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1. TITLE PAGE

Study Title:	A Phase 1, Single Center Randomized, Three-Way Crossover, Double-Blinded, Placebo- and Moxifloxacin-Controlled Thorough QT (TQT) Study to Determine the Effects of Sertraline (Zoloft®) on the Cardiac Repolarization in Healthy Subjects
Investigational Product:	Sertraline Hydrochloride
Indication:	Major depression
Sponsor:	Pfizer Inc
Protocol Number:	A0501104
Phase of Development:	Phase 1
Study Initiation Date:	First Subject First Visit (FSFV): 07 January 2016
Primary Completion Date:	06 September 2016
Study Completion Date:	Last Subject Last Visit (LSLV): 06 September 2016
Sponsor's Signatories:	[redacted]
Report Date:	05 March 2017
Previous Report Date(s):	Not Applicable.
Investigators:	See below.

Country	Center	Principal Investigator
[redacted]	[redacted]	[redacted]

[redacted]

GOOD CLINICAL PRACTICE (GCP) STATEMENT

This study was conducted in compliance with GCP guidelines and, where applicable, local country regulations relevant to the use of new therapeutic agents in the country of conduct, including the archiving of essential documents.

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2. SYNOPSIS

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16.1. Study Information

[redacted]

[redacted]

Individual Subject Data Listings to be submitted will be provided in Module 5 of the Common Technical Document (CTD) for New Drug Applications (USA).

4. LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Definition
%CV	percent coefficients of variation
%RE	percent relative error
Abs	absolute
AE	adverse event
ALT	alanine aminotransferase
ALP	alkaline phosphatase
AM	ante meridiem
AST	aspartate aminotransferase
AUC	area under the plasma concentration-time profile
AUC_{24}	area under the plasma concentration-time profile from time 0 to 24 hours
AUC_{24}(dn)	dose-normalized AUC_{24}
AUC_{extrap}%	percent of the area under the plasma concentration-time curve from time 0 to infinite time, obtained by forward extrapolation
AUC_{inf}	area under the plasma concentration-time curve from time 0 to infinite time
AUC_{last}	area under the plasma concentration-time profile from time 0 to the time of the last quantifiable concentration (C_{last})
β-hCG	beta-subunit of human chorionic gonadotropin
BID	twice a day
BLQ	below lower limit of quantification
BP	blood pressure
BUN	blood urea nitrogen
CI	confidence interval
C-SSRS	Columbia - Suicide Severity Rating Scale
C_{max}	maximum plasma concentration
C_{max}(dn)	dose-normalized C_{max}
C_{min}	minimum observed concentration during the dosing interval
CO_2	carbon dioxide
CRO	contract research organization
CRU	clinical research unit
CSR	clinical study report
DCT	data collection tool
ECG	electrocardiogram
FSH	follicle-stimulating hormone
GCP	Good Clinical Practice
GGT	gamma-glutamyl transferase
HCl	hydrochloride
HR	hours
HPF	high power field
ICD	informed consent document
ICH	International Council for Harmonization
ID	identification

Abbreviation	Definition
IEC	Independent Ethics Committee
INR	international normalized ratio
IP	investigational product
k_{el}	terminal phase rate constant
LFT	liver function test
LLOQ	lower limit of quantification
ln	natural-log transformed
LS	least squares
MCH	mean corpuscular hemoglobin
MCHC	mean corpuscular hemoglobin concentration
MCV	mean corpuscular volume
MedDRA	Medical Dictionary for Regulatory Activities
MHP	mental health professional
MR	metabolite to parent ratio
MW	molecular weight
NA	not applicable
NC	not calculated
PCRU	Pfizer clinical research unit
PIMS	Phase 1 Management System
pH	hydrogen ion concentration (negative log)
PK	pharmacokinetic
PM	post meridiem
PTR	peak-to-trough ratio
PT	prothrombin time
QC	quality control
QD	once daily
QT	time from ECG Q-wave to the end of the T-wave corresponding to electrical systole
QTc	corrected time from ECG Q-wave to the end of the T-wave corresponding to electrical systole for heart rate
QTcB	QT corrected for heart rate using Bazett's formula
QTcF	QT corrected for heart rate using Fridericia formula
QTcI	individually corrected QT interval
QTcN	QT corrected for heart rate using a study population-based approach
r^2	goodness-of-fit statistic from the regression
R_{ac}	observed accumulation ratio of AUC
$R_{ac,Cmax}$	observed accumulation ratio for C_{max}
RBC	red blood cell
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SSRI	selective serotonin reuptake inhibitor
SOP	standard operating procedure

[redacted]

Abbreviation	Definition
$t_{½}$	plasma terminal elimination half-life
TEAE	treatment-emergent adverse event
T_{max}	time to reach maximum concentration
TQT	thorough QT
ULN	upper limit of normal
vs	versus
WBC	white blood cell

5. ETHICS

5.1. Independent Ethics Committee or Institutional Review Board

The final protocol (Section 16.1.1), and informed consent documentation (Section 16.1.3.2) were reviewed and approved by the Independent Ethics Committee (IEC) at the investigational center participating in the study. The IEC is listed in Section 16.1.3.1. Investigators were required to inform the IEC of the study's progress and occurrence of any serious and/or unexpected adverse events (AEs).

5.2. Ethical Conduct of the Study

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of study participants.

5.3. Subject Information and Consent

A signed and dated informed consent was required before any screening procedures were done. The investigator explained the nature, purpose, and risks of the study to each subject. Each subject was informed that he/she could withdraw from the study at any time and for any reason. Each subject was given sufficient time to consider the implications of the study before deciding whether to participate. Subjects who chose to participate signed an informed consent document (ICD) (Section 16.1.3.2).

Some subjects might have been prescreened by the investigator under an IEC-approved generic consent document, which allowed for collection of standard safety data for the purpose of identifying potential subjects. In such situations, screening data were obtained prior to the date the subject signed the ICD for this study.

6. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

The study was managed by Pfizer Inc (the sponsor) and conducted at a Pfizer clinical research unit (PCRU). The investigators ( ) were responsible for adhering to the study procedures described in the protocol, for keeping records of study drug, and for accurately completing the Phase 1 Management System (PIMS), the data collection tool (DCT) supplied by the sponsor. Data management, data analysis, biostatistics, and medical writing were completed by the sponsor (or its designee).

The study was conducted at 1 center in . Study drug was packaged, labeled, and shipped by the study sponsor. The clinical laboratory sample analyses were performed by . Pharmacokinetic (PK) sample analysis and method validation was performed by .

The names, addresses, services and dates provided by contract research organizations (CROs) used during the study are provided in .

7. INTRODUCTION

Sertraline is a selective serotonin reuptake inhibitor (SSRI). Zoloft® (Sertraline hydrochloride) is indicated for the treatment of major depressive disorder; obsessions and compulsions in patients with obsessive-compulsive disorder; panic disorder, with or without agoraphobia, as defined in Diagnostic and Statistical Manual of Mental Disorders-I; posttraumatic stress disorder; premenstrual dysphoric disorder; and social anxiety disorder, also known as social phobia, in adults. The mechanism of action of sertraline is presumed to be linked to its inhibition of central nervous system neuronal uptake of serotonin. Studies at clinically relevant doses in man have demonstrated that sertraline blocks the uptake of serotonin into human platelets. In vitro studies in animals also suggest that sertraline is a potent and selective inhibitor of neuronal serotonin reuptake and has only very weak effects on norepinephrine and dopamine neuronal reuptake. The chronic administration of sertraline was found in animals to down regulate brain norepinephrine receptors, as has been observed with other drugs effective in the treatment of major depressive disorder. Sertraline does not inhibit monoamine oxidase. [1]

PK of sertraline has been extensively evaluated following approved therapeutic doses of 50 to 200 mg. Sertraline undergoes extensive first pass metabolism. The principal initial pathway of metabolism for sertraline is N-demethylation. N-desmethylsertraline has a plasma terminal elimination half-life ($t_{½}$) of 62 to 104 hours. Both in vitro biochemical and in vivo pharmacological testing have shown N-desmethylsertraline to be substantially less active than sertraline. Both sertraline and N-desmethylsertraline undergo oxidative deamination and subsequent reduction, hydroxylation, and glucuronide conjugation.

In vitro protein binding studies performed with radiolabeled H^3-sertraline showed that sertraline is highly bound to serum proteins (98%) in the range of 20 to 500 ng/mL. However, at up to 300 and 200 ng/mL concentrations, respectively, sertraline and N-desmethylsertraline did not alter the plasma protein binding of 2 other highly protein bound drugs, ie, warfarin and propranolol.[1]

This study was conducted to fulfill a United States Food and Drug Administration post marketing requirement and the study design was in accordance with the ICH E14 Guidance for thorough time from electrocardiogram (ECG) Q-wave to the end of the T-wave corresponding to electrical systole (thorough QT [TQT]) study.[2] This study was designed to assess effect of sertraline on corrected time from ECG Q-wave to the end of the T-wave corresponding to electrical systole for heart rate (QTc) interval at supratherapeutic concentrations.

8. STUDY OBJECTIVES

Primary:

- To determine the effect of sertraline on QTc intervals relative to time-matched placebo in healthy subjects.

Secondary:

- To evaluate study sensitivity by evaluating the effect of moxifloxacin on QTc intervals relative to time-matched placebo at moxifloxacin historical time to reach maximum concentration (T_{max}; 3 hours postdose);
- To evaluate the safety and tolerability of sertraline in healthy subjects;
- To evaluate the relationship of the QTc interval with plasma concentrations of sertraline and its metabolite, N-desmethylsertraline.

Tertiary:

- To evaluate the PK of sertraline and its metabolite, N-desmethylsertraline.

9. INVESTIGATIONAL PLAN

9.1. Overall Study Design and Plan: Description and Flow Chart

This was a Phase 1, single-center, randomized, double-blinded, placebo- and moxifloxacin-controlled, 3-period, 6-sequence, 3-treatment (sertraline and placebo blinded; moxifloxacin open-label), 3-way crossover TQT study of the effects of sertraline on cardiac repolarization in approximately 54 healthy subjects.

A sample size of 42 subjects (7 per sequence) was estimated to be required for this study to attain reasonable power to show lack of effect of sertraline on QTc and also show assay sensitivity. To allow for dropouts, approximately 54 subjects (9 per sequence) were planned to be randomized to have 42 evaluable subjects. Subjects were not to be replaced. However, if the total number of subjects went below 36, additional subjects were to be randomized. These additional subjects were to be randomized in multiples of 6 (block size).

Sertraline (Treatment A), moxifloxacin (Treatment B), and placebo (Treatment C) were administered in a randomized sequence in Periods 1, 2 or 3 as indicated in Table 1.

Table 1. Randomization Scheme

	Treatment		
	Period 1	**Period 2**	**Period 3**
Sequence 1 (n = 9)	Treatment A	Treatment B	Treatment C
Sequence 2 (n = 9)	Treatment C	Treatment B	Treatment A
Sequence 3 (n = 9)	Treatment B	Treatment C	Treatment A
Sequence 4 (n = 9)	Treatment C	Treatment A	Treatment B
Sequence 5 (n = 9)	Treatment A	Treatment C	Treatment B
Sequence 6 (n = 9)	Treatment B	Treatment A	Treatment C

Source: [redacted]
Abbreviation: n = number of subjects.

[redacted]

The following treatments were administered:

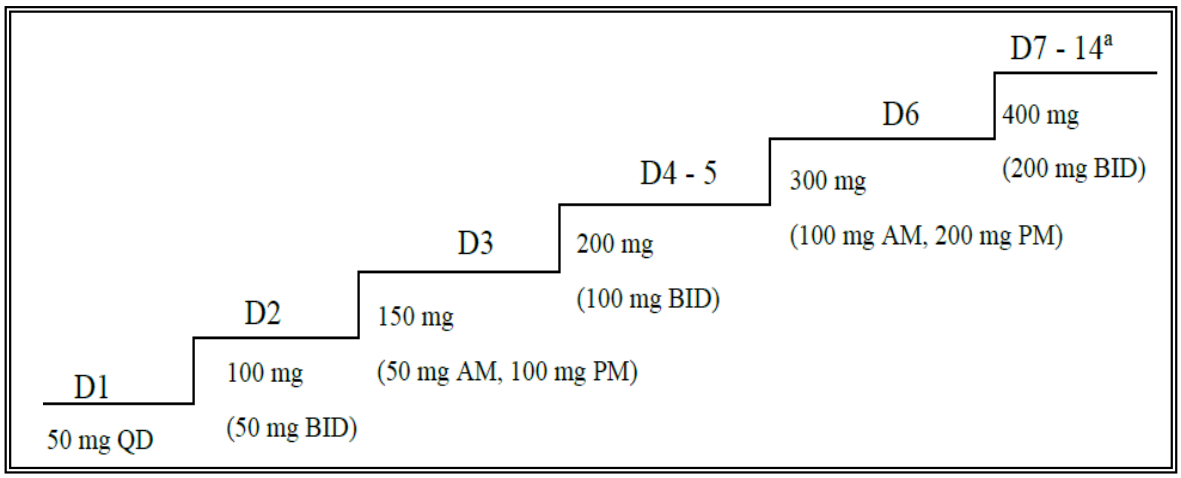
- **Treatment A (Sertraline Hydrochloride - Double-Blinded):** Dose titrated from a starting single dose of 50 mg sertraline hydrochloride in the morning on Day 1 followed by twice a day (BID) (given at approximately 12 hours apart) escalating doses administered on Days 2 through 6, followed by 400 mg/day BID on Days 7 through 13, and on Day 14 only the morning dose of 200 mg was administered, and no evening dose was administered, according to the dose titration scheme in Figure 1.

- **Treatment B (Moxifloxacin - Positive Control, Open-Label):** Double-blinded placebo (matching for sertraline hydrochloride) was given from Day 1 to Day 13, according to dose titration scheme in Figure 1. On Day 14, a single dose of 400 mg moxifloxacin (Avelox) was administered open-label.

- **Treatment C (Placebo - Double-Blinded):** Placebo control – placebo administered on Days 1 through 14, according to the dose titration scheme in Figure 1.

Sertraline 50 mg tablets and matching placebo tablets were used in the study.

Figure 1. Dose Titration Scheme for Treatment A – Sertraline Hydrochloride Administration



Source: [redacted]
Treatment A = sertraline hydrochloride - double-blinded.
Abbreviations: AM = ante meridiem; BID = twice a day; D = day; PM = post meridiem; QD = once daily.
a = On Day 14, only the morning dose of 200 mg was administered, and no evening dose was administered.

Each subject participated in the study for approximately 4 months, including screening, study periods, and washout. It was estimated that the clinical portion of the study was completed in approximately 3 months (ie, 93 days). Participation included a screening evaluation conducted within 28 days before dosing in Period 1, admission to PCRU on study Day 0 and a subsequent 17-nights inpatient stay, respectively, for treatments A, B and C. There was a washout period of at least 14 days after completion of treatment A, B and C.

[redacted]

Subjects had undergone screening evaluation within 28 days of dosing. Day 0 was defined as the day prior to first day of dosing (Day 1) for each period. Eligible subjects were admitted to PCRU on Day 0 and remained at the PCRU until the last PK sample was collected at the end of the treatment period. Double-blind test article or placebo administration occurred on Days 1 through 14 for Treatment A and C (sertraline and placebo treatment, respectively). Double-blind placebo administration also occurred for Treatment B (moxifloxacin) on Days 1 to 13 following by single dose of open-label moxifloxacin 400 mg on Day 14. An overnight fast of at least 10 hours observed before the morning dose administrations on Days 1 and 14 (when PK and ECG assessments were planned), and the evening dose on Day 1 could be given with food, and a fasted morning dose on Day 15 when obtaining trough measurement for all treatments. Breakfast was completed by 30 minutes prior to drug administration on other study days (Days 3 through 13) of study Treatments A, B and C.

