intercept, β is the slope and ε is the error term.

Dose independence will be assessed for t½ and CL/F by performing a regression analysis of the untransformed parameters versus dose with a fixed effect for dose and a random effect for subject. For each parameter a point estimate and corresponding 95% confidence interval will be calculated for the slope of the regression line.

Derived pharmacokinetic parameters will be presented graphically for mean C_{max}, AUC_{0-t}, AUC_{0-inf}, t½ and CL/F versus dose.

11. PHARMACODYNAMIC ANALYSIS

Descriptive statistics of absolute and change from baseline for peripheral blood flow cytometry data will be presented at each timepoint by dose.

Descriptive statistics of absolute and change from baseline for Galectin-3 plasma concentration data will be presented at each timepoint by dose.

Exhaled breath condensate data will be presented as a data listing.

PG Assessments: Descriptive statistics of absolute and change from baseline of mRNA expression levels from blood leucocytes will be presented at each timepoint by dose.

12. SAFETY ANALYSIS

All adverse events will be coded using the MedDRA dictionary, version 16.1.

The descriptive statistics N, n, mean, SD, minimum, median and maximum will be presented for continuous data.

The frequency descriptive statistics N, n and % will be presented for categorical data. The percentages will be presented to 1 decimal place.

No repeat assessments will be included within summary information. Only the original values will be used within the summary presentations (tables and figures).

12.1 Vital Signs

Vital signs parameters will be listed with any out of normal range values flagged. Descriptive statistics of absolute and change from baseline (pre-dose) supine systolic and diastolic blood pressure, supine pulse rate, respiration rate, oral temperature and O_2 saturation at each time point, up to and including Day 14, will be tabulated by dose.

The mean change from baseline data will also be plotted by dose across time, up to and including Day 14.

12.2 12-Lead ECG Data

12-Lead ECG parameters will be listed with any out of normal range values flagged. Descriptive statistics of absolute and change from baseline (pre-dose) heart rate, PR interval, QRS interval, QT interval and QTcB interval at each time point, up to and including day 14, will be tabulated by dose.

The mean change from baseline data will also be plotted by dose across time, up to and including Day 14.

In addition, frequencies of QTcB data will be calculated according to the following categories:

For absolute values

- QTcB > 450 mSec
- QTcB > 480 mSec
- QTcB > 500 mSec

For change from baseline

- QTcB increase > 30 mSec
- QTcB increase > 60 mSec

12.3 Laboratory Safety Data

Biochemistry, haematology and urinalysis parameters will be listed with any out of normal range values flagged. Laboratory test results that are out of normal range will also be presented separately along with normal reference ranges. Descriptive statistics of absolute and change from baseline (pre-dose) values for each biochemistry and haematology parameter at each time point, up to and including Day 2, will be tabulated by dose.

12.4 Adverse Events

All adverse events, including those that occur prior to the first administration of the study drug, will be listed. Only treatment-emergent adverse events (TEAEs), i.e. existing conditions that worsen or events that occur during the course of the study after administration of study drug, will be included within the summary tables. Adverse event summaries will be presented by treatment and overall (data from all dose groups will be pooled).

An overall summary of adverse events will be produced including the number of TEAEs; the number and percentage of subjects reporting at least one: TEAE, serious TEAE, TEAE leading to withdrawal from the study; the number and percentage of subjects reporting TEAEs by severity and relationship to study drug.

The number of TEAEs and the number and percentage of subjects reporting at least one TEAE will be tabulated by system organ class (SOC) and preferred term (PT). A subject reporting multiple episodes of a particular adverse event within a study period will only contribute one count towards the corresponding system organ class and preferred term within that study period.

In addition, the number and percentage of subjects reporting TEAEs will be tabulated by maximum severity and strongest relationship to study drug. For the summary of TEAEs by severity, if a subject has multiple events occurring within the same SOC or preferred term, the event with the highest severity will be counted. Similarly, for TEAEs by relationship to study drug, if a subject has multiple events occurring within the same SOC or preferred term, the event with the highest association to study drug will be counted.

13. OTHER ANALYSES

13.1 Disposition

Frequencies of the total number of subjects randomised, completed, and prematurely discontinued (including reason for discontinuation) from the study will be summarised by dose. Additionally the frequency of subjects within each analysis population (safety, PK) will be summarised by dose.

13.2 Demographics

Demographic data will be listed and descriptive statistics will be tabulated for the continuous variables age, height, weight and BMI and frequencies for the categorical variable race. These descriptive statistics will be presented by dose and overall.

14. CHANGES FROM PROTOCOL

None.

15. REFERENCES

None.

16. TABLES, FIGURES & LISTINGS

The default tables, figures and listings (TFL) layout will be as follows:

Orientation	A4 Landscape
Margins	Top: 2.54 cm Bottom: 2.54 cm Left: 2.54 cm Right: 2.54 cm
Font	Courier New 7pt
Headers (Centre)	Sponsor Protocol Number, TFL Number, Title, Population
Footers (Left)	Source Listing, Date/Time TFL Generated, TFL Version (Left), Page Number, i.e. Page X of Y (Right)

The font size may be reduced as necessary to allow additional columns to be presented, but not at the expense of clarity. Also the orientation of the table may be changed to portrait if appropriate.

At the time of programming footnotes will be added to the listing, table or figure as needed. All footnotes will be used for purposes of clarifying the presentation.

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16.2.5.4 Plasma Half-Life Calculations: SEE LIST OF FIGURES

16.2.5.5 Urine Concentration Data:

- Not applicable

16.2.5.6 Faecal Concentration Data:

- Not applicable

Appendix 16.2.6: Pharmacodynamics / Pharmacogenetics

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Table 14.1.1
Summary of Study Disposition
Safety Population

	Number (%) of Subjects							
	Placebo (N=12)	0.15mg TD139 (N=4)	1.5mg TD139 (N=4)	3mg TD139 (N=4)	10mg TD139 (N=4)	20mg TD139 (N=4)	50mg TD139 (N=4)	Overall (N=36)
Dosed	x	x	x	x	x	x	x	x
Completed Study	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Early Study Termination	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Reason for Early Termination								
Adverse event	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Violation of selection criteria	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Other Protocol violation	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Safety Population	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
PK Population	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
PD Population	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)

NB. Percentages are based on the total number of dosed subjects within the treatment group.