Each subject was to participate in 3 study periods and receive all 3 treatments. The study was planned for a single investigational site.

A standard breakfast, lunch and dinner was provided at appropriate times. Subjects abstained from drinks, including water, for 0.5 hours prior to any ECG measurement. Subjects were restricted to consuming ambient temperature beverages in each study period. During the treatment periods, subjects who experience repeated episodes of vomiting were assessed by the principal investigator (PI) for potential discontinuation from the study.

Schedule of activities are presented in Table 2 and PK sampling and ECG assessment time points are added in Table 3.

[redacted]

Table 2. Schedule of Activities

Visit Identifier	Screening	Periods 1, 2 and 3 (Treatments A, B and C)																	
		D 0	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9	D 10	D 11	D 12	D 13	D 14	D 15	D 16	D 17/Early Termination
Informed consent	X																		
CRU confinement		X[a]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Inclusion/exclusion criteria	X	X[b]																	
Medical history[c]	X	X[d]																	
Physical examination[e]	X	X																	X[f]
Height and weight	X																		
Safety laboratory	X	X							X[g]							X[g]			X[f]
12-lead ECG (single)	X																		
12-lead ECG (triplicates)[h]			X	X												X	X	X	X[f]
Demography	X																		
Vital signs (BP/pulse rate, temperature)	X		X	X															X[f]
Pregnancy test[i]	X	X																	X
FSH[j]	X																		
Confirm proper contraception was being used	X	X																	X
Urine drug screen	X	X																	
Study treatment administration[k]			X	X	X	X	X	X	X	X	X	X	X	X	X	X			
PK blood sampling[l]			X	X												X	X	X	X
Baseline symptoms/ AE monitoring		X----------																	----------X
Prior/concomitant treatment	X	X[m]----------																	----------X
Suicidality assessment[n]	X	X														X			X[o]
Discharge from unit																			X

Table 2. Schedule of Activities

Source: [redacted]

Treatment A = sertraline hydrochloride - double-blinded; Treatment B = moxifloxacin - positive control, open-label; Treatment C = placebo - double-blinded.
Abbreviations: AE = adverse event; BP = blood pressure; CRU = clinical research unit; C-SSRS = Columbia - Suicide Severity Rating Scale; D = day; ECG = electrocardiogram; FSH = follicle-stimulating hormone; PK = pharmacokinetic.

a. Subjects were admitted on Day 0 and were discharged after collection of the 72-hour (following Day 14 dosing) PK sample and ECG reading on Day 17.
b. Period 1 only.
c. Medical history updated on Day 0 (Period 1 only).
d. Medical history included complete history of all prescription and non-prescription drugs and dietary and herbal supplements taken 28 days prior to the planned first dose, as well as illegal drug, alcohol and tobacco use.
e. Full physical examination either at screening or Day 0 Period 1; otherwise brief examination if findings during previous examination or new/open AEs if appropriate at investigator discretion.
f. Conducted on Day 17, Period 3 and for Periods 1 and 2 at principal investigator discretion or upon early withdrawal.
g. Predose.
h. Detailed ECG collection time points were provided in PK and ECG assessment flow chart below.
i. Female of childbearing potential. Also at discharge of each period.
j. Serum FSH evaluation was done for any female who was amenorrheic for at least 12 consecutive months.
k. Treatment A was active drug given on Day 1 to 14 based on escalation schema specified in Section 9.1. Treatment C (matching placebo) administered on Days 1 to 14 using the same escalation schema as active drug. Treatment B (matching placebo) on Days 1 to 13 using the same escalation schema as active drug, and a single dose, open-label administration of moxifloxacin on Day 14. The washout period between treatments was of 14 days.
l. Detailed PK sample collection time points are provided in PK sampling and ECG assessment flow chart below (Table 3).
m. Repeated if subjects discharged to home after 72-hour assessment.
n. C-SSRS - lifetime/Baseline assessment at screening; all other assessments were since last visit assessment.
o. Performed upon early termination.

[redacted]

Table 3. Pharmacokinetic Sampling and Electrocardiogram Assessment

Protocol Assessment	**Periods 1, 2 and 3 (Treatments A, B and C)**																							
Study Day	**Day 1**											**Day 2**	**Day 14**									**Day 15**	**Day 16**	**Day 17**
Hours Postdose	**-1**	**-0.5**	**0[a]**	**1**	**2**	**3**	**4**	**5**	**6**	**8**	**12**	**24**	**0[a]**	**1**	**2**	**3**	**4**	**5**	**6**	**8**	**12**	**24**	**48**	**72**
PK blood sampling[b]			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
12-lead ECG (triplicates)[c]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Source: [redacted]

Treatment A = sertraline hydrochloride - double-blinded; Treatment B = moxifloxacin - positive control, open-label; Treatment C = placebo - double-blinded.

Abbreviations: ECG = electrocardiogram; PK = pharmacokinetic; QTc = corrected QT interval.

a. The predose PK sampling (0-hour) occurred immediately prior to the morning dose.

b. All study treatments had identical sample collection time points. Placebo samples need to be analyzed only if deemed necessary. For moxifloxacin treatment, Day 14 plasma samples were analyzed for the 1, 2, 3, 4, and 5-hour time points if a positive signal (QTc prolongation) was not observed; moxifloxacin samples were to be held until notification by the clinical team before analysis.

c. ECG assessment was triplicate recorded approximately 2 minutes apart, the predose assessments (-1, -0.5 and 0 hours) occurred immediately prior to the morning dose on Day 1.

[redacted]

9.2. Discussion of Study Design, Including Choice of Control Groups

This study consisted of 3 periods and 3 treatments (supratherapeutic dose of the drug, placebo, and moxifloxacin). To achieve supratherapeutic concentrations of the drug and its active metabolite in healthy subjects, slow escalation of doses over a 2-week period was required for tolerability reasons. Similarly a washout period of approximately 2 weeks (14 days) was necessary due to the long half-lives of the drug and its metabolite. Moxifloxacin was administered in this study in order to confirm assay sensitivity for detecting increases in QTc of 5 msec or greater.[2] A single dose of moxifloxacin was chosen as a positive control in the majority of TQT studies as it typically has a peak occurring between 1 and 3 hours postdose in the range of 8 to 15 msec and a lower bound of the 1-sided 95% confidence interval (CI) above 5 msec.[3,4] In this study, the same procedure for administering the study drug, moxifloxacin and placebo, taking blood samples, and collecting the ECG data was used.[4] A single dose of moxifloxacin was administered on Day 14.

The largest increases in exposure to sertraline occurred in hepatic impairment subjects. The exposure increased approximately 3-fold for sertraline and approximately 2-fold for desmethylsertraline in chronic mild hepatic impairment patients. Therefore, the supratherapeutic dose could ideally achieve plasma exposure to drug in the current study of approximately 3 and 2-fold above plasma concentrations of sertraline and desmethylsertraline, respectively, normally observed for the highest recommended doses of sertraline.

9.3. Selection of Study Population

Subjects had to meet all inclusion criteria and not meet any exclusion criteria to participate in this study.

9.3.1. Inclusion Criteria

Eligible subjects were expected to meet the following and all other qualifying criteria:

1. Healthy female subjects and/or male subjects who at the time of screening were between the ages of 18 and 55 years, inclusive. Healthy was defined as no clinically relevant abnormalities identified by a detailed medical history, full physical examination, including blood pressure (BP) and pulse rate measurement, 12-lead ECG and clinical laboratory tests.

   Female subjects of non-childbearing potential must meet at least 1 of the following criteria:

   a. Achieved postmenopausal status, defined as follows: cessation of regular menses for at least 12 consecutive months with no alternative pathological or physiological cause; and have a serum follicle-stimulating hormone (FSH) level confirming the post-menopausal state;

   b. Had undergone a documented hysterectomy and/or bilateral oophorectomy;

   c. Had medically confirmed ovarian failure.

All other female subjects (including females with tubal ligations) were considered to be of childbearing potential.

2. Body mass index of 17.5 to 30.5 kg/m^2; and a total body weight >50 kg (110 lbs).

3. Evidence of a personally signed and dated ICD indicating that the subject was informed of all pertinent aspects of the study.

4. Subjects who were willing and able to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures.

9.3.2. Exclusion Criteria

Subjects were ineligible to participate in this study if any of the following criteria were met:

1. Evidence or history of clinically significant hematological, renal, endocrine, pulmonary, gastrointestinal, cardiovascular, hepatic, psychiatric, neurologic, or allergic disease (including drug allergies, but excluding untreated, asymptomatic, seasonal allergies at time of dosing).

2. Any condition possibly affecting drug absorption (eg, gastrectomy).

3. A positive urine drug screen.

4. History of regular alcohol consumption exceeding 14 drinks/week for females or 21 drinks/week for males (1 drink = 5 ounces [150 mL] of wine or 12 ounces [360 mL] of beer or 1.5 ounces [45 mL] of hard liquor) within 6 months of screening.

5. Treatment with investigational product (IP) within 30 days (or as determined by the local requirement) or 5 half-lives preceding the first dose of IP (whichever was longer).

6. Screening supine BP ≥140 mm Hg (systolic) or ≥90 mm Hg (diastolic), following at least 5 minutes of rest. If BP was ≥140 mm Hg (systolic) or ≥90 mm Hg (diastolic), the BP was repeated 2 more times and the average of the 3 BP values was used to determine the subject's eligibility.

7. Screening supine 12-lead ECG demonstrating the QT corrected for heart rate using Fridericia formula (QTcF) >450 or a QRS interval >120 msec. If QTcF exceeded 450 msec, or QRS exceeded 120 msec, the ECG was to be repeated 2 more times and the average of the 3 QTcF values was to be used to determine the subject's eligibility.

8. Subjects with any of the following abnormalities in clinical laboratory tests at screening, as assessed by the study-specific laboratory and confirmed by a single repeat, if deemed necessary:

    - Aspartate aminotransferase (AST)/serum glutamic oxaloacetic transaminase or alanine aminotransferase (ALT)/serum glutamic pyruvic transaminase ≥1.5 × upper limit of normal (ULN);

- Total bilirubin ≥1.5 × ULN; subjects with a history of Gilbert's syndrome might have a direct bilirubin measured and would be eligible for this study provided the direct bilirubin was ≤1 × ULN.

9. Pregnant female subjects; breastfeeding female subjects; male subjects with partners currently pregnant; male subjects able to father children and female subjects of childbearing potential who were unwilling or unable to use at least 1 highly effective method of contraception as outlined in Section 9.3.4.4 for the duration of the study and for at least 28 days after the last dose of IP or longer based upon the compound's $t_{½}$ characteristics.

10. Use of prescription or nonprescription drugs and dietary supplements within 7 days or 5 half-lives (whichever was longer) prior to the first dose of IP. Herbal supplements and hormone replacement therapy were to be discontinued 28 days prior to the first dose of IP. As an exception, acetaminophen/paracetamol could have been used at doses of ≤1 g/day. Limited use of non-prescription medications that were not believed to affect subject safety or the overall results of the study might be permitted on a case-by-case basis following approval by the sponsor. Contraceptive methods are allowed as described in Section 9.3.4.4.

11. Blood donation (excluding plasma donations) of approximately 1 pint (500 mL) or more within 56 days prior to dosing.

12. History of sensitivity to heparin or heparin-induced thrombocytopenia.

13. History of known QTc prolongation or ECG abnormalities.

14. Suicidal ideation associated with actual intent and a method or plan in the past year: "Yes" answers on items 4 or 5 of the Columbia - Suicide Severity Rating Scale (C-SSRS). In addition, subjects deemed by the investigator to be at significant risk of suicidal or violent behavior were to be excluded.

15. Individuals with known hypersensitivity reactions to sertraline or SSRI.

16. Individuals with a known hypersensitivity to moxifloxacin or quinolones.

17. Subjects, who according to the product label for moxifloxacin, would be at increased risk if dosed with moxifloxacin (ie, including but not limited to subjects with history of myasthenia gravis, tendinitis/tendon rupture).

18. Unwilling or unable to comply with the lifestyle guidelines described in Section 9.3.4.

19. Other severe, acute, or chronic medical or psychiatric condition or laboratory abnormality that might increase the risk associated with study participation or IP administration or might interfere with the interpretation of study results and, in the judgment of the investigator, would make the subject inappropriate for entry into this study.

20. Subjects who were investigational site staff members directly involved in the conduct of the study and their family members, site staff members otherwise supervised by the investigator, or subjects who were sponsor employees directly involved in the conduct of the study.

21. Self-reported history of risk factors for QT prolongation or torsades de pointes (eg, organic heart disease, congestive heart failure, hypokalemia, hypomagnesemia, congenital long QT syndrome, myocardial ischemia or infarction, congenital deafness, and family history of sudden death, or a family history of congenital QT syndrome.)

22. Self-reported history of sick sinus syndrome, first, second, or third degree atrioventricular block, myocardial infarction, pulmonary congestion, cardiac arrhythmia, prolonged QT interval or conduction abnormalities, or any other clinically significant cardiovascular disease history.

23. Use of tobacco- or nicotine-containing products in excess of the equivalent of 5 cigarettes per day.

9.3.3. Removal of Subjects From Therapy or Assessment

Subjects could have withdrawn from the study at any time at their own request, or they could have withdrawn at any time at the discretion of the investigator or sponsor for safety or, behavioral reasons, or the inability of the subject to comply with the protocol-required schedule of study visits or procedures at a given study site. The early termination visit only applied to subjects who were randomized and then were prematurely withdrawn from the study.

If a subject did not return for a scheduled visit, every effort was made to contact the subject. The investigator or site staff should have attempted to contact the subject twice. After 2 attempts, CRU staff might have sent a registered letter. If no response was received from the subject, the subject was to be considered lost to follow-up. All attempts to contact the subject and information received during contact attempts were to be documented in the subject's medical record. In any circumstance, every effort was made to document subject outcome, if possible. The investigator should have inquired about the reason for withdrawal, requests the subject to return for a final visit, if applicable, and follow-up with the subject regarding any unresolved AEs.

It might be appropriate for the subject to return to the clinic for final safety assessments scheduled as early as practically feasible following the decision to withdraw from the study. Subjects were questioned regarding their reason for withdrawal. At the early withdrawal visit, every effort was made to complete the following assessments:

- Assess symptoms by spontaneous reporting of AEs and by asking the subjects to respond to a non-leading question such as "How do you feel?";
- Obtain information regarding the occurrence of AEs;
- Assess supine BP, pulse rate and oral temperature;

- Obtain triplicate 12-lead ECG measurement;
- Collect a blood sample for PK analysis;
- Collect blood and urine samples for safety laboratory tests;
- Collect serum pregnancy test for females of childbearing potential;
- Conduct a limited physical examination if there was a new or open AE or clinically significant abnormal physical finding from the last visit;
- Confirm proper contraception was used;
- Administer the since last visit C-SSRS;
- Assess concomitant treatments;
- Discharge from unit.

Lack of completion of all or any of the early termination procedures were not viewed as protocol deviations so long as the subject's safety was preserved. If the subject withdraws from the study and also withdraws consent for disclosure of future information, no further evaluations were performed and no additional data were collected. The sponsor retained and could have continued to use any data collected before the withdrawal of consent.