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Table 14.1.2
Summary of Demographic Data
Safety Population

Parameter	Statistic	Placebo (N=12)	0.15mg TD139 (N=4)	1.5mg TD139 (N=4)	3mg TD139 (N=4)	10mg TD139 (N=4)	20mg TD139 (N=4)	50mg TD139 (N=4)	Overall (N=36)
Age (yrs)	n	x	x	x	x	x	x	x	x
	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Min	x	x	x	x	x	x	x	x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Max	x	x	x	x	x	x	x	x
Height (cm)	n	x	x	x	x	x	x	x	x
	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Min	x	x	x	x	x	x	x	x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Max	x	x	x	x	x	x	x	x
Weight (kg)	n	x	x	x	x	x	x	x	x
	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Min	x	x	x	x	x	x	x	x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Max	x	x	x	x	x	x	x	x
BMI (kg/m^2)	n	x	x	x	x	x	x	x	x
	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Min	x	x	x	x	x	x	x	x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Max	x	x	x	x	x	x	x	x
Race: CAUCASIAN	n (%)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)

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Table 14.2.1
Summary of Derived Plasma TD139 Pharmacokinetic Parameters
PK Population

Dose	Summary Statistic	C_{max} (ng/ml)	T_{max} (h)	$AUC_{(0-t)}$ (ng*h/ml)	$AUC_{(0-inf)}$ (ng*h/ml)	Kel (1/h)	t1/2 (h)	CL/F (L/h)	$AUC_{\%extrap}$ (%)
0.15mg TD139 (N=4)	n	x	x	x	x	x	x	x	x
	Mean	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xx
	SD	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxx
	Min	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.x
	Median	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xx
	Max	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.x
	CV%	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Geo Mean	x.xxx	N/a	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xx
1.5mg TD139 (N=4)	n	x	x	x	x	x	x	x	x
	Mean	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xx
	SD	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxx
	Min	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.x
	Median	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xx
	Max	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.x
	CV%	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Geo Mean	x.xxx	N/a	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xx
3mg TD139 (N=4)	n	x	x	x	x	x	x	x	x
	Mean	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xx
	SD	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxx
	Min	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.x
	Median	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xx
	Max	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.x
	CV%	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Geo Mean	x.xxx	N/a	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xx

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Table 14.2.2
Summary of Statistical Analysis of Dose Proportionality
PK Population

	0.15mg TD139 (N=4)	1.5mg TD139 (N=4)	3mg TD139 (N=4)	10mg TD139 (N=4)	20mg TD139 (N=4)	50mg TD139 (N=4)	Slope	95% C.I. for Slope
				Dose Proportionality Geometric LSmean				
C_{max} (ng/L)	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xxx	x.xxx - x.xxx
AUC_{0-t} (ng*hr/L)	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xxx	x.xxx - x.xxx
AUC_{0-inf} (ng*hr/L)	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xxx	x.xxx - x.xxx
				Dose Independence LSmean				
t½ (hr)	x.x	x.x	x.x	x.x	x.x	x.x	x.xxx	x.xxx - x.xxx
CL/F(L/hr)	x.x	x.x	x.x	x.x	x.x	x.x	x.xxx	x.xxx - x.xxx

NB. Results for Cmax and AUCs obtained using an ANOVA on log-transformed data with a fixed effect of log-transformed dose.
Results for t½ obtained using same method on non-transformed data.

Source Listing: Listing 16.2.5.3.1; Produced: 23JAN2014 12:17; Draft

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Table 14.3.1.1
Summary of Peripheral Blood Flow Cytometry Data
PD Population

		Actual						Change from Baseline					
Dose	Time	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Placebo (N=12)	Pre-Dose	x	x.xx	x.xxx	x.x	x.xx	x.x						
	30 Min	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	2 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	18 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	24 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
0.15mg TD139 (N=4)	Pre-Dose	x	x.xx	x.xxx	x.x	x.xx	x.x						
	30 Min	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	2 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	18 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	24 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
1.5mg TD139 (N=4)	Pre-Dose	x	x.xx	x.xxx	x.x	x.xx	x.x						
	30 Min	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	2 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	18 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	24 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x

NB. Baseline defined as 0 h

Source Listing: Listing 16.2.6.1.1; Produced: 23JAN2014 12:17; Draft

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Table 14.3.1.2
Summary of Galectin-3 Plasma Concentration Data
PD Population

		Actual						Change from Baseline					
Dose	Time	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Placebo (N=12)	Pre-Dose	x	x.xx	x.xxx	x.x	x.xx	x.x						
	5 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	48 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
0.15mg TD139 (N=4)	Pre-Dose	x	x.xx	x.xxx	x.x	x.xx	x.x						
	5 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	48 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
1.5mg TD139 (N=4)	Pre-Dose	x	x.xx	x.xxx	x.x	x.xx	x.x						
	5 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	48 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
3mg TD139 (N=4)	Pre-Dose	x	x.xx	x.xxx	x.x	x.xx	x.x						
	5 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	48 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
10mg TD139 (N=4)	Pre-Dose	x	x.xx	x.xxx	x.x	x.xx	x.x						
	5 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	48 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x

NB. Baseline defined as 0 h

Source Listing: Listing 16.2.6.1.2; Produced: 23JAN2014 12:17; Draft

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Table 14.3.2.1
Summary of mRNA Expression Levels
Safety Population