9.3.4. Lifestyle Guidelines

9.3.4.1. Meals and Dietary Restrictions

- Days 1 and 14 (days when PK and ECG evaluations were planned) - morning dosing occurred on these days following an overnight fast of at least 10 hours before the morning dose administrations (PK and ECG assessments), and subjects were required to continue fasting for 4 hours post-morning dose. Water was permitted until 1 hour prior to IP administration. Water could be consumed without restriction beginning 1 hour after dosing;
- Subjects fasted on Day 15 when obtaining trough ECG and PK measurement for all treatments;
- Other days - breakfast could be completed 30 minutes prior to IP administration on other study days (Days 2 to 13) of Treatments A, B and C;
- The time of meals was standardized between study days and study periods;
- Subjects were restricted to consuming ambient temperature beverages in each study period until the 24-hour ECG collection;

- Subjects had to abstain from all food and drink (except water) at least 4 hours prior to any safety laboratory evaluations and 8 hours prior to the start of PK sample collections;

- Subjects had to abstain from drinks, including water, for 0.5 hours prior to any ECG measurement. Non-caffeinated drinks (except grapefruit or grapefruit-related citrus fruit juices – see below) could be consumed with meals and the evening snack;

- Lunch was provided approximately 4 hours after morning dosing for each period;

- Dinner was provided approximately 9 to 10 hours after morning dosing;

- An evening snack was permitted;

- Subjects were not allowed to eat or drink grapefruit or grapefruit-related citrus fruits (eg, Seville oranges, pomelos) from 7 days prior to the first dose of study IP until collection of the final PK blood sample;

- While confined, the total daily nutritional composition was approximately 55% carbohydrate, 30% fat and 15% protein. The daily caloric intake per subject not exceeded approximately 3200 kcal.

9.3.4.2. Alcohol, Caffeine and Tobacco

- Subjects had to abstain from alcohol for 24 hours prior to admission to the CRU and continued abstaining from alcohol until the final PK sample of each study period had been collected. Subjects could have undergone an alcohol breath test or blood alcohol test at the discretion of the investigator;

- Subjects had to abstain from caffeine-containing products for 24 hours prior to the start of dosing until the final PK sample of each study period had been collected;

- Subjects had to abstain from the use of tobacco- or nicotine-containing products for 24 hours prior to dosing and during confinement in the research unit.

9.3.4.3. Activity

- Subjects had to abstain from strenuous exercise (eg, heavy lifting, weight training, calisthenics, and aerobics) for at least 48 hours prior to each blood collection for clinical laboratory tests. Walking at a normal pace was permitted.

9.3.4.4. Contraception

All male subjects who were able to father children and female subjects who were of childbearing potential and who were sexually active and at risk for pregnancy agreed to use at least 1 highly effective method of contraception consistently and correctly for the duration of the active treatment period and for at least 28 days after the last dose of IP.

If at least 1 form of highly effective contraception from the list was used, then contraception used by the partner was enough provided that the male subject knows it must be used consistently and correctly, tells the investigator it was being used consistently and correctly and the investigator documented the conversation. If the subject was unable to confirm that his partner was reliably and correctly taking her contraception, then the subject was needed to use another form of highly effective contraception (and the use of a condom alone without spermicide was not regarded as a highly effective form of contraception).

The investigator or his/her designee, in consultation with the subject, confirmed that the subject had selected the most appropriate method of contraception for the individual subject and his or her partner from the permitted list of contraception methods (see below) and instructed the subject in its consistent and correct use. Subjects needed to affirm that they met the criteria for the correct use of at least 1 of the selected methods of contraception. The investigator or his/her designee discussed with the subject the need to use highly effective contraception consistently and correctly according to the schedule of activities (Table 2) and documented such conversation in the subject's chart. In addition, the investigator or his/her designee instructed the subject to call immediately if the selected contraception methods were discontinued or if pregnancy was known or suspected in the subject or subject's partner.

Highly effective methods of contraception were those that, alone or in combination, resulted in a failure rate of <1% per year when used consistently and correctly (ie, perfect use) and included the following:

- Established use of oral, inserted, transdermal, injected, or implanted hormonal methods of contraception was allowed provided the subject planned to remain on the same treatment throughout the entire study and was using that hormonal contraceptive for an adequate period of time to ensure effectiveness.

- Correctly placed copper-containing intrauterine device.

- Male condom or female condom used with a spermicide (ie, foam, gel, film, cream, or suppository). For countries where spermicide was not available or condom plus spermicide was not accepted as highly effective contraception, this option was not appropriate.

- Male sterilization with absence of sperm in the postvasectomy ejaculate.

- Bilateral tubal ligation/bilateral salpingectomy or bilateral tubal occlusive procedure (provided that occlusion was confirmed in accordance with the device's label).

- Female partner who met the criteria for non-childbearing potential as described below.

  Female subjects of non-childbearing potential had to meet at least 1 of the following criteria:

[redacted]

a. Achieved postmenopausal status, defined as follows: cessation of regular menses for at least 12 consecutive months with no alternative pathological or physiological cause; and have a serum FSH level confirming the post-menopausal state;

b. Undergone a documented hysterectomy and/or bilateral oophorectomy;

c. Medically confirmed ovarian failure.

All other female subjects (including females with tubal ligations) were considered to be of childbearing potential.

All sexually active male subjects agreed to prevent potential transfer of and exposure to drug through semen to their partners by using a condom consistently and correctly, beginning with the first dose of IP and continuing for at least 28 days after the last dose.

9.4. Treatments

9.4.1. Treatments Administered

Sertraline 50 mg tablets and matching placebo tablets and moxifloxacin 400 mg (Avelox) tablets were packaged at the PCRU in individual dosing containers by 2 operators, one of whom was a qualified pharmacist.

Following an overnight fast of at least 10 hours (PK Days 1, 14 and 15 only), subjects received IPs at approximately 08:00 hours (±2 hours). Administration of IP on the other days occurred under the conditions described in Section 9.3.4.1. Investigator site personnel administered IP during each period with ambient temperature water to an approximately volume of 240 mL. Subjects were to swallow the IP as a whole, and were not to manipulate or chew the medication prior to swallowing.

For the sertraline treatment period, sertraline and the matching placebo (Treatments A and C) were administered BID on Days 2-13. Dosing for Day 1 was a 50 mg in the morning, for Day 2 a 50 mg sertraline was administered BID, for Day 3 doses were 50 mg for the morning and a 100 mg for the evening, on Days 4-5 a 100 mg was administered BID, for Day 6 a 100 mg dose was administered in the morning and a 200 mg dose in the evening, for Days 7-13 a dose of 200 mg was administered BID, on Day 14 a 200 mg was administered in the morning only. Sertraline doses were given in multiples of 50 mg.

For Treatment B, a single 400 mg dose of moxifloxacin was administered as open-label on Day 14, blind placebo was administered on Days 1-13.

The total number of tablets or matching placebo dispensed for Treatments A or C and Treatment B are given in Table 4 and Table 5 respectively.

[redacted]

Table 4. Total Number of Tablets or Matching Placebo Dispensed for Treatments A or C

Visit Day	Number of Sertraline Hydrochloride 50 mg or Matching Placebo Tablets Dispensed	
	Morning (AM)	Evening (PM)
D1	1	0
D2	1	1
D3	1	2
D4 - D5	2	2
D6	2	4
D7 - D13	4	4
D14	4	0

Source: [redacted]
Treatment A = sertraline hydrochloride - double-blinded; Treatment C = placebo - double-blinded.
Abbreviations: AM = ante meridiem; D = day; PM = post meridiem.

Table 5. Total Number of Tablets Dispensed for Treatment B

Visit Day	Number of Placebo for Sertraline 50 mg Tablets Dispensed		Number of Moxifloxacin 400 mg Tablets Dispensed
	Morning (AM)	Evening (PM)	
D1	1	0	0
D2	1	1	0
D3	1	2	0
D4 - D5	2	2	0
D6	2	4	0
D7 - D13	4	4	0
D14	0	0	1

Source: [redacted]
Treatment B = moxifloxacin - positive control, open-label.
Abbreviations: AM = ante meridiem; D = day; PM = post meridiem.

In order to standardize the conditions on PK sampling days, all subjects were required to refrain from lying down (except when required for BP, pulse rate, and ECG measurements), eating, and drinking beverages other than water during the first 4 hours after dosing.

9.4.2. Identity of Investigational Products

Sertraline hydrochloride 50 mg tablets and matching placebo tablets were used in the study. Sertraline hydrochloride 50 mg tablets and matching placebo were supplied to the sponsor CRU pharmacy in bulk by the sponsor.

Moxifloxacin (Avelox) 400 mg film-coated tablets were supplied locally by the sponsor CRU.

[redacted]

The single reference safety document for moxifloxacin (Avelox) was the summary of product characteristics (Avelox).[5]

IPs were presented to the subjects in individual dosing containers. IP description is provided in Table 6.

Table 6. Investigational Product Description

Investigational Product Description	Vendor Lot Number	Pfizer Lot Number	Strength/Potency	Dosage Form
Placebo for sertraline HCl 50 mg blue film coated tablet	[redacted]	[redacted]	0 mg	Tablet
Sertraline HCl 50 mg blue film coated tablet (unmarked)	[redacted]	[redacted]	50 mg	Tablet

Source: [redacted]
Abbreviation: HCl = hydrochloride.

IPs were stored in its original container and in accordance with the label. Storage conditions stated in the Single Reference Safety Document (eg, United States package insert) were superseded by the storage conditions stated on the product label.

9.4.3. Method of Assigning Subjects to Treatment Groups

The investigator's knowledge of the treatment (moxifloxacin) should not have influenced the decision to enroll a particular subject or affect the order in which subjects were enrolled.

The investigative site assigned subject numbers to the subjects as they were screened for this study. The sponsor provided a randomization schedule to the investigator and, in accordance with the randomization numbers, the subject received the study treatment regimen assigned to the corresponding randomization number ([redacted]).

9.4.4. Selection of Doses in the Study

The approved therapeutic dosage regimen for sertraline hydrochloride is an initial dose of 25 or 50 mg administered once daily, and the dose may be increased up to a maximum of 150 mg/day or 200 mg/day, depending on the indication.[1]

The proposed starting dose for this study was 50 mg on Day 1. Thereafter, the dose was increased in increments of 50 mg/day or 100 mg/day to a maximum dose of 400 mg/day, achieved on Day 7. The 400 mg/day dose was then continued from Day 8 to Day 14 (on Day 14 only the morning dose of 200 mg was administered, and no evening dose was administered). This dose escalation schema was anticipated to be tolerated in healthy volunteers and was designed to achieve supratherapeutic concentrations by Day 14.

It was anticipated that by Day 14, the supratherapeutic concentration of sertraline following the 400 mg/day dose was about 3-fold higher than the concentration achieved after the maximum therapeutic dose of 200 mg/day.

9.4.5. Selection and Timing of Dose for Each Subject

Refer to Section 9.4.4 for selection of dose and Section 9.4.1 for timing of dose.

9.4.6. Blinding

The subjects, investigator and site personnel involved in the study (except for the pharmacy staff) were blinded to IPs (except open-label moxifloxacin), while the sponsor was un-blinded for other details please see Section 9.4.1.

At the initiation of the study, the study site was instructed on the method for breaking the blind. The method was an electronic process. Blinding codes were to broken only in emergency situations for reasons of subject safety. Whenever possible, the investigator or subinvestigator needed to consult with a member of the study team prior to breaking the blind. When the blinding code was broken, the reason was fully documented and entered into PIMS.

9.4.7. Prior and Concomitant Medications and Procedures

Treatments taken within 28 days before the first dose of study IP were documented as a prior treatment. Treatments taken after the first dose of study IP were documented as concomitant treatments. Restrictions on prior and concomitant medication are described in Section 9.3.2.

Subjects were to abstain from all concomitant treatments, except for the treatment of AEs and drugs listed in exclusion criteria number 10 in Section 9.3.2. Limited use of nonprescription medications that were not believed to affect subject safety or the overall results of the study were permitted on a case-by-case basis following approval by the sponsor. Hormonal contraception treatments were allowed.

All concomitant treatments taken during the study were recorded with indication, daily dose, and start and stop dates of administration. All subjects were questioned about concomitant treatment at each clinic visit.

9.4.8. Treatment Compliance

Study treatment was administered under the supervision of investigator site personnel. The oral cavity of each subject was examined following dosing to assure the study drug was taken.

9.5. Efficacy, Safety, Pharmacokinetic and Pharmacodynamic Evaluations

9.5.1. Appropriateness of Measurements

The measures of PK and safety in this study were standard measurements, widely used and generally recognized as reliable, accurate, and relevant. The safety measurements recorded in this clinical study are those employed in most clinical studies, including the recording of AEs. Medical Dictionary for Regulatory Activities (MedDRA), Version 19.0 coding was applied.

9.5.2. Efficacy Evaluations (Not Applicable)

There were no efficacy evaluations done in this study.

9.5.3. Other Evaluations (Not Applicable)

There were no additional nonsafety evaluations in this study.

9.5.4. Pharmacokinetic Evaluations

9.5.4.1. Pharmacokinetic Sampling

During all study periods, blood samples (4 mL) to provide approximately 1.5 mL plasma for PK analysis were collected into appropriately labeled tubes containing sodium heparin at times specified in Table 2 and Table 3.

The actual times might have changed but the number of samples remained the same. All IPs had identical sample collection timepoints. All efforts were made to obtain the PK samples at the exact nominal time relative to dosing. However, samples obtained within 10% of the nominal time (eg, within 6 minutes of a 60 minute sample) from dosing were not captured as a protocol deviation, as long as the exact time of the sample collection was noted on the source document and DCT.

- Samples from Treatment A were analyzed using a validated analytical method for sertraline hydrochloride and its metabolite in compliance with sponsor standard operating procedures (SOPs). Samples for Treatment C (placebo) were only analyzed if deemed necessary. Samples from Treatment B (moxifloxacin) on Day 14 (1, 2, 3, 4 and 5 hours only) were analyzed if deemed necessary;

- The PK samples were processed and shipped as indicated to maintain sample integrity. Any deviations from the PK processing steps, including any actions taken, were documented and reported to the sponsor. On a case-by-case basis, the sponsor could have made a determination as to whether sample integrity had been compromised. Any sample deemed outside of established stability, or of questionable integrity, was considered a protocol deviation;

- As part of understanding the PK of the study drug, samples might have been used for metabolite identification and/or evaluation of the bioanalytical method, as well as for other internal exploratory purposes. These data is not included in this clinical study report (CSR). Samples collected for this purpose were retained in accordance with local regulations and, if not used within this timeframe, will be destroyed. These data will be used for internal exploratory purposes and is not included in this CSR.

9.5.4.2. Pharmacokinetic Analytical Methods

Plasma samples were analyzed for sertraline and N-desmethylsertraline concentrations at Covance using a validated analytical assay in compliance with Pfizer SOPs. Sertraline and N-desmethylsertraline samples were assayed using a validated, sensitive and specific liquid chromatography tandem mass spectrometric method. The performance of the method during validation is documented in CRO/Pfizer method validation report [redacted]

[redacted]

Plasma specimens were stored at approximately -70°C until analysis and assayed within the 249 days of established stability data generated during validation. Calibration standard responses were linear over the range of 0.500 to 250 ng/mL; using a weighted ($1/concentration^2$) linear least squares regression. Those samples with concentrations above the upper limits of quantification were adequately diluted into calibration range. The lower limit of quantification (LLOQ) for sertraline and N-desmethylsertraline was 0.500 ng/mL. Clinical specimens with plasma sertraline and N-desmethylsertraline concentrations below the LLOQ are reported as below lower limit of quantification (BLQ).

Sertraline:

The between-day assay accuracy, expressed as percent relative error (%RE), for Quality Control (QC) concentrations, ranged from -3.5% to 0.0% for the low, low-medium, medium, high and diluted QC samples. Assay precision, expressed as the between-day percent coefficients of variation (% CV) of the mean estimated concentrations of QC samples was ≤4.5% for low (1.50 ng/mL), low-medium (15.0 ng/mL), medium (100 ng/mL), high (200 ng/mL) and diluted (1000 ng/mL) concentrations.

N-Desmethylsertraline:

The between-day assay accuracy, expressed as %RE, for QC concentrations, ranged from - 1.6% to 0.7% for the low, low-medium, medium, high and diluted QC samples. Assay precision, expressed as the between-day percent coefficients of variation (%CV) of the mean estimated concentrations of QC samples was ≤9.3% for low (1.50 ng/mL), low-medium (15.0 ng/mL), medium (100 ng/mL), high (200 ng/mL) and diluted (1000 ng/mL) concentrations.

The sample analysis report corresponding to this work is included in [redacted]

9.5.4.3. Calculation of Pharmacokinetic Parameters

The following PK parameters for sertraline and its metabolite N-desmethylsertraline were calculated for each subject and treatment, as applicable, using noncompartmental analysis of concentration-time data as listed in Table 7. Samples below the lower limit of quantitation were set to 0 for analysis. Actual sample collection times were used for the PK analysis.

[redacted]

[redacted]

Table 7. Pharmacokinetic Parameters Determined

Parameter	Definition	Method of Determination
Single Dose		
C_{max}	Maximum plasma concentration.	Observed directly from data.
$C_{max}(dn)$[a]	Dose normalized C_{max}.	C_{max}/Dose.
T_{max}	Time for C_{max}.	Observed directly from data as time of first occurrence.
AUC_{24}	Area under the plasma concentration-time profile from time 0 to 24 hours postdose.	Linear/Log trapezoidal method.
$AUC_{24}(dn)$[a]	Dose normalized AUC_{24}.	AUC_{24}/Dose.
MR[b]	Metabolite to parent ratio for AUC_{24} (the ratio of the metabolite AUC_{24} to the parent AUC_{24}, corrected for molecular weights [MW]).	(AUC_{24} metabolite/AUC_{24} parent) × (MW parent/MW metabolite).
Multiple Dose		
C_{max}	Maximum plasma concentration.	Observed directly from data.
$C_{max}(dn)$[a]	Dose normalized C_{max}.	C_{max}/Dose.
T_{max}	Time for C_{max}.	Observed directly from data as time of first occurrence.
AUC_{24}	Area under the plasma concentration-time profile from time 0 to 24 hours post dose.	Linear/Log trapezoidal method.
$AUC_{24}(dn)$[a]	Dose normalized AUC_{24}.	AUC_{24}/Dose.
AUC_{last}	Area under the concentration-time curve from time 0 to the time of the last quantifiable concentration (C_{last}).	Linear/Log trapezoidal method.
$t_{½}$[c]	Terminal half-life.	$Log_e(2)/k_{el}$, where k_{el} is the terminal phase rate constant calculated by a linear regression of the log-linear concentration-time curve. Only those data points judged to describe the terminal log-linear decline will be used in the regression.
C_{min}	Minimum plasma concentration over the 0-24 hour period after the last dose on Day 14.	Observed directly from data.
R_{ac}	Observed accumulation ratio for AUC_{24}.	Day 14 $AUC_{24}(dn)$/Day 1 $AUC_{24}(dn)$.
$R_{ac,Cmax}$	Observed accumulation ratio for C_{max}.	Day 14 $C_{max}(dn)$/Day 1 $C_{max}(dn)$.
MR[b]	Metabolite to parent ratio for AUC_{24} (the ratio of the metabolite AUC_{24} to the parent AUC_{24}, corrected for MW).	(AUC_{24} metabolite/AUC_{24} parent) × (MW parent/MW metabolite).

Source: [redacted]
Abbreviation: MW = molecular weight.
Pharmacokinetic parameter values were calculated using an internally validated electronic noncompartmental analysis software, eNCA (Version 2.2.4).

a. For sertraline only; dose = 50 mg on Day 1 and 200 mg on Day 14.
b. For metabolite only; MW = molecular weight = 306.2 for parent (sertraline) and 292.2 for metabolite (n-desmethylsertraline).
c. If data permit.

[redacted]

Supporting data from the estimation of $t_{½}$ were also reported: terminal phase rate constant (k_{el}); the first, last, and number of time points used for the log-linear regression ($k_{el,t(lo)}$, $k_{el,t(hi)}$, and $k_{el,t(n)}$); goodness-of-fit statistic from the regression (r^2); and the percent of the area under the plasma concentration-time curve from time 0 to infinite time, AUC_{inf}, obtained by forward extrapolation (AUC_{extrap}%).

Unless otherwise noted, parameters marked "if data permit" were reported only where a well-characterized terminal phase was observed. A well-characterized terminal phase is defined as one with at least 3 data points, $r^2 \geq 0.9$, and $AUC_{extrap}\% \leq 20$.

9.5.5. Pharmacodynamic Evaluations (Not Applicable)

There were no pharmacodynamic evaluations done in this study.

9.5.6. Pharmacogenomic Evaluations (Not Applicable)

There were no pharmacogenomic samples collected in this study.

9.5.7. Safety Evaluations

9.5.7.1. Adverse Events

The investigator obtained and recorded in PIMS all observed or volunteered AEs, the severity (mild, moderate, or severe) of the events, and the investigator's opinion of the relationship to the study drug. These AEs included adverse drug reactions, illnesses with onset during the study, and exacerbation of previous illnesses. Additionally, the investigator recorded as AEs any clinically significant changes in physical examination findings and abnormal objective test findings (eg, ECG, laboratory). See the final protocol ([redacted]) for additional details concerning AE reporting.

For all AEs, the investigator pursued and obtained information adequate to determine both the outcome of the AE and whether it met the criteria for classification as a serious adverse event (SAE, Section 9.5.7.2). If the AE or its sequelae persisted, follow-up was required until resolution or stabilization occurred at a level acceptable to the investigator and sponsor. For all AEs, sufficient information had to be obtained by the investigator to determine the causality of the AE.

Medication errors could have resulted in this study from the administration or consumption of the wrong product, by the wrong subject, at the wrong time, or at the wrong dosage strength. Such medication errors occurring to a study participant were to be captured on the medication error PIMS which was a specific version of the AE page and on the SAE form when appropriate. In the event of medication dosing error, the sponsor was to be notified immediately.

Medication errors were reportable irrespective of the presence of an associated AE/SAE, including:

- Medication errors involving subject exposure to the study drug;

[redacted]

- Potential medication errors or uses outside of what was foreseen in the protocol that did or did not involve the participating subject.

Whether or not the medication error was accompanied by an AE, as determined by the investigator, the medication error and, if applicable, any associated AE(s) was captured on an AE PIMS page.

9.5.7.2. Serious Adverse Events

Regardless of treatment group or suspected relationship to the IP, all SAEs (as defined below) were to be reported immediately to the sponsor.

An SAE was defined as any AE at any dose that:

- Resulted in death;
- Was life threatening (immediate risk of death);
- Required inpatient hospitalization or prolongation of existing hospitalization;
- Resulted in a persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions); or
- Resulted in congenital anomaly/birth defect.

Other important medical events were considered SAEs if they jeopardized the subject or required medical or surgical intervention to prevent 1 of the outcomes listed in this definition.

Regardless of the above criteria, any AE that the sponsor or investigator considered serious was to have been immediately reported as an SAE.

SAE or death was reported immediately if it occurred or came to the attention of the investigator at any time during the study through the last follow-up visit or 28 calendar days after the last dose of the IP, whichever was later. Any SAE occurring at any other time after completion of the study was promptly reported if a causal relationship to the IP was suspected.

For all SAEs, the investigator was obligated to pursue and provide information on the PIMS and additional information as requested by the sponsor. Generally, this included a detailed description of the AE, which allowed a complete assessment of the case and determination of the possible causality by the sponsor. The investigator's assessment of causality was also provided. If causality was unknown and the investigator did not know whether the IP caused the event, then it was attributed to the IP. If a subject died and an autopsy was performed, a summary of available autopsy findings was submitted to the sponsor.

9.5.7.3. Potential Cases of Drug-Induced Liver Injury

Liver Function Tests (LFTs) were not required as a routine safety monitoring procedure in this study. However, when investigator deem it necessary to run LFTs because of clinical sign/symptom presentation in a subject, such LFT results were to be handled and followed up as described below.

Abnormal values in AST and/or ALT levels concurrent with abnormal elevations in total bilirubin level that meet the criteria outlined below in the absence of other causes of liver injury were to be considered potential cases of drug-induced liver injury (potential Hy's law cases) and were to be always considered important medical events.

The threshold of laboratory abnormalities for a potential case of drug-induced liver injury depended on the subject's individual baseline values and underlying conditions. Subjects who presented with the following laboratory abnormalities were evaluated further to definitively determine the etiology of the abnormal laboratory values:

- Subjects with AST or ALT and total bilirubin baseline values within the normal range who subsequently present with AST or ALT values ≥3 × ULN concurrent with a total bilirubin value ≥2 × ULN with no evidence of hemolysis and an alkaline phosphatase (ALP) value ≤2 × ULN or not available;

- For subjects with preexisting ALT or AST or total bilirubin values above the ULN, the following threshold values were used in the definition mentioned above:

    - For subjects with preexisting AST or ALT baseline values above the normal range: AST or ALT values ≥2 times the baseline values and ≥3 × ULN, or ≥8 × ULN (whichever was smaller).

- Concurrent with:

    - For subjects with preexisting values of total bilirubin above the normal range: total bilirubin level increased from baseline by an amount of at least 1 × ULN or if the value reaches ≥3 × ULN (whichever was smaller).

The subject returned to the investigational site and evaluated as soon as possible, preferably within 48 hours from awareness of the abnormal results. This evaluation included laboratory tests, detailed history and physical assessment.

In addition to repeating measurements of AST and ALT, laboratory tests included albumin, creatine kinase, total bilirubin, direct and indirect bilirubin, gamma-glutamyl transferase, prothrombin time/international normalized ratio, and ALP. A detailed history, including relevant information, such as review of ethanol, acetaminophen, recreational drug and supplement consumption, family history, occupational exposure, sexual history, travel history, history of contact with a jaundiced person, surgery, blood transfusion, history of liver or allergic disease, and work exposure, were collected. Further testing for acute hepatitis A, B, or C infection and liver imaging (eg, biliary tract) was warranted. All cases confirmed on

repeat testing as meeting the laboratory criteria defined above, with no other cause for LFT abnormalities identified at the time, were to be considered potential Hy's law cases irrespective of availability of all the results of the investigations performed to determine etiology of the abnormal LFTs. Such potential Hy's law cases were to be reported as SAEs.

9.5.7.4. Laboratory Evaluations

The laboratory evaluations as listed in Table 8 were performed at times defined in Table 2. Additional laboratory results could be reported on these samples as a result of the method of analysis or the type of analyzer used by the clinical laboratory; or as derived from calculated values. These additional tests could not require additional collection of blood. Unscheduled clinical laboratory could be obtained at any time during the study to assess any perceived safety concerns.

Table 8. Laboratory Tests

Hematology	Chemistry	Urinalysis	Other
Hemoglobin	BUN/urea and creatinine	pH	FSH[b]
Hematocrit	Glucose (fasting)	Glucose (qual)	Urine drug screening[c]
RBC count	Calcium	Protein (qual)	β-hCG[d]
MCV	Sodium	Blood (qual)	
MCH	Potassium	Ketones	
MCHC	Chloride	Nitrites	
Platelet count	Total CO_2 (bicarbonate)	Leukocyte esterase	
WBC count	AST, ALT	Urobilinogen	
Total neutrophils (Abs)	Total bilirubin	Urine bilirubin	
Eosinophils (Abs)	Alkaline phosphatase	Microscopy[a]	
Monocytes (Abs)	Uric acid		
Basophils (Abs)	Albumin		
Lymphocytes (Abs)	Total protein		
	Additional Tests (Needed for Hy's Law)		
	AST, ALT (repeat)		
	Total bilirubin (repeat)		
	Albumin (repeat)		
	Alkaline phosphatase (repeat)		
	Direct bilirubin		
	Indirect bilirubin		
	Creatine kinase		
	GGT		
	PT/INR		

Source: [redacted]

Abbreviations: β-hCG = beta-subunit of human chorionic gonadotropin; Abs = absolute; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CO_2 = carbon dioxide; FSH = follicle-stimulating hormone; GGT = gamma-glutamyl transferase; INR = international normalized ratio; MCH = Mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; MCV = mean corpuscular volume; pH = hydrogen ion concentration (negative log); PT = prothrombin time; qual = qualitative; RBC = red blood cell; WBC = white blood cell.

a. Only if urine dipstick was positive for blood, protein, nitrites or leukocyte esterase.
b. At Screening only, in females who were amenorrheic for at least 12 consecutive months.
c. At Screening and Day 0 only.
d. Serum β-hCG for females of childbearing potential.

[redacted]

Minimum requirement for drug screening included: cocaine, tetrahydrocannabinol, opiates/opioids, benzodiazepines and amphetamines.

Subjects might have undergone random urine drug screening at the discretion of the investigator. Drug screening conducted prior to dosing must be negative for subjects to receive IP.

All clinically important abnormal laboratory tests occurring during the study were repeated at appropriate intervals until laboratory values:

- Returned to baseline;
- Returned to a level deemed acceptable by the investigator and the sponsor or the designated representative; or
- Were explained by a diagnosis.

9.5.7.5. Other Safety Measures

The below mentioned other safety measures were collected or measured at time points as detailed in Table 2. Additional collection times, or changes to collection times of BP and pulse rate was permitted, as necessary, to ensure appropriate collection of safety data.

9.5.7.5.1. Pregnancy Testing

For female subjects of childbearing potential, a serum pregnancy test, with sensitivity of at least 25 mIU/mL, was performed at Screening, admission (Day 0) of all study periods, and prior to discharge on Day 17 of Period 3 (end of study) or early withdrawal. Results were obtained prior to dosing during each period.

A negative pregnancy result was required before the subject may have been received the study drug. Pregnancy tests were also done whenever 1 menstrual cycle was missed during the active treatment period (or when potential pregnancy was otherwise suspected). Pregnancy tests may have also been repeated as per request of IRB or if required by local regulations.

9.5.7.5.2. Physical Examinations

Physical examinations were conducted by a physician, trained physician's assistant, or nurse practitioner as acceptable according to local regulation. A full physical examination included head, ears, eyes, nose, mouth, skin, heart and lung examinations, lymph nodes, gastrointestinal, musculoskeletal, and neurological systems. The limited or abbreviated physical examination was focused on general appearance, the respiratory and cardiovascular systems, as well as towards subject reported symptoms. For measuring weight, a scale with appropriate range and resolution was used.

9.5.7.5.3. Vital Signs: Blood Pressure, Pulse Rate and Temperature

Supine BP was measured with the subject's arm supported at the level of the heart, and recorded to the nearest mm Hg after at least 5 minutes of rest. The same arm (preferably the dominant arm) was used throughout the study. BP from the arm with an intravenous infusion was not recorded. Subjects were instructed not to speak during measurements.

The same properly sized and calibrated BP cuff was used to measure BP at each time. The use of an automated device for measuring BP and pulse rate was acceptable, although, when done manually, pulse rate was measured in the brachial/radial artery for at least 30 seconds. At the times when the timing of these measurements coincided with a blood collection, BP and pulse rate were obtained prior to the nominal time of the blood collection.

Temperature was measured orally. No eating, drinking or smoking was allowed for 15 minutes prior to the measurement.

9.5.7.5.4. Electrocardiogram

ECG evaluations were done at time specified in Table 2 and Table 3. Subjects abstained from drinks, including water, for approximately 0.5 hours prior to any ECG measurement.

All scheduled ECGs were performed after the subject had rested quietly for at least 10 minutes in a supine position.

Triplicate 12-lead ECGs were obtained approximately 2 minutes apart; the predose assessments (-1, -0.5 and 0 hours) occurred immediately prior to the ante meridiem (AM) dose on Day 1; the average of the 3 triplicate ECG measurements collected predose on Day 1 (ie, -1 hour, -0.5 hour, and 0 hour time points) of each period served as each subject's baseline QTc value. When the timing of these measurements coincided with a blood collection, the ECG was obtained prior to the nominal time of the blood collection, BP, pulse rate and temperature. The actual times could change but the number of ECGs collected remained the same.

During the treatment with active drug or placebo, if any subject demonstrated a change in QTc value from baseline of >45 msec or QT values of >500 msec the PI assessed the subject for potential discontinuation from this study.

To ensure safety of the subjects, a qualified individual at the investigator site made comparisons to baseline measurements.