		Actual						Change from Baseline					
Dose	Time	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Placebo (N=12)	Pre-Dose	x	x.xx	x.xxx	x.x	x.xx	x.x						
	30 Min	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	2 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	18 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	24 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
0.15mg TD139 (N=4)	Pre-Dose	x	x.xx	x.xxx	x.x	x.xx	x.x						
	30 Min	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	2 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	18 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	24 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
1.5mg TD139 (N=4)	Pre-Dose	x	x.xx	x.xxx	x.x	x.xx	x.x						
	30 Min	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	2 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	18 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	24 h	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x

NB. Baseline defined as 0 h

Source Listing: Listing 16.2.6.2.1; Produced: 23JAN2014 12:17; Draft

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Table 14.4.1
Summary of Treatment Emergent Adverse Events
Safety Population

	Placebo (N=12)	0.15mg TD139 (N=4)	1.5mg TD139 (N=4)	3mg TD139 (N=4)	10mg TD139 (N=4)	20mg TD139 (N=4)	50mg TD139 (N=4)	Overall (N=36)
Number of TEAEs	x	x	x	x	x	x	x	x
Number(%) of subjects reporting at least one:								
TEAE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Serious TEAE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
TEAE Leading to Withdrawal	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Number(%) of subjects with TEAE by severity:								
Mild	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Moderate	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Severe	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Number(%) of subjects with TEAE by relationship to study drug:								
Almost Definite	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Probable	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Possible	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Unlikely	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Unrelated	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)

NB. A subject with multiple occurrences of an AE is counted only once within each level of severity or relationship.

Source Listing: Listing 16.2.7.1.1; Produced: 23JAN2014 12:17; Draft

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Table 14.4.2
Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Number of Events / Subjects (%) Placebo (N=12)	0.15mg TD139 (N=4)	1.5mg TD139 (N=4)	3mg TD139 (N=4)	10mg TD139 (N=4)	20mg TD139 (N=4)	50mg TD139 (N=4)	Overall (N=36)
GASTROINTESTINAL DISORDERS	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)
DIARRHOEA	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)
VOMITING	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)
INFLUENZA LIKE ILLNESS	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)
INJECTION SITE ANAESTHESIA	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)
INJECTION SITE DISCOMFORT	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)
INJECTION SITE REACTION	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)
NERVOUS SYSTEM DISORDERS	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)
HEADACHE	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)
PARAESTHESIA	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)
TREMOR	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)
VASCULAR DISORDERS	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)
HAEMATOMA	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)	x / x (x.x)

NB. A subject is counted only once per system organ class and preferred term

Source Listing: Listing 16.2.7.1.1; Produced: 23JAN2014 12:17; Draft

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Table 14.4.3
Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term	Severity	Number of Subjects (%) Placebo (N=12)	0.15mg TD139 (N=4)	1.5mg TD139 (N=4)	3mg TD139 (N=4)	10mg TD139 (N=4)	20mg TD139 (N=4)	50mg TD139 (N=4)	Overall (N=36)
GASTROINTESTINAL DISORDERS									
TOTAL	MILD	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	MODERATE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	SEVERE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
ABDOMINAL DISCOMFORT	MILD	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
ABDOMINAL PAIN UPPER	MILD	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
DIARRHOEA	MILD	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	MODERATE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
VOMITING	MILD	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
INVESTIGATIONS									
TOTAL	MILD	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
BLOOD PRESSURE INCREASED	MILD	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)

NB. A subject with multiple occurrences of an AE is counted only once at the maximum level of severity within that System Organ Class and Preferred Term.

Source Listing: Listing 16.2.7.1.1; Produced: 23JAN2014 12:17; Draft

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Table 14.4.4
Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Relationship
Safety Population

System Organ Class Preferred Term	Relationship	Number of Subjects (%) Placebo (N=12)	0.15mg TD139 (N=4)	1.5mg TD139 (N=4)	3mg TD139 (N=4)	10mg TD139 (N=4)	20mg TD139 (N=4)	50mg TD139 (N=4)	Overall (N=36)
GASTROINTESTINAL DISORDERS									
TOTAL	UNRELATED	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	UNLIKELY	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	POSSIBLE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	PROBABLE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
ABDOMINAL DISCOMFORT	POSSIBLE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
ABDOMINAL PAIN UPPER	POSSIBLE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
DIARRHOEA	POSSIBLE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	PROBABLE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
VOMITING	PROBABLE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
INVESTIGATIONS									
TOTAL	UNLIKELY	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
BLOOD PRESSURE INCREASED	UNLIKELY	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)

NB. A subject with multiple occurrences of an AE is counted only once at the highest association to study drug within that System Organ Class and Preferred Term.

Source Listing: Listing 16.2.7.1.1; Produced: 23JAN2014 12:17; Draft

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Table 14.5.1
Summary of Absolute and Change from Baseline Biochemistry Data
Safety Population

ALT (U/L)

		Actual						Change from Baseline					
Dose	Study Day	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Placebo (N=12)	Day -1	x	x.xx	x.xxx	x.x	x.xx	x.x						
	Day 1	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	Day 2	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
0.15mg TD139 (N=4)	Day -1	x	x.xx	x.xxx	x.x	x.xx	x.x						
	Day 1	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	Day 2	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
1.5mg TD139 (N=4)	Day -1	x	x.xx	x.xxx	x.x	x.xx	x.x						
	Day 1	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	Day 2	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
3mg TD139 (N=4)	Day -1	x	x.xx	x.xxx	x.x	x.xx	x.x						
	Day 1	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	Day 2	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
10mg TD139 (N=4)	Day -1	x	x.xx	x.xxx	x.x	x.xx	x.x						
	Day 1	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	Day 2	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x

NB. Baseline defined as Day -1

Source Listing: Listing 16.2.7.2.1; Produced: 23JAN2014 12:17; Draft

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Table 14.5.2
Summary of Absolute and Change from Baseline Haematology Data
Safety Population

Red Blood Cells (10^12/L)