If the QTc interval was increased by ≥45 msec from the baseline, or an absolute QTc value was ≥500 msec for any scheduled ECG, then 2 additional ECGs were collected, approximately 2 minutes apart, to confirm the original measurement. If either of the QTc values from these repeated ECGs remained above the threshold value (≥45 msec from the baseline; or was ≥500 msec), then a single ECG was repeated at least hourly until QTc values from 2 successive ECGs fell below the threshold value that triggered the repeated measurement.

If the average of QTc values from the triplicate measurements remained above the threshold value (≥45 msec from the baseline; or was ≥500 msec for QTc), then a single ECG was

repeated at least hourly until QTc values from 2 successive ECGs fell below the threshold value that triggered the repeated measurement.

If QTc values remained ≥500 msec (or ≥45 msec from the baseline) for >4 hours (or sooner at the discretion of the investigator); or QTc intervals get progressively longer, the subject underwent continuous ECG monitoring. A cardiologist was to be consulted if QTc intervals did not return to <500 msec (or to <45 msec above the baseline) after 8 hours of monitoring (or sooner at the discretion of the investigator).

In some cases, it may have been appropriate to repeat abnormal ECGs to rule out improper lead placement as contributing to the ECG abnormality. It was important that leads were placed in the same positions each time in order to achieve precise ECG recordings. If a machine-read QTc value was prolonged, as defined above, repeated measurements may not have been necessary if a qualified physician's interpretation determines that the QTc values were in the acceptable range.

The ECG source data for analyses on TQT studies conducted in healthy subjects were automated readings validated by trained human readers (semi-automated method).

9.5.7.5.5. Assessment of Suicidal Ideation and Behavior

The C-SSRS was an interview based rating scale to systematically assess suicidal ideation and suicidal behavior (SIB). Versions were available for Screening/Baseline (Lifetime) and follow-up visits (Since Last Visit).

The C-SSRS were collected at times specified in Table 2, by an appropriately trained PCRU staff member. The C-SSRS could also be administered at any time in this study at the discretion of the investigator based on any reasonable concern.

At each suicidal assessment, subjects who had significant suicidal ideation with actual plan and intent or suicidal behavior (based on C-SSRS results), were evaluated by a clinician/mental health professional (MHP) skilled in the evaluation of suicidality in the subjects by virtue of training or experience (eg, psychiatrist, licensed clinical psychologist) who determined if it was safe for the subject to participate/continue in this study. Specific criteria that indicated a need for such an assessment were:

- Suicidal ideation associated with actual intent and/or plan in the past year; "YES" answer to C-SSRS questions 4 "some intent to act without specific plan" or 5 "specific plan and intent";
- Previous history of suicide behaviors in the past 10 years (a "YES" answer to any of the suicidal behavior items of the C-SSRS with the behavior occurring in the past 10 years);
- In the investigator's judgment a risk assessment or exclusion was warranted.

A written copy of the risk assessment may have been included in the subject's clinical record (source documentation).

Other possible suicidality AEs or other clinical observations could, based on the judgment of the investigator, also trigger a risk assessment and require a narrative.

Suicidality AEs or other clinical observations could, based on the judgment of the investigator and clinician/MHP, also triggered a risk assessment and a narrative using information from the C-SSRS, and available information, prior to screening and baseline information, and the clinician/MHP assessment. When there was a positive response to any question on the C-SSRS, the investigator was to determine whether an AE had occurred.

At the Baseline visit (Screening or could have be performed Day 0, Period 1), a risk assessment was done by qualified staff at the PCRU to determine whether it was safe for the subject to be enrolled or to continue to participate in this study.

Any subject that responded yes to items 4 and 5 on the suicidal ideation subscale of the C-SSRS or yes to any behavioral question – at the Screening visit or Baseline or Post-Baseline visit had to be simply excluded from this study.

9.5.8. Biospecimen Banking (Not Applicable)

9.6. Data Quality Assurance

As this study was performed at PCRU, personnel at the unit were responsible for reviewing study procedures, comparing PIMS data to original clinical records, resolving data queries and providing details of protocol deviations in accordance with the unit's SOPs.

This CSR has been subject to QC review by the sponsor or the sponsor's designee. The QC processes were reviewed by the sponsor's own independent quality assurance group.

9.7. Statistical Methods Planned in the Protocol

9.7.1. Statistical and Analytical Plans

Detailed methodology for summarization and statistical analyses of the data collected in this study was documented in a statistical analysis plan (SAP) [redacted]).

9.7.2. Determination of Sample Size

A sample size of 42 subjects (7 per sequence) provided at least 99% power to exclude that upper bound of a 2-sided 90% CI (1-sided 95% CI) of time-matched difference between sertraline hydrochloride and placebo was >10 msec at each time point. The overall study power for 9 postdose time points on Day 14 was supposed to be at least 90%. These calculations were based upon the assumptions that expected mean difference between sertraline hydrochloride and placebo was no >5 msec at each time point and intra-subject variability was 5.36 msec.

Given a 1-sided significance of 0.05, 42 subjects provided 99% power to detect at least 5 msec difference between moxifloxacin and placebo at 3 hours postdose (historical moxifloxacin median T_{max}) to demonstrate assay sensitivity.

[redacted]

To allow for dropouts, 54 subjects (9 per sequence) were randomized to have 42 evaluable subjects.

9.7.3. Analysis of Pharmacokinetic Parameters

The PK concentration population was defined as all subjects enrolled and treated who had at least 1 concentration determined.

The PK parameter analysis population was defined as all subjects enrolled and treated who had at least 1 of the PK parameters of primary interest determined.

Sertraline and metabolite PK parameters were calculated using noncompartmental methods and subsequently summarized descriptively by treatment and day as specified in Table 9.

Table 9. Summary Statistics for Pharmacokinetic Parameters

Day	Parameter	Summary Statistics	Analysis Scale
Single dose	C_{max}, C_{max}(dn), AUC_{24}, AUC_{24}(dn), MR	N, arithmetic mean, median, %CV, SD, minimum, maximum, geometric mean and geometric %CV	ln
	T_{max}	N, median, minimum, maximum	R
Multiple dose	C_{max}, C_{max}(dn), AUC_{24}, AUC_{24}(dn), AUC_{last}, R_{ac} (R_{ac} [obs] and R_{ac} [C_{max}]) MR and C_{min}	N, arithmetic mean, median, %CV, SD, minimum, maximum, geometric mean and geometric %CV	ln
	T_{max}	N, median, minimum, maximum	R
	$t_{½}$	N, arithmetic mean, median, %CV, SD, minimum, maximum	R

Source: [redacted]
For PK parameter definitions please see Table 7.
Abbreviations: %CV = percent coefficients of variation; C_{min} = minimum observed concentration during the dosing interval; ln = natural-log transformed; MR = metabolite to parent ratio; N = number; PK = pharmacokinetic; R = raw (untransformed); SD = standard deviation.

Supporting data from the estimation of $t_{½}$ were listed by treatment: k_{el}; goodness of fit statistic from the r^2; and the first, last, and number of time points used in the estimation of k_{el}.

9.7.4. Pharmacokinetic and Pharmacodynamic (Exposure-Response) (Electrocardiogram) Analysis

A linear mixed effect modeling approach was undertaken to characterize the relationship between baseline corrected QTc (QT corrected for heart rate using Bazett's formula [QTcB], QTcF, and/or estimated QT corrected for heart rate using a study population-based approach [QTcN]) interval and plasma concentrations of sertraline/N-desmethylsertraline. The following linear mixed model was used to characterize that relationship.

$$\Delta QTc_{ijk} = \left(\mu + TRT_j + t_k + \eta_{\mu,i}\right) + \theta_0\left(B_{QTc,i} - \bar{B}\right) + \left(\theta_1 + \eta_{C,i}\right)C_{ijk} + \varepsilon_{ijk}$$

where i is the i^{th} subject, j is the j^{th} treatment, k is the k^{th} time point relative to dosing, μ is the intercept, TRT is the j^{th} treatment effect, k is the k^{th} time effect, $B_{QTc,i}$ is the baseline QTc for the i^{th} subject for the j^{th} treatment, $\bar{B}$ is the population mean baseline QTc, C_{ijk} is the

[redacted]

concentration at the k^{th} time point for Treatment j for Subject i, ΔQTc_{ijk} is the change from baseline in QTc at the k^{th} time point for Treatment j for Subject i, θ_0 is the change in the baseline QTc, θ_1 is the slope. Under this model, the intercept is treatment-specific for each subject. An unstructured covariance matrix is the preferred random effects covariance matrix because it does not impose constraints on the variances. $\eta_{\mu,i}$ and $\eta_{C,i}$ were the subject-specific random effects for the intercept and slope, respectively, having mean [0, 0] and unstructured covariance. ε are independent residuals having mean 0 and variance σ^2. The average of the triplicate QTc values at each time point was used for this analysis. Visual and statistical metrics were used to assess the adequacy of linear models.

9.7.5. Safety Parameters

All subjects who received at least 1 dose of IP were included in the safety analyses and listings.

AEs, ECGs, BP, vital signs, pulse rate, and safety laboratory data were reviewed and summarized on an ongoing basis during the study to evaluate the safety of subjects. Any clinical laboratory, ECG, BP, and PR abnormalities of potential clinical concern as defined in [redacted] were described. Suicidality was assessed using C-SSRS. Safety data were presented in tabular and/or graphical format and summarized descriptively, where appropriate.

Medical history and physical examination and neurologic examination information, as applicable, collected during the course of the study was considered source data and was not reported, unless otherwise noted. However, any untoward findings identified on physical and/or neurologic examinations conducted after the administration of the first dose of IP was captured as an AE, if those findings meet the definition of an AE. Data collected at screening that was used for inclusion/exclusion criteria, such as laboratory data, ECGs and vital signs were considered source data, and are not reported, unless otherwise noted. Demographic data collected at screening was reported.

9.7.5.1. Adverse Events

AEs were reported in accordance with the sponsor's reporting standards. SAE presentations were derived from a combination of data in the clinical study database and the corporate safety database. The corporate safety database was a separate, centralized, AE monitoring database that was continuously updated based on rapidly communicated reports from the investigators to the sponsor (as per Section 9.5.7.2). The clinical study database was based on information provided from the PIMS. Consequently, occasional differences in data may exist between the centralized safety database and the clinical study database.

9.7.5.2. Clinical Laboratory Parameters

Safety laboratory parameters (Table 8) were listed in accordance with the sponsor's reporting standards.

[redacted]

9.7.5.3. Other Safety Parameters

9.7.5.3.1. Vital Signs

The baseline measurement was the average of the predose measurements taken on Day 1 of each period. For each planned timepoint, baseline values and change from Baseline in vital signs (supine BP and pulse rate) was summarized with descriptive statistics (using sponsor default standards) by treatment. These data was listed in accordance with the sponsor reporting standards. Additionally, standing vital signs were listed only.

9.7.5.3.2. Suicidality Assessment Columbia – Suicide Severity Rating Scale

Assessment of SIB based on C-SSRS was listed by treatment as per the sponsor's reporting standards.

9.7.5.3.3. Electrocardiogram Analysis

Primary ECG Analysis Population: The primary ECG analysis population was defined as all subjects randomized and treated who had at least 1 postdose ECG measurement in at least 1 period. Analysis sets might contain different numbers of subjects for different ECG parameters based on availability of data.

Completer ECG Analysis Population: The completer ECG analysis population was defined as all subjects randomized and treated and completed all 3 treatment periods, at least up to Day 15 (24-hour Day 14) ECG measurements.

Derivation of ECG Parameters Prior to Analysis:

The average of the triplicate ECGs collected at each time was calculated. Baseline was defined as the mean of the 3 average triplicate measurements taken at the following 3 time points (-1 hour, -0.5 hour, 0 hour) before dosing within each period. The QT intervals, QTcF, QTcB, PR intervals, RR, QRS interval and heart rate were recorded at each assessment time indicated in Table 2 and Table 3. If QTcF was not supplied then it was derived using Fridericia's heart rate correction formula:

- $QTcF(msec) = QT(msec)/(RR)^{1/3}$ where RR(sec) = 60/heart rate (if not provided)

If not supplied, QTcB intervals were derived using Bazett's heart rate correction formula:

- $QTcB(msec) = QT(msec)/(RR)^{1/2}$ where RR(sec) = 60/heart rate (if not provided)

Changes from baseline for QTcF, QTcB uncorrected QT, PR, QRS, and heart rate were calculated for each subject and treatment at each time point.

The maximum absolute postdose value and the maximum increase from baseline for QTcF, QTcB, uncorrected QT, PR, QRS, and heart rate were determined for each subject and treatment.

Additionally, individually corrected QT interval (QTcI) and QTcN were computed using individual and population correction methods.

[redacted]

Averages of triplicate ECG measurements were used in all statistical analyses.

If subjects vomited on Day 14 within 2 hours of dosing, data from subjects on this day were excluded from PK and ECG statistical analyses.

Primary Analysis: Primary analysis was conducted in the primary ECG analysis population.

The postdose QTcF intervals were analyzed (Day 14 data for sertraline hydrochloride, placebo, and moxifloxacin) with baseline as a covariate. Analysis of covariance using a mixed effect model with sequence, period, treatment, time, and treatment-by-time interaction as fixed effects, subject within sequence as a random effect and baseline QTcF as a covariate was conducted.

If a significant period effect was found, a mixed effect model with sequence, period, treatment, period-by-treatment interaction, carry-over, time, treatment-by-time interaction as fixed effects, subject within sequence as a random effect and baseline QTcF as a covariate was to be conducted.

The 90% CIs (equivalent to a 1-sided 95% CI) for time-matched change from placebo in QTcF at each time point on Day 14 was computed for both sertraline hydrochloride and moxifloxacin, separately.

Lack of Effect of Sertraline on QTc Intervals Assessment: A lack of an effect of sertraline hydrochloride on QTc intervals was concluded if the upper bounds of the 2-sided 90% (equivalent to 1-sided 95%) CIs for all the time-matched mean differences between sertraline hydrochloride and placebo were <10 msec.

Assay Sensitivity Assessment: This study had been deemed adequately sensitive to detect QT/QTc prolongation if the lower bound of the 2-sided 90% CI for the mean difference between moxifloxacin and placebo was >5 msec at the historic T_{max} of moxifloxacin (3 hours postdose).

Sensitivity Analysis: At the completion of the study, if >10% of subjects dropped out or had missing data for 1 or more treatment periods, primary analysis outlined above was conducted in the Completer ECG Analysis Population also.

Additional Analyses: Additional analysis was conducted in the primary ECG analysis population. Relationship between QTc prolongation and sertraline/metabolite plasma concentration was examined graphically. Exposure response analysis was performed to establish relationship between change in QTc from baseline and drug concentration. Categorical analysis of QTcF of both absolute postdose maximum and maximum increase from baseline was provided.

QT, QTcF, PR, heart rate, and QRS were summarized by treatment group, study day, and time point - both observed and change from baseline. Analyses conducted on QTcF were repeated on QTcB, QTcI and QTcN if deemed necessary.

9.8. Changes in the Conduct of the Study or Planned Analyses

There were no changes to the planned protocol and analysis.

10. STUDY SUBJECTS

10.1. Disposition of Subjects

Subject disposition is summarized in Table 10. A total of 54 subjects were randomized into the study. Fifty-two (52) subjects received sertraline and 50 subject each received moxifloxacin and placebo during the 3 periods of the study. A total of 9 subjects discontinued treatment during the double-blind period (5 subjects receiving sertraline, 3 subjects receiving placebo and 1 subject receiving moxifloxacin). Two (2) subjects receiving sertraline were discontinued from the study due to AEs (Tables 14.1.1.2, 14.3.1.1.1 [redacted]).

- Subject [redacted] was discontinued after receiving sertraline 200 mg in double-blind period due to an AE (asthma exacerbation).
- Subject [redacted] was discontinued after receiving sertraline 200 mg in double-blind period due to an AE (psychotic decompensation).
- Subject [redacted] receiving sertraline was withdrawn due to behavior problem.