		Actual						Change from Baseline					
Dose	Study Day	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Placebo (N=12)	Day -1	x	x.xx	x.xxx	x.x	x.xx	x.x						
	Day 1	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	Day 2	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
0.15mg TD139 (N=4)	Day -1	x	x.xx	x.xxx	x.x	x.xx	x.x						
	Day 1	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	Day 2	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
1.5mg TD139 (N=4)	Day -1	x	x.xx	x.xxx	x.x	x.xx	x.x						
	Day 1	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	Day 2	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
3mg TD139 (N=4)	Day -1	x	x.xx	x.xxx	x.x	x.xx	x.x						
	Day 1	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	Day 2	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
10mg TD139 (N=4)	Day -1	x	x.xx	x.xxx	x.x	x.xx	x.x						
	Day 1	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	Day 2	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x

NB. Baseline defined as Day -1

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Table 14.6.1
Summary of Absolute and Change from Baseline Vital Signs Data
Safety Population

Supine Systolic Blood Pressure (mmHg)

		Actual						Change from Baseline					
Dose	Time	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Placebo (N=12)	-30 min	x	x.x	x.xx	x	x.x	x						
	5 min	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	15 min	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	30 min	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	2hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	6hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	24hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	48hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
0.15mg TD139 (N=4)	-30 min	x	x.x	x.xx	x	x.x	x						
	5 min	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	15 min	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	30 min	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	2hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	6hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	24hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	48 hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x

NB. Baseline defined as Day 1, -30 min

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Table 14.7.1
Summary of Absolute and Change from Baseline 12-Lead ECG Data
Safety Population

PR Interval (mSec)

		Actual						Change from Baseline					
Dose	Time	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Placebo (N=12)	-30 min	x	x.x	x.xx	x	x.x	x						
	30 min	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	2hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	24hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
0.15mg TD139 (N=4)	-30 min	x	x.x	x.xx	x	x.x	x						
	30 min	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	2hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	24hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
1.5mg TD139 (N=4)	-30 min	x	x.x	x.xx	x	x.x	x						
	30 min	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	2hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	24hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
3mg TD139 (N=4)	-30 min	x	x.x	x.xx	x	x.x	x						
	30 min	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	2hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	24hr	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x

NB. Baseline defined as Day 1, -30 min

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Table 14.7.2
Summary of 12-Lead ECG QTcB Parameters by Categories
Safety Population

		Number of Subjects (%)									
Dose	Time	QTcB > 450 mSec		QTcB > 480 mSec		QTcB > 500 mSec		QTcB Increase > 30 mSec		QTcB Increase > 60 mSec	
Placebo (N=12)	-30 min	x	(x.x)	x	(x.x)	x	(x.x)				
	30 min	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)
	2hr	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)
	24hr	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)
0.15mg TD139 (N=4)	-30 min										
	30 min	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)
	2hr	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)
	24hr	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)
1.5mg TD139 (N=4)	-30 min	x	(x.x)	x	(x.x)	x	(x.x)				
	30 min	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)
	2hr	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)
	24hr	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)
3mg TD139 (N=4)	-30 min	x	(x.x)	x	(x.x)	x	(x.x)				
	30 min	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)
	2hr	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)
	24hr	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)	x	(x.x)

NB. Baseline defined as Day 1, -30 min

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Figure 16.2.5.2.1
Individual Plasma TD139 Concentration - Time Curves on a Linear Scale
Safety Population

Dose = 1.5mg TD-139

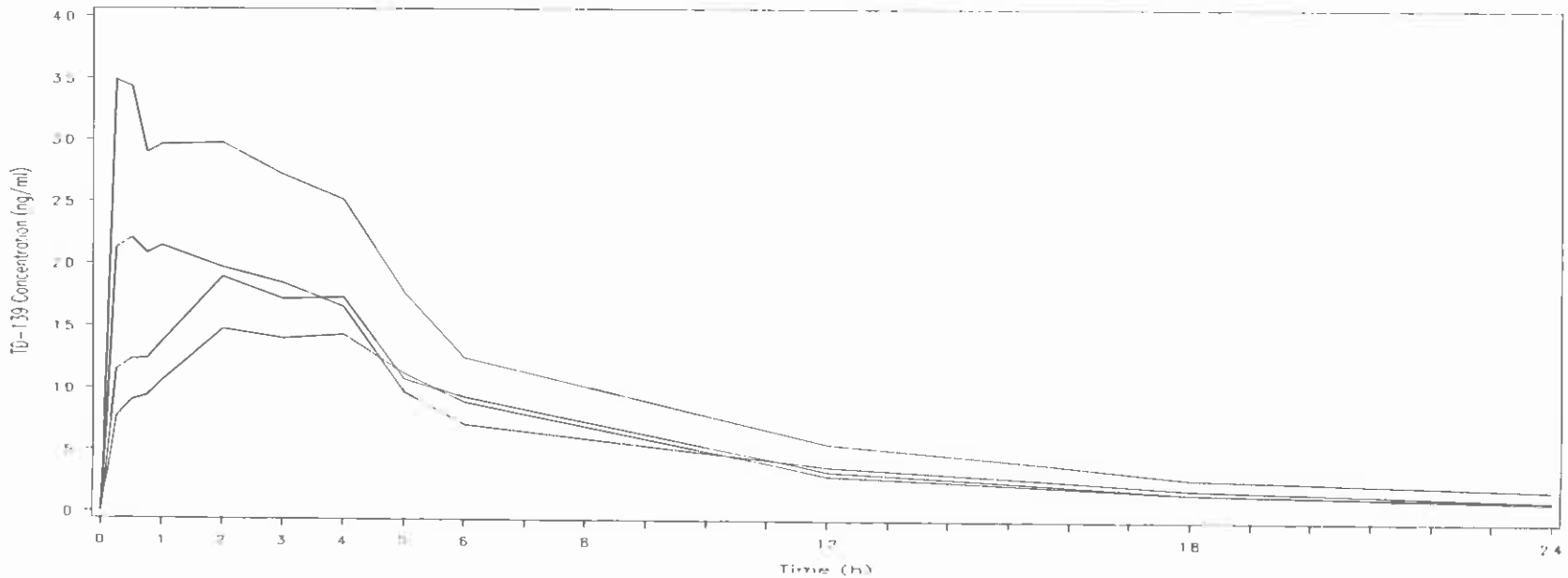

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Figure 16.2.5.2.2
Individual Plasma TD139 Concentration - Time Curves on a Semi-Logarithmic Scale
Safety Population

Dose = 1.5mg TD-139

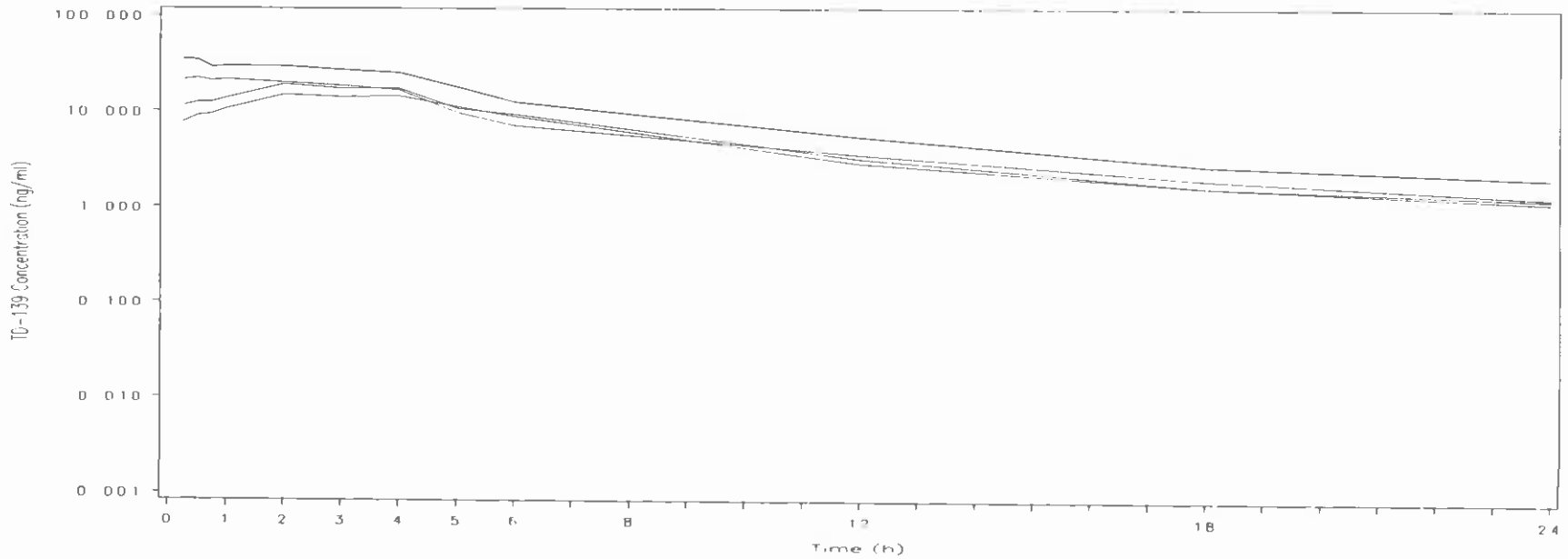

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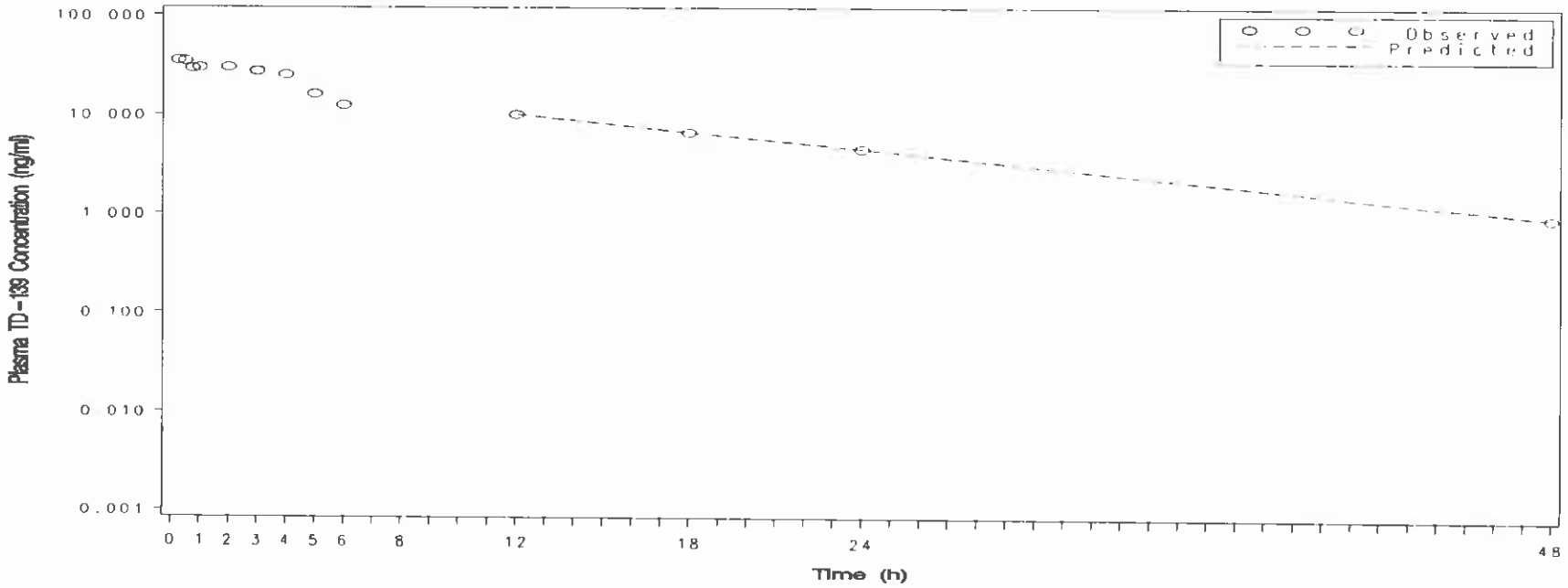
Figure 16.2.5.4.1
Plasma TD139 Half-Life Calculations
Safety Population