The other 6 subjects discontinued as they were no longer willing to participate in the study.

[redacted]

[redacted]

Table 10. Subject Disposition

Number (%) of Subjects	Sertraline	Moxifloxacin	Placebo
Assigned to study treatment 54			
Treated	52	50	50
Completed	47 (90.4)	49 (98.0)	47 (94.0)
Discontinued	5 (9.6)	1 (2.0)	3 (6.0)
Relation to study drug not defined	3 (5.8)	1 (2.0)	3 (6.0)
No longer willing to participate in study	2 (3.8)	1 (2.0)	3 (6.0)
Other	1 (1.9)	0	0
Related to study drug	1 (1.9)	0	0
Adverse event	1 (1.9)	0	0
Not related to study drug	1 (1.9)	0	0
Adverse event	1 (1.9)	0	0
Analyzed for pharmacokinetics			
Concentration	52 (100.0)	0	0
Parameter	52 (100.0)	0	0
Analyzed for ECG			
Primary ECG analysis population	52 (100.0)	50 (100.0)	50 (100.0)
Completer ECG analysis population	46 (88.5)	46 (92.0)	46 (92.0)
Analyzed for safety			
Adverse events	52 (100.0)	50 (100.0)	50 (100.0)
Laboratory data	52 (100.0)	50 (100.0)	50 (100.0)

Source: Tables 14.1.1.1 and 14.1.1.2
Discontinuations were attributed to the last study treatment received.
Abbreviation: ECG = electrocardiogram.

10.2. Protocol Deviations

[redacted] lists the protocol deviations recorded for this study including, subjects who deviated from the conduct of the study after the start of IP and those subjects who did not participate in study assessments (or use "evaluations") as required by the protocol. A total of 25 protocol deviations occurred in this study (Table 11). None of the protocol deviations resulted in clinically significant events or were deemed to adversely impact the primary endpoint or overall interpretation of the study results.

A formal acknowledgment by the study team was made that deviations were reviewed and GCP compliance was maintained. [redacted].

[redacted]

Table 11. Protocol Deviations

Protocol Deviation Category	Protocol Deviation Subcategory	Number of Deviations
Laboratory	PK samples collected outside 10% of nominal time	3
	PK samples not collected at protocol required time	1
Procedures/tests	Contraception check not performed in accordance with protocol required time	1
	ECG not taken at protocol required time	3
	ECG recordings not performed in accordance with protocol	15
	Safety laboratories not performed in accordance with the protocol	2

Source: [redacted]
Abbreviations: ECG = electrocardiogram; PK = pharmacokinetic.

10.3. Prior and Concomitant Treatments

Twenty-three (23) subjects received concomitant drug treatment during the study. The most common concomitant drug treatment was perdolan (paracetamol). Concomitant drug treatments during the study are presented in Table 16.2.5.2. No subject received concomitant non-drug treatment. Some women reported to have taken prior oral contraception.

11. ELECTROCARDIOGRAM, PHARMACOKINETIC AND PHARMACODYNAMICS EVALUATIONS

11.1. Data Sets Analyzed

All 52 subjects treated with sertraline were included in the PK analysis. Due to discontinuations only 50 subjects had PK data for Day 14, and 1 subject on Day 14 had only limited PK parameters due to an incomplete concentration-time profile ([redacted] last sample was 12 hours postdose). All subjected treated with sertraline, moxifloxacin and placebo were evaluated for safety and primary ECG analysis (Table 10).

11.2. Demographic and Other Baseline Characteristics

A total of 54 subjects (43 male and 11 female) were enrolled in the study.
Mean age (standard deviation) of the subjects was 36.5 years (9.7). Majority of subjects were white (46/54). Demographic data are presented in Table 12.

[redacted]

Table 12. Demographic Characteristics

	All Subjects (N = 54)		
	Male	**Female**	**Total**
Number (%) of Subjects	43	11	54
Age (years)			
<18	0	0	0
18-25	7 (16.3)	1 (9.1)	8 (14.8)
26-35	16 (37.2)	2 (18.2)	18 (33.3)
36-45	11 (25.6)	5 (45.5)	16 (29.6)
>45	9 (20.9)	3 (27.3)	12 (22.2)
Mean (SD)	36.0 (9.7)	38.5 (9.9)	36.5 (9.7)
Range (minimum, maximum)	22, 53	20, 54	20, 54
Race			
White	36 (83.7)	10 (90.9)	46 (85.2)
Black	3 (7.0)	0	3 (5.6)
Asian	1 (2.3)	0	1 (1.9)
Other	3 (7.0)	1 (9.1)	4 (7.4)
Weight (kg)			
Mean (SD)	75.9 (10.0)	68.7 (10.1)	74.4 (10.3)
Range (minimum, maximum)	56.4, 96.0	54.3, 87.4	54.3, 96.0
Body mass index (kg/m^2)			
Mean (SD)	24.7 (2.8)	25.1 (3.6)	24.8 (3.0)
Range (minimum, maximum)	18.1, 30.1	19.9, 30.5	18.1, 30.5
Height (cm)			
Mean (SD)	175.3 (6.5)	165.5 (6.8)	173.3 (7.6)
Range (minimum, maximum)	163, 193	156, 179	156, 193

Source: Table 14.1.2
Body mass index was defined as weight/(height × 0.01)^2.
Abbreviations: N = number; SD = standard deviation.

11.3. Measurements of Treatment Compliance

IPs were administered under the supervision of investigator site personnel. The oral cavity of each subject was examined following dosing to assure the IP was taken. Randomization treatment assigned and treatment received is presented in [redacted] All 54 subjects were randomized and received at least 1 study treatment. For discontinuation details please see Section 10.1.

11.4. Electrocardiogram and Pharmacokinetic Results

11.4.1. Statistical/Analytical Issues

No additional statistical or analytical issues other than those described in Section 9.7 (Statistical Methods Planned in the Protocol) were identified.

11.4.1.1. Adjustments for Covariates

The baseline QTc from each period was used as a covariate in the statistical model.

[redacted]

11.4.1.2. Handling of Dropouts or Missing Data

11.4.1.2.1. Concentrations Below the Limit of Quantification

In all data presentations (except listings), BLQ concentrations were set to 0. In listings, BLQ values were reported as "<LLOQ".

11.4.1.2.2. Deviations, Missing Concentrations and Anomalous Values

In summary tables and plots of median profiles, statistics were calculated having set concentrations to missing if 1 of the following cases was true:

1. A concentration had been collected as ND (ie, not done) or NS (ie, no sample);

2. A deviation in sampling time was of sufficient concern or a concentration had been flagged anomalous by the pharmacokineticist.

Note that summary statistics were not presented at a particular time point if >50% of the data were missing.

11.4.1.2.3. Pharmacokinetic Parameters

Actual PK sampling times were used in the derivation of PK parameters.

If a PK parameter could not be derived from a subject's concentration data, the parameter was coded as NC (ie, not calculated).

(Note that NC values were not generated beyond the day that a subject discontinued).

In summary tables, statistics were calculated by setting NC values to missing; and statistics were presented for a particular dose with ≥3 evaluable measurements. For statistical analyses (ie, analysis of variance), PK parameters coded as NC were set to missing; and analyses was not be performed for a particular parameter if >50% of the data were NC.

11.4.2. Electrocardiogram Results

A summary of the statistical analyses of QTcF for sertraline and moxifloxacin compared with placebo at each postdose time point on Day 14 are presented in Table 13 and Table 14, respectively. Figure 2 plots the estimated mean differences (90% CI) for sertraline versus (vs) placebo and moxifloxacin vs placebo, at each postdose time point on Day 14.

For moxifloxacin, the lower bound of the 2-sided 90% CIs for least square (LS) mean differences between moxifloxacin and placebo was more than the predefined cutoff of 5 msec (9.813 msec) at moxifloxacin T_{max} (3 hours postdose) on Day 14 (Table 14). Therefore, this study was adequately sensitive to assess the effect of sertraline on QTcF interval.

In the primary analysis, at 4 hour postdose time point on Day 14, the upper bounds of the 2-sided 90% CI for the time-matched LS mean difference of QTcF between sertraline and placebo (11.666 msec) was greater than the predefined threshold of 10 msec. At remaining

8 postdose time points on Day 14 the upper bound of the 2-sided 90% CIs were all less than the predefined threshold of 10 msec (Table 13). Out of 9 postdose time points on Day 14, 5 time points (2, 3, 4, 5, and 24 hours postdose) had lower bounds of 90% CI above 5 msec.

Scatter plot of QT vs RR and log transformed QT vs RR (Predose) are presented in Figures 14.3.4.3.1.2.1 and 14.3.4.3.1.2.2, respectively.

Scatter plot of observed predose QT and RR data were used to determine a suitable relationship between QT and RR to derive population and individual QT correction method (Figures 14.3.4.3.1.2.1 and 14.3.4.3.1.2.2). Based upon results obtained ([redacted] and Figures 14.3.4.3.1.3.2, 14.3.4.3.1.3.3 and 14.3.4.3.1.3.4), it was determined that primary analysis on QTcF was sufficient to evaluate effect of sertraline on QTc.

Linear regression plot of QTcB, QTcF, QTcI and QTcN vs RR are presented in Figures 14.3.4.3.1.3.1, 14.3.4.3.1.3.2, 14.3.4.3.1.3.3 and 14.3.4.3.1.3.4, respectively.

Preliminary mixed effect model fit of QTcF data indicated that period effect was not statistically significant, therefore a full model with carry-over effect was not analyzed.

Table 13. Summary of Statistical Comparisons of QTcF Between Sertraline and Placebo at Each Time Point Postdose on Day 14 - Primary ECG Analysis Population

Nominal Time Postdose (Hours)	Least Squares Mean (msec)		Least Squares Difference (msec) (Sertraline - Placebo)	90% Confidence Interval
	Sertraline N = 50	Placebo N = 50		
1	414.299	407.341	6.957	(4.942, 8.973)
2	415.625	407.775	7.851	(5.835, 9.866)
3	416.465	408.641	7.824	(5.808, 9.840)
4	418.252	408.601	9.651	(7.635, 11.666)
5	411.285	403.908	7.377	(5.362, 9.393)
6	408.985	402.475	6.511	(4.495, 8.526)
8	408.732	403.135	5.597	(3.582, 7.613)
12	411.019	405.341	5.677	(3.662, 7.693)
24	414.294	406.948	7.346	(5.331, 9.360)

Source: Table 14.3.4.3.5.1
Baseline was defined as the mean of the 3 average triplicate measurements taken at the following 3 time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect and baseline QTcF as a covariate were used.
Unplanned readings had been excluded from the presentation.
Primary ECG analysis population was defined as all subjects randomized and treated who had at least 1 post-dose ECG measurement in at least 1 period.
For primary analysis, ECG measurements on Day 14 up to 24 hours were used.'
Abbreviations: ECG = electrocardiogram; N = number of subjects; QTcF = QT corrected for heart rate using Fridericia formula.

[redacted]

Table 14. Summary of Statistical Comparisons of QTcF Between Moxifloxacin and Placebo at Each Time Point Postdose on Day 14 - Primary ECG Analysis Population

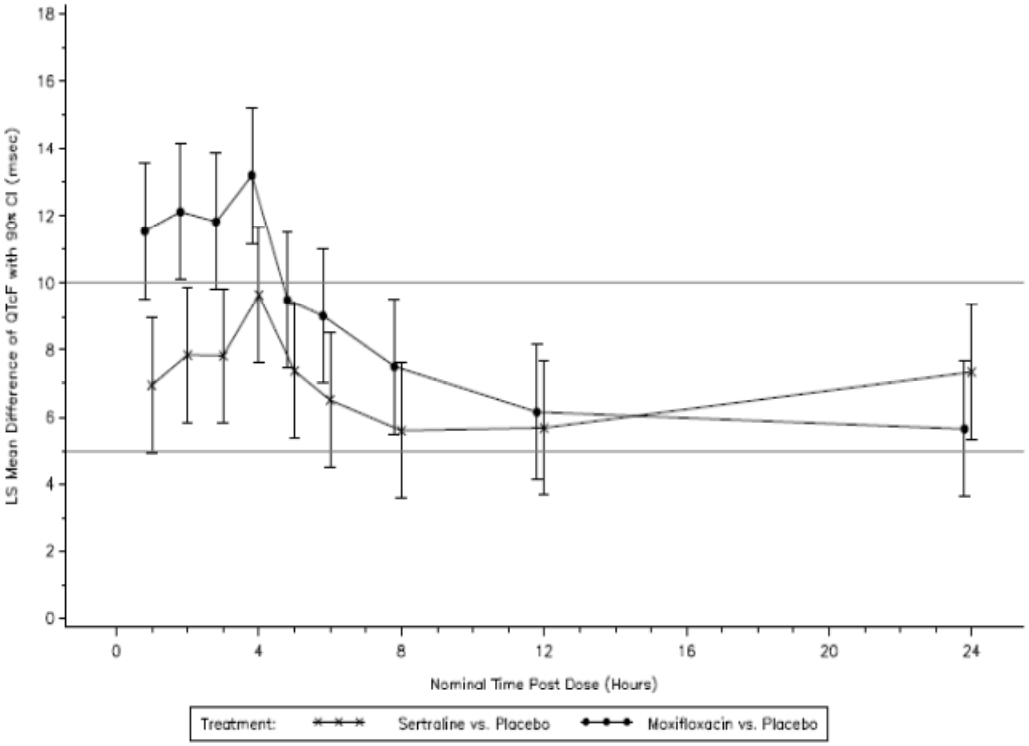
Nominal Time Postdose (Hours)	Least Squares Mean (msec)		Least Squares Difference (msec) (Moxifloxacin - Placebo)	90% Confidence Interval
	Moxifloxacin N = 50	Placebo N = 50		
1	418.886	407.341	11.544	(9.526, 13.563)
2	419.899	407.775	12.124	(10.106, 14.143)
3	420.473	408.641	11.831	(9.813, 13.849)
4	421.799	408.601	13.198	(11.179, 15.216)
5	413.413	403.908	9.504	(7.486, 11.523)
6	411.493	402.475	9.018	(6.999, 11.036)
8	410.639	403.135	7.504	(5.486, 9.523)
12	411.493	405.341	6.151	(4.133, 8.169)
24	412.599	406.948	5.651	(3.633, 7.669)

Source: Table 14.3.4.3.6.2
Baseline was defined as the mean of the 3 average triplicate measurements taken at the following 3 time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect and baseline QTcF as a covariate were used.
Primary ECG analysis population was defined as all subjects randomized and treated who had at least 1 post-dose ECG measurement in at least 1 period.
Unplanned readings had been excluded from the presentation.
Abbreviations: ECG = electrocardiogram; N = number of subjects; QTcF = QT corrected for heart rate using Fridericia formula.

[redacted]

[redacted]

Figure 2. Plot of LS Mean Difference of QTcF (msec) Between Sertraline vs Placebo and Moxifloxacin vs Placebo at Each Time Point Postdose on Day 14 - Primary ECG Analysis Population



Source: Figure 14.3.4.3.7.2
Unplanned readings had been excluded from the presentation.
Primary ECG analysis population was defined as all subjects randomized and treated who had at least 1 postdose ECG measurement in at least 1 period.
Abbreviations: ECG = electrocardiogram; LS = least square; QTcF = QT corrected for heart rate using Fridericia formula; vs = versus.

Categorical summary of postdose ECG data based on pre-specified criteria of potential clinical concern, QT/QTcF and QT/QTcB categorization is provided in Table 15. No subject had an absolute PR interval of ≥300 msec or increase from baseline in PR interval of ≥25% (baseline >200 msec)/50% (baseline ≤200 msec) after receiving any treatment. No subject had an absolute QRS interval of ≥200 msec or increase from baseline in QRS interval of ≥25% (baseline >100 msec)/50% (baseline ≤100 msec) after receiving any treatment. None of the subjects met categorical criterion of absolute QTcF interval of ≥500 msec or increase from baseline in QTcF and QTcB interval ≥60 msec after receiving any treatment.

Absolute ECG values and mean change from Baseline are presented in Tables 14.3.4.3.1 and 14.3.4.3.2, respectively.

Table 15. Categorical Summary of Postdose ECG Data – Absolute Values and Increases From Baseline

Parameters (Units)	Criteria	Sertraline N = 52	Moxifloxacin N = 50	Placebo N = 50
		n (%)	n (%)	n (%)
Maximum Absolute Values				
Maximum heart rate (bpm)	>120	0	0	0
	<40	0	0	0
Maximum PR interval (msec)	≥300	0	0	0
Maximum QRS complex (msec)	≥200	0	0	0
Maximum QT interval (msec)	450 to <480	12 (23.1)	11 (22.0)	9 (18.0)
	480 to <500	0	1 (2.0)	1 (2.0)
	≥500	1 (1.9)	0	0
Maximum QTcB interval (msec)	450 to <480	6 (11.5)	7 (14.0)	6 (12.0)
	480 to <500	0	0	0
	≥500	0	0	0
Maximum QTcF interval (msec)	450 to <480	1 (1.9)	3 (6.0)	3 (6.0)
	480 to <500	0	0	0
	≥500	0	0	0
Maximum Increases From Baseline in				
Maximum PR interval (msec)	≥25%/50%	0	0	0
Maximum QRS complex (msec)	≥25%/50%	0	0	0
Maximum QT interval (msec)	≥30 to <60	6 (11.5)	10 (20.0)	4 (8.0)
	≥60	1 (1.9)	0	0
Maximum QTcB interval (msec)	≥30 to <60	9 (17.3)	5 (10.0)	0
	≥60	0	0	0
Maximum QTcF interval (msec)	≥30 to <60	0	1 (2.0)	0
	≥60	0	0	0

Source: Tables 14.3.4.3.2.1 and 14.3.4.3.2.2
Baseline was defined as the mean of the 3 average triplicate measurements taken at the following 3 time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Abbreviations: bpm = beats per minute; ECG = electrocardiogram; N = number of subjects evaluated against criteria; n = number of subjects that met criteria; QTcB = QT corrected for heart rate using Bazett's formula; QTcF = QT corrected for heart rate using Fridericia formula.

Mean difference from placebo for adjusted baseline ECG data (heart rate, QT and QTcF) is presented in Table 14.3.4.3.3.1. Maximum absolute values (postdose) for ECG data (QTcF, QT, PR, RR, QRS and heart rate) is presented in Table 14.3.4.3.4.1. Maximum increase from Baseline for ECG data (QTcF, QT, PR, RR, QRS and heart rate) is presented in Table 14.3.4.3.4.2. Mean difference from placebo of adjusted baseline ECG value in heart rate, QT and QTcF vs time are presented in Figures 14.3.4.3.3.2.1, 14.3.4.3.3.2.2 and 14.3.4.3.3.2.3, respectively.

Sensitivity Analysis:

Out of 54 subjects randomized and treated, only 46 subjects completed all 3 treatment periods. Since >10% of subjects dropped out of study or had missing data for ≥1 treatment periods, sensitivity analysis proposed was conducted. Results of sensitivity analysis was

similar to the primary ECG analysis which are presented in Table 14.3.4.3.5.2 and Table 14.3.4.3.6.4.

11.4.2.1. Pharmacokinetics and Pharmacodynamics (Exposure-Response) (Electrocardiogram) Analysis

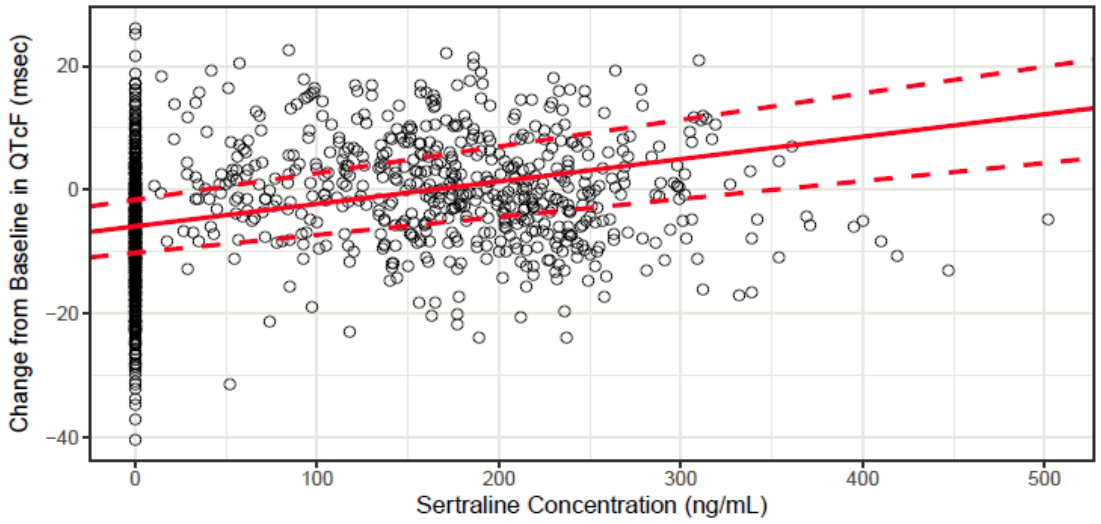
The relationship between change from baseline in QTcF (ΔQTcF) vs sertraline plasma concentration is provided in Figure 3. Linear mixed effect modeling showed an increase in QTcF values with increasing sertraline ($p<0.0001$) and N-desmethylsertraline ($p<0.0001$) concentrations. The estimated slope (90% CI) for ΔQTcF vs sertraline plasma concentration was 0.036 msec/(ng/mL) (0.029, 0.043), which translates to predicted ΔQTcF of 3.57 msec (90% CI: 2.92 to 4.23 msec) at the mean therapeutic maximum plasma concentration (C_{max}) (86 ng/mL). The predicted ΔQTcF was 8.93 msec (90% CI: 7.42 to 10.45 msec) at the mean supratherapeutic C_{max} (234 ng/mL) on Day 14. Based on this model, plasma concentration value has to be >223.5 ng/mL for predicted upper bound of 2-sided 90% CI to cross threshold of 10 msec. This concentration is approximately 2.6 fold larger than mean therapeutic C_{max} (86 ng/mL). Predicted change from baseline in QTcF adjusted for placebo and associated 2-sided 90% CI for different plasma concentration values are provided in [redacted].

The exposure-response analysis report corresponding to this work is included in [redacted]

The estimated slope (90% CI) for ΔQTcF vs N-desmethylsertraline plasma concentration relationship was 0.036 msec/(ng/mL) (0.029, 0.042), which translates to predicted ΔQTcF of 3.46 msec at the mean therapeutic C_{max} (100 ng/mL). Similarly, the relationship between change from baseline in QTcF (ΔQTcF) vs N-desmethylsertraline plasma concentration is provided in Figure 4.

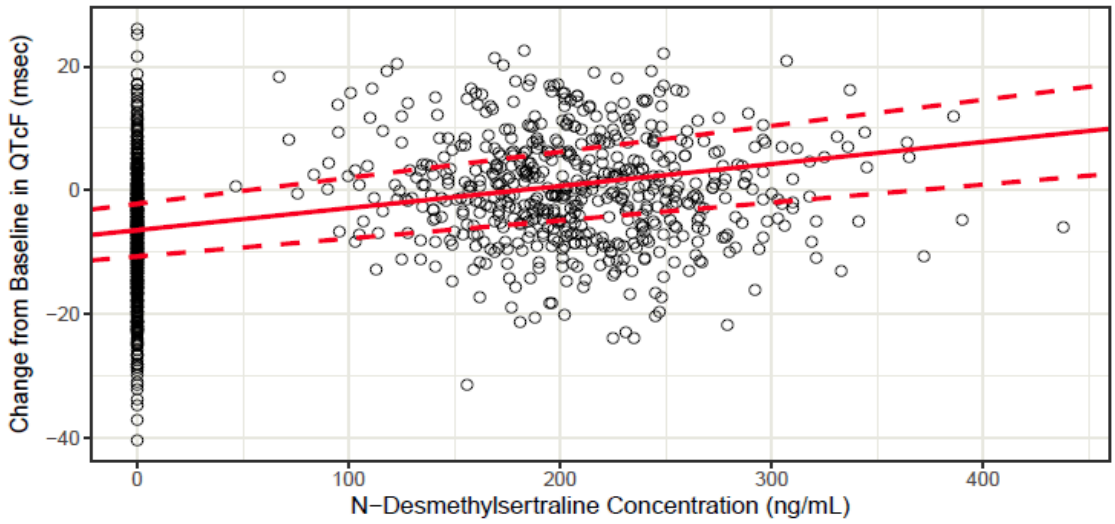
[redacted]

Figure 3. Observed and Predicted (Regression Line) Change From Baseline in QTcF Versus Sertraline Plasma Concentrations on Day 14



Source: Figure 6 in the exposure-response analysis report in [redacted]
Open circle represents observed data, solid red line represents regression line and dotted red line represents 90% confidence interval.
Abbreviation: QTcF = QT corrected for heart rate using Fridericia formula.

Figure 4. Observed and Predicted (Regression Line) Change From Baseline in QTcF Versus N-Desmethylsertraline Plasma Concentrations on Day 14



Source: Figure 8 in the exposure-response analysis report in [redacted]
Open circle represents observed data, solid redline represents regression line and dotted redline represents 90% confidence interval.
Abbreviation: QTcF = QT corrected for heart rate using Fridericia formula.

[redacted]

11.4.3. Pharmacokinetic Results

The PK of sertraline and its metabolite, N-desmethylsertraline, were assessed on Days 1 and 14. The dosing titration scheme consisted of a single dose of 50 mg sertraline in the morning on Day 1 followed by BID (given at approximately 12 hours apart) escalating doses of 50 mg BID on Day 2; 50 mg AM and 100 mg post meridiem (PM) on Day 3; 100 mg BID on Days 4 and 5; 100 mg AM and 200 mg PM on Day 6; 200 mg BID on Days 7 to 13; and 200 mg AM on Day 14.

11.4.3.1. Sertraline Pharmacokinetic Results

Median plasma sertraline concentration-time profiles on Day 1 and Day 14 are presented in Figure 5. PK parameters for Days 1 and 14 are summarized in Table 16. Individual and geometric mean dose normalized area under the plasma concentration-time profile from time 0 to 24 hours (AUC_{24}) and C_{max} are plotted by day in Figure 6.

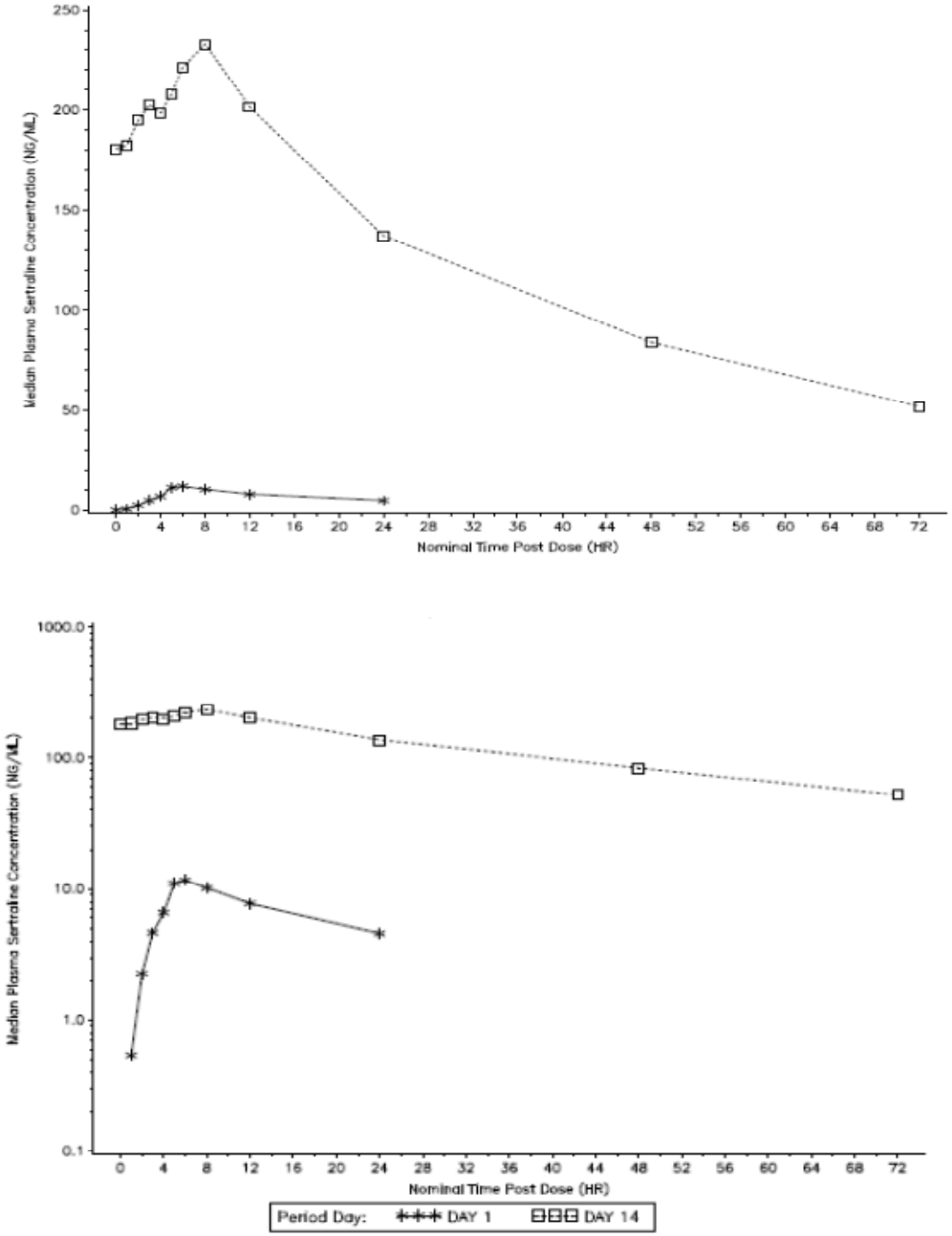
As expected, median plasma sertraline concentrations on Day 14 following multiple dosing were higher in comparison to those observed following single dose administration on Day 1 (Figure 5). Sertraline was slowly absorbed with C_{max} achieved at median T_{max} of 5.06 hours and 7.15 hours postdose on Day 1 and Day 14, respectively. Mean $t_{½}$ following the last dose on Day 14 was about 27 hours. The $t_{½}$ was reported for 23 out of 50 subjects on Day 14 where a well-characterized terminal phase was present as defined in Section 9.5.4.3. Supporting data for $t_{½}$ estimations is included in Table 16.2.5.5.1.5.

Geometric mean sertraline C_{max} and AUC_{24} values of sertraline on Day 14 were 234.2 ng/mL and 4388 ng•h/mL, respectively. The geometric mean Day 14 C_{max} (234.2 ng/mL) achieved in this study, with titration dosing to a maximum dose of 200 mg BID (400 mg/day), was approximately 3-fold higher than the steady-state C_{max} value of 86.1 ng/mL observed at the highest approved therapeutic dosing level of 100 mg BID (200 mg/day) sertraline in a previous multiple-dose PK study in healthy volunteers,[6] indicating that supratherapeutic concentrations of sertraline were achieved.

Variability of sertraline exposure based on geometric %CV for AUC_{24} was 34% on Day 1 and 36% on Day 14, and for C_{max} was 37% on Day 1 and 34% on Day 14 (Table 16).