Subject = 1
Rsq = 1.0 Rsq_adjusted = 1.0 HL_Lambda_z = 12.4867
(4 points used in calculation)
Uniform Weighting



Source Listing: Listing 16.2.5.1.1; Produced: 23JAN2014 12:17; Draft

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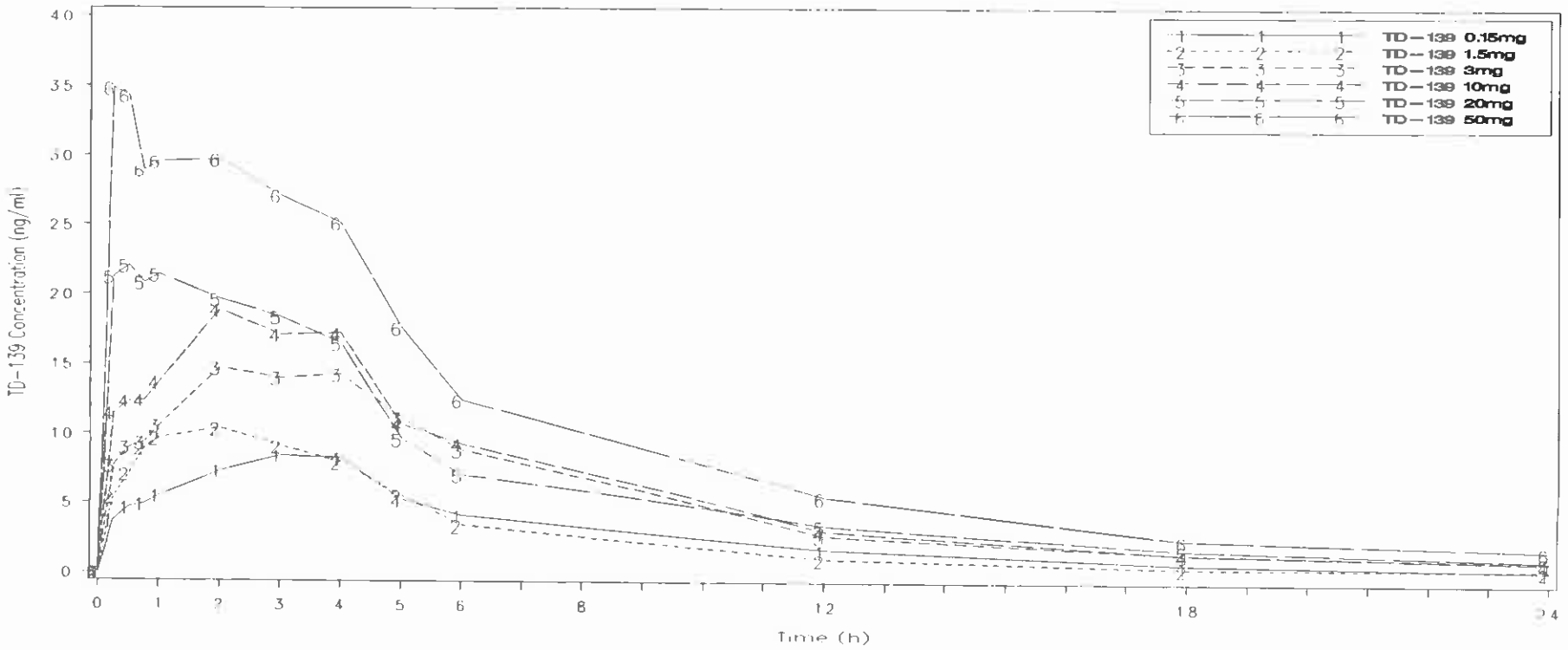
Figure 14.2.1
Mean Plasma TD139 Concentration - Time Curve on a Linear Scale
PK Population



Source Listing: Listing 16.2.5.1.1; Produced: 23JAN2014 12:17; Draft

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Figure 14.2.2
Mean Plasma TD139 Concentration - Time Curve on a Semi-Logarithmic Scale
PK Population

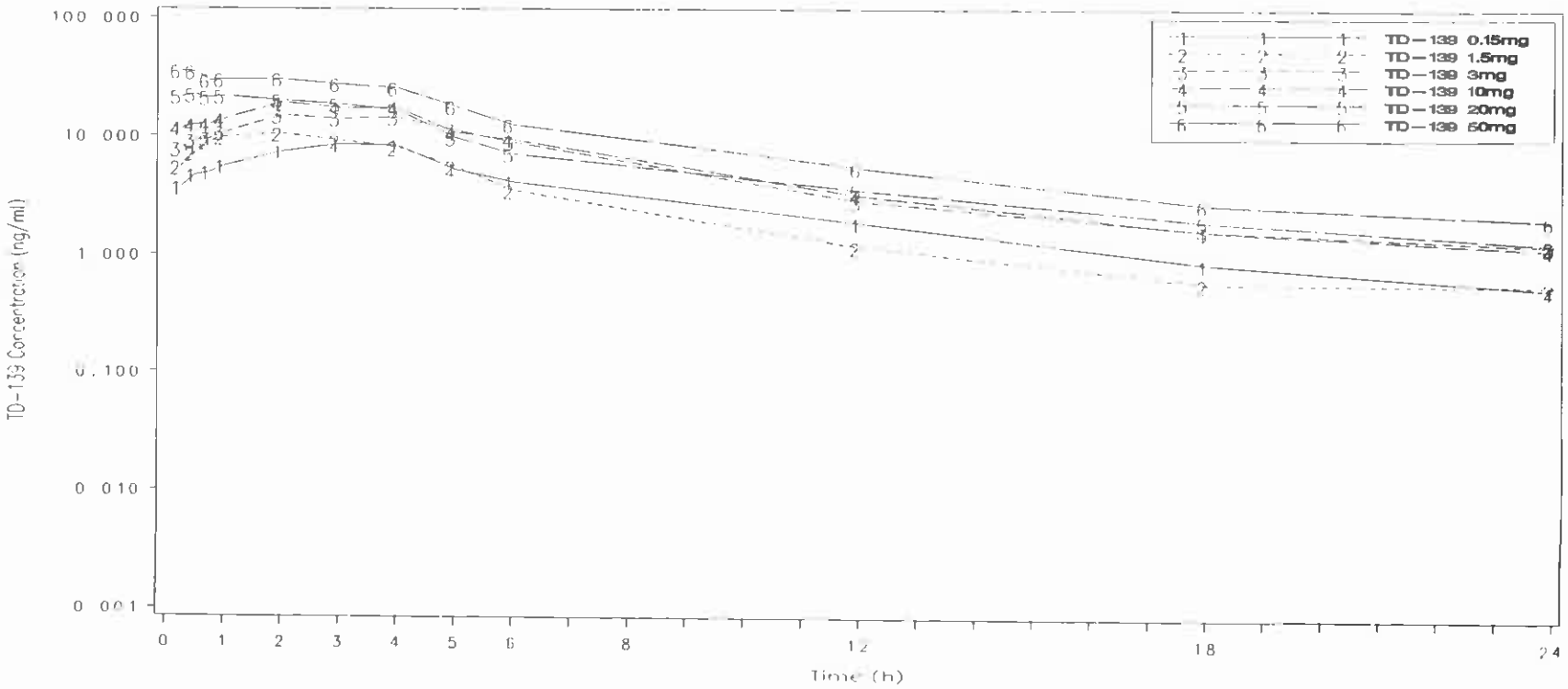

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Figure 14.2.3
Dose Response of Derived Pharmacokinetic Parameters
PK Population

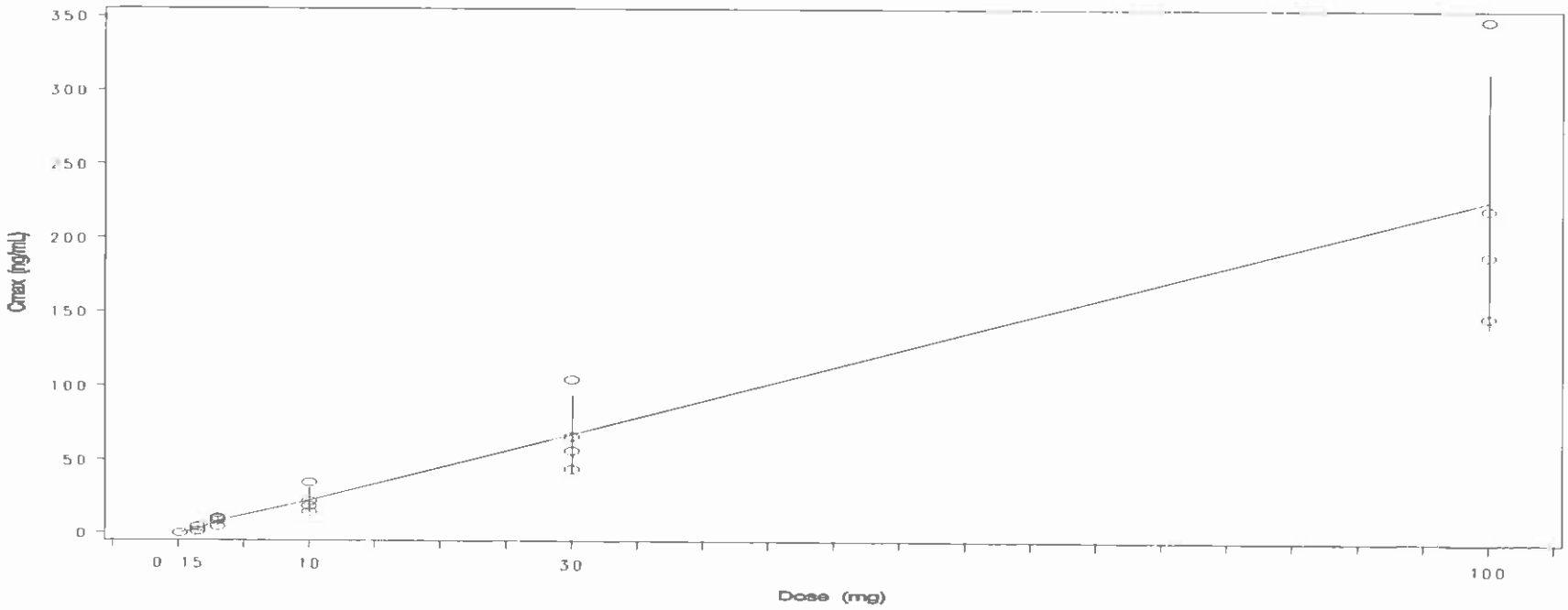

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Figure 14.6.1
Mean Change from Baseline Vital Signs Data
Safety Population

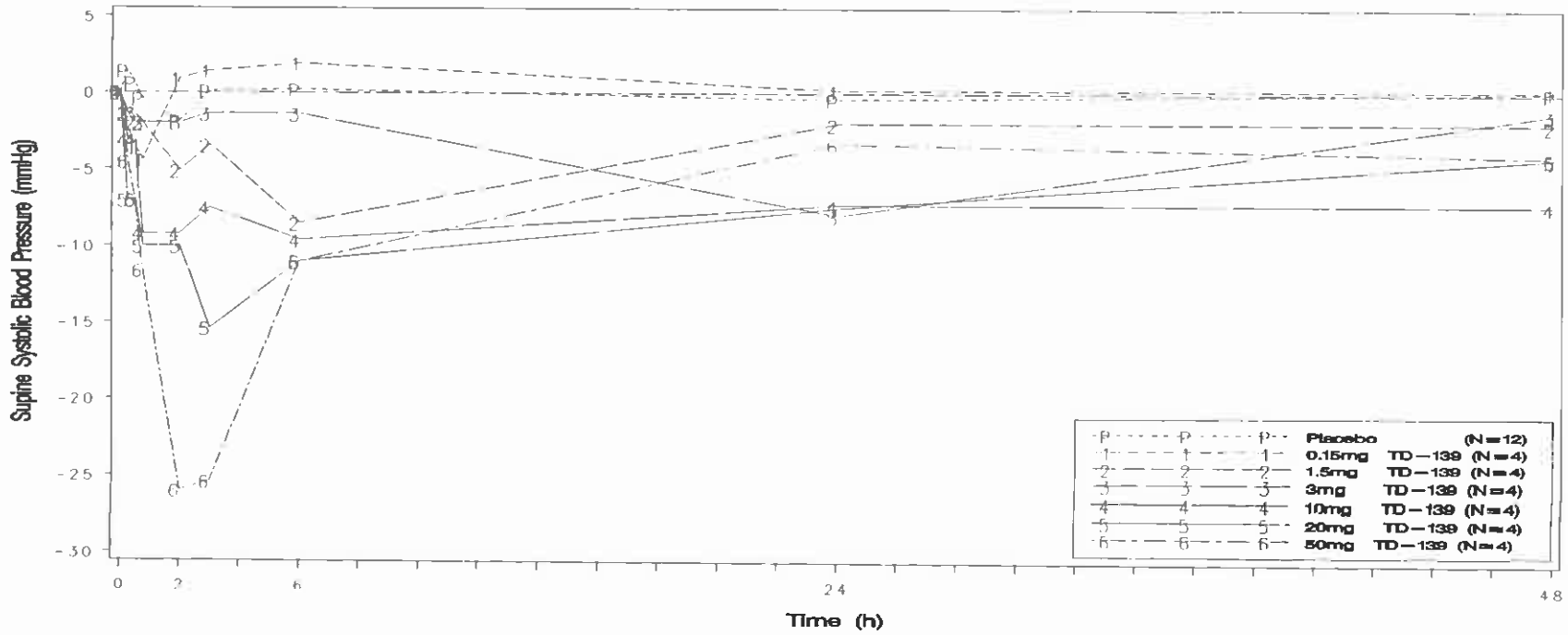

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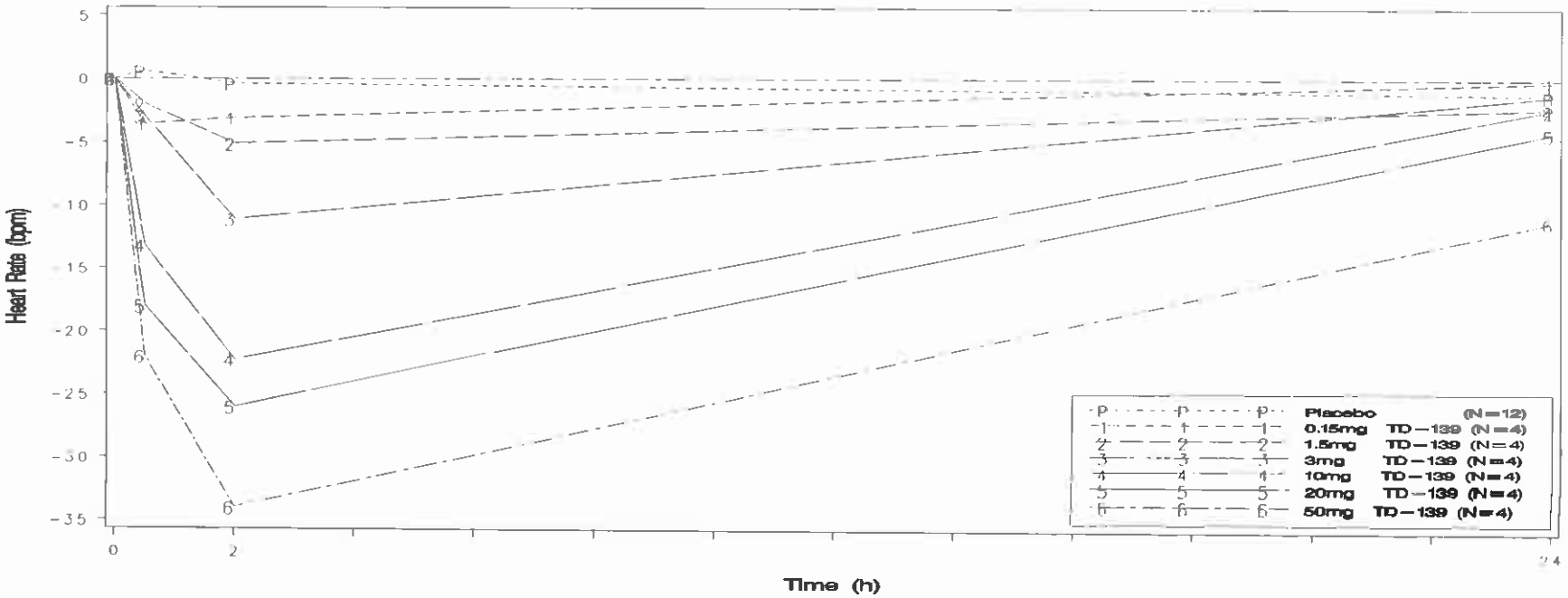
Figure 14.7.1
Mean Change from Baseline 12-Lead ECG Data
Safety Population



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