[redacted]

Figure 5. Median Plasma Sertraline Concentration-Time Profiles on Day 1 and Day 14



Source: Figures 14.4.2.2.1 and 14.4.2.2.2
Summary statistics was calculated by setting concentration values below the lower limit of quantification to 0.
The lower limit of quantification was 0.500 ng/mL.
Upper and lower panels are linear and semi-logarithmic scales, respectively.
For corresponding mean plots, see Figures 14.4.2.2.3 and 14.4.2.2.4.
Abbreviation: HR = hours.

Table 16. Descriptive Summary of Plasma Sertraline Pharmacokinetic Parameter Values on Day 1 and Day 14

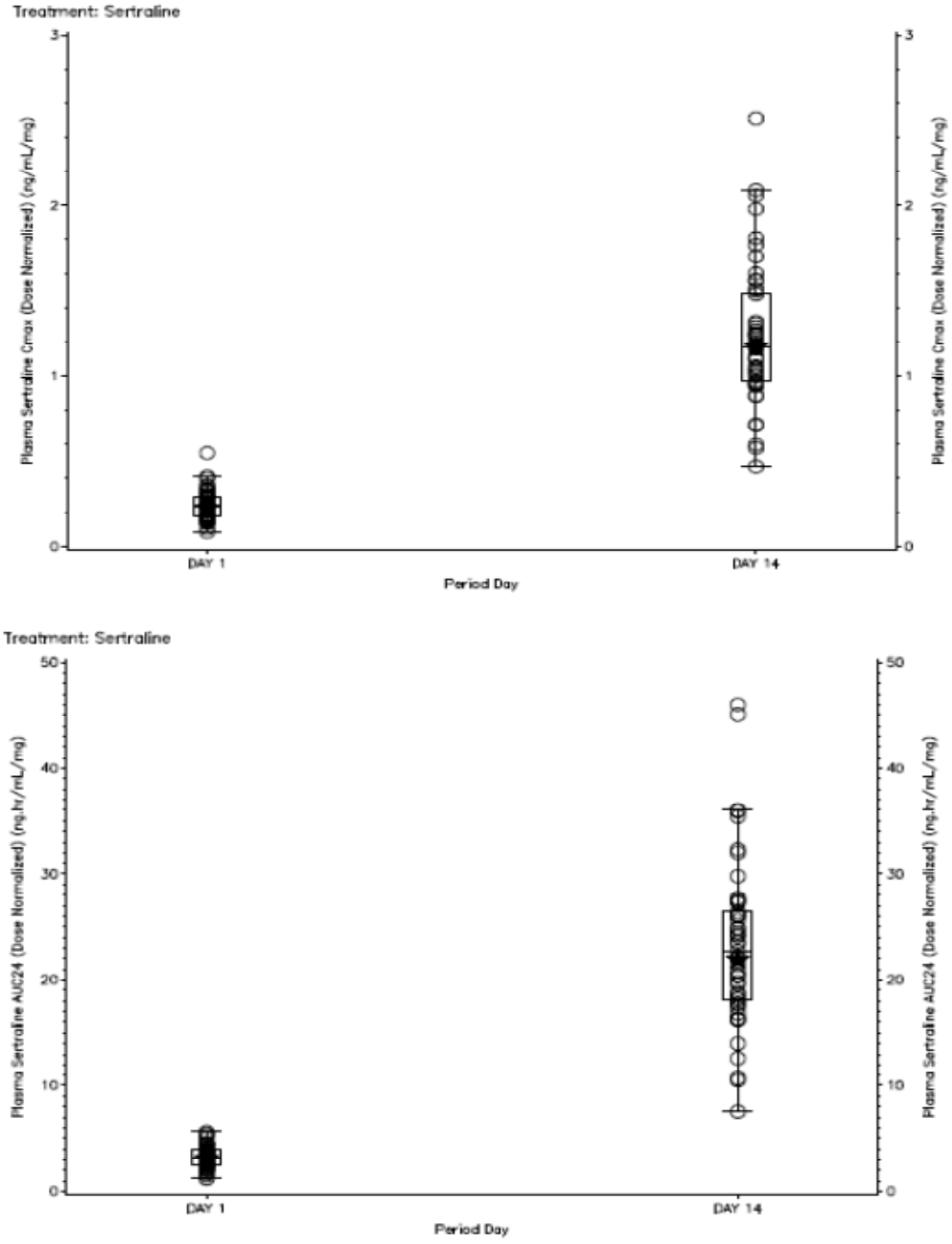
Parameter (Units)	Parameter Summary Statistics[a]	
	Day 1 (Single Dose)	Day 14 (Multiple Dose)
N, n	52	50[b], 23
C_{max} (ng/mL)	11.39 (37)	234.2 (34)
C_{max}(dn) (ng/mL/mg)	0.2277 (37)	1.173 (34)
T_{max} (h)	5.06 (4.02 - 8.05)	7.15 (3.00 - 8.08)
AUC_{24} (ng•h/mL)	154.3 (34)	4388 (36)
AUC_{24}(dn) (ng•h/mL/mg)	3.086 (34)	21.94 (36)
AUC_{last} (ng•h/mL)	NA	8489 (43)
$t_{½}$ (h)	NA	26.93 ± 2.71
C_{min} (ng/mL)	NA	135.3 (43)
R_{ac}	NA	7.238 (23)
$R_{ac,Cmax}$	NA	5.206 (32)

Source: Tables 14.4.3.1.1 and 14.4.3.1.2
Pharmacokinetic parameters are defined in Table 7.
Abbreviations: AUC = area under the plasma concentration-time profile; %CV = percent coefficients of variation; N = number of subjects in the treatment group and contributing to the mean; n = number of subjects with reportable $t_{½}$ (Day 14 only; see Table 16.2.5.5.1.5 supporting data for sertraline $t_{½}$); NA = not applicable; SD = standard deviation.

a. Geometric mean (%CV) for all except: median (range) for T_{max} and arithmetic mean ± SD for $t_{½}$.
b. N = 49 for all AUC parameters, C_{min}, and R_{ac} due to an incomplete profile for 1 subject.

[redacted]

Figure 6. Individual and Geometric Mean Plasma Sertraline Dose-Normalized C_{max} (Upper Panel) and AUC_{24} (Lower Panel) Values by Study Day



Source: Figures 14.4.3.2.1 and 14.4.3.2.2
Pharmacokinetic parameters are defined in Table 7.
Geometric mean was calculated for each period day.
C_{max} (upper panel) and AUC_{24} (lower panel).
Open circles represent individual subject values and star represents the geometric mean.
Box plot provides median and 25%/75% quartiles with whiskers to the last data point within 1.5 times the interquartile range.

[redacted]

11.4.3.2. N-Desmethylsertraline Pharmacokinetic Results

Median plasma N-desmethylsertraline concentration-time profiles on Day 1 and Day 14 are presented in Figure 7. PK parameters for Day 1 and Day 14 are summarized in Table 17.

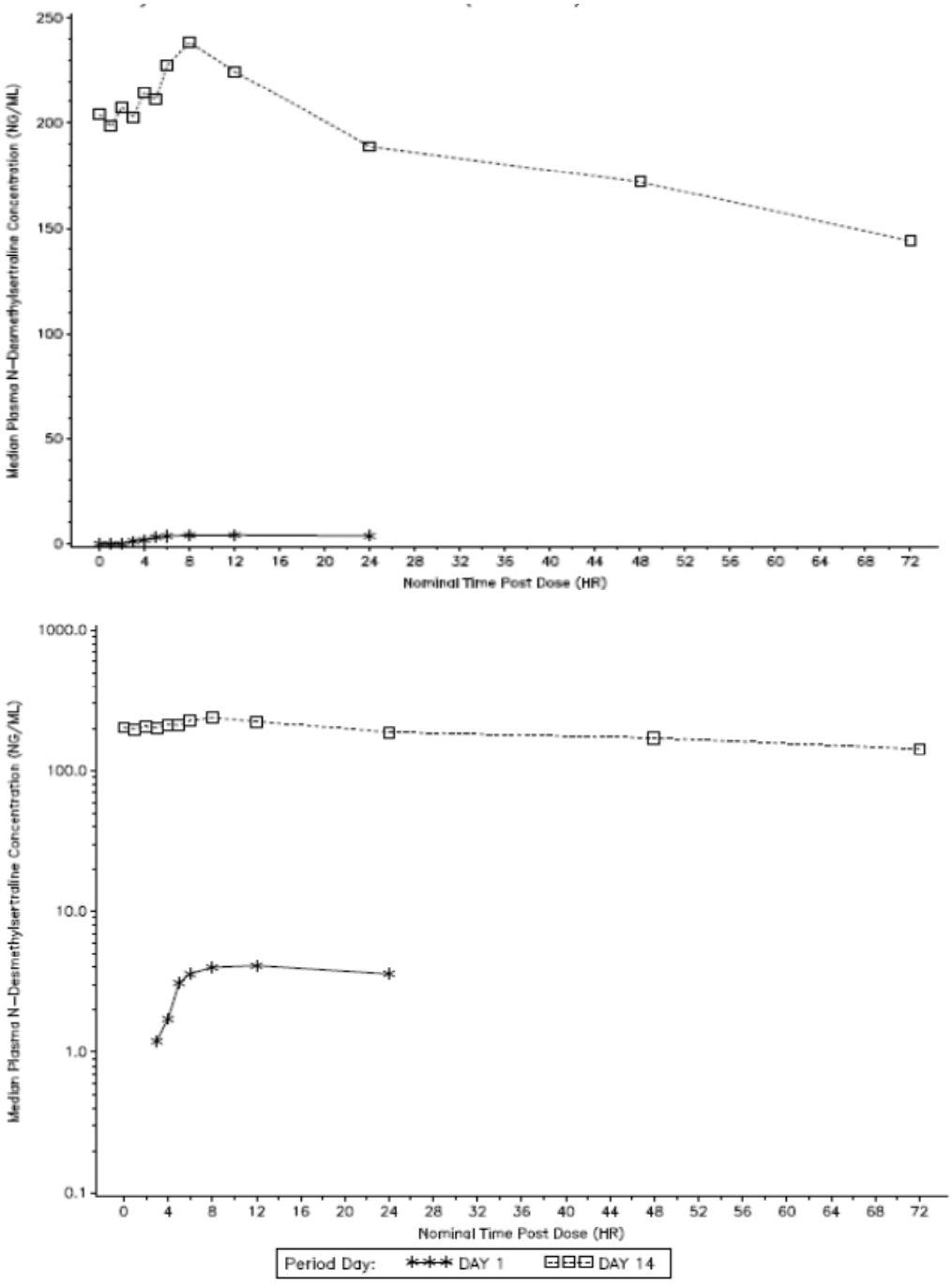
As expected, median plasma N-desmethylsertraline concentrations on Day 14 following multiple dosing of sertraline were higher in comparison to those observed following single dose administration on Day 1 (Figure 7). Median T_{max} was 12.0 hours and 8.0 hours postdose on Day 1 and Day 14, respectively. Terminal $t_{½}$ for N-desmethylsertraline was not reportable for any subjects on Day 14 due to lack of a well-characterized terminal phase as defined in Section 9.5.4.3. Supporting data for $t_{½}$ estimations is included in Table 16.2.5.5.1.6.

N-desmethylsertraline geometric mean AUC_{24} and C_{max} values on Day 14 were 5227 ng•h/mL and 249.6 ng/mL, respectively. The geometric mean Day 14 C_{max} (249.6 ng/mL) achieved in this study, with titration dosing to a maximum sertraline dose of 200 mg BID (400 mg/day), was approximately 3-fold higher than the steady-state C_{max} value of 85.5 ng/mL observed at the highest approved therapeutic dosing level of 100 mg BID (200 mg/day) in the previous multiple-dose PK study in healthy volunteers.[6]

The metabolite to parent ratio for AUC_{24} was 0.52 on Day 1 and 1.2 on Day 14, indicating that N-desmethylsertraline plasma exposure was less than sertraline exposure on Day 1, and greater than sertraline exposure on Day 14.

Summary plots presenting parent and metabolite concentration-time profiles on the same page are presented in Figures 14.4.2.2.9 - 14.4.2.2.16. Variability of N-desmethylsertraline exposure based on geometric %CV for AUC_{24} was 24% on Day 1 and 22% on Day 14, and for C_{max} was 27% on Day 1 and 23% on Day 14 (Table 17).

Figure 7. Median Plasma N-Desmethylsertraline Concentration-Time Profiles on Day 1 and Day 14



Source: Figures 14.4.2.2.5 and 14.4.2.2.6
Upper and lower panels are linear and semi-logarithmic scales, respectively.
Summary statistics was calculated by setting concentration values below the lower limit of quantification to 0.
The lower limit of quantification was 0.500 ng/mL.
For corresponding mean plots, see Figures 14.4.2.2.7 and 14.4.2.2.8.
Abbreviation: HR = hours.

[redacted]

Table 17. Descriptive Summary of Plasma N-Desmethylsertraline Pharmacokinetic Parameter Values on Day 1 and Day 14

Parameter (Units)	Parameter Summary Statistics[a]	
	Day 1 (Single Dose)	Day 14 (Multiple Dose)
N, n	52	50[b], 0
C_{max} (ng/mL)	4.269 (27)	249.6 (23)
T_{max} (h)	12.0 (5.00 - 23.9)	8.00 (1.07 - 12.1)
AUC_{24} (ng•h/mL)	76.87 (24)	5227 (22)
AUC_{last} (ng•h/mL)	NA	13110 (25)
$t_{½}$ (h)	NA	NC
C_{min} (ng/mL)	NA	184.1 (23)
MR	0.5222 (34)	1.248 (24)

Source: Tables 14.4.3.1.3 and 14.4.3.1.4
Pharmacokinetic parameters are defined in Table 7.
Abbreviations: %CV = percent coefficients of variation; AUC = area under the plasma concentration-time profile; MR = metabolite to parent ratio; N = number of subjects in the treatment group and contributing to the mean; n = number of subjects with reportable $t_{½}$ (Day 14 only; see Table 16.2.5.5.1.6 supporting data for N-desmethylsertraline $t_{½}$); NA = not applicable; NC = not calculated; SD = standard deviation.
a. Geometric mean (%CV) for all except: median (range) for T_{max} and arithmetic mean ± SD for $t_{½}$.
b. N = 49 for all AUC parameters and C_{min} due to an incomplete profile for 1 subject.

11.4.3.3. Pharmacokinetic Supporting Data

Summary PK tables and figures are presented in Tables 14.4.2.1.1, 14.4.2.1.2, 14.4.3.1.1 - 14.4.3.1.4, Figures 14.4.2.2.1 - 14.4.2.2.16, 14.4.3.2.1 and 14.4.3.2.2. Individual PK data including concentration-time listings and figures, parameters, and supporting data for $t_{½}$ estimations are provided in [redacted]

11.4.4. By Subject Displays

By-subject displays of PK data are referenced under Section 11.4.3.3.

11.4.5. Electrocardiogram and Pharmacokinetic Conclusions

- In the primary analysis, at 4-hours postdose time point, the supratherapeutic dose of 400 mg/day was shown to exceed the threshold (ie, the time-matched LS mean difference of QTcF between sertraline and placebo was greater than the predefined threshold of 10 msec) for a positive thorough QT/QTc study in healthy subjects.

- Moxifloxacin demonstrated assay sensitivity, suggesting that the study was adequately sensitive to assess the effect of sertraline on QTcF interval.

- Exposure-response analysis indicated a slightly positive relationship between QTcF and sertraline/N-desmethylsertraline concentrations.

    - At therapeutic C_{max} of sertraline (86 ng/mL), predicted QTcF prolongation was not clinically significant (Mean 3.57 msec; 90% CI of 2.92 to 4.23 msec).

[redacted]

- At supratherapeutic C_{max} of sertraline on Day 14 (234 ng/mL), predicted 2-sided 90% CI of QTcF prolongation exceeds 10 msec (Mean 8.93 msec; 90% CI of 7.42 to 10.45 msec).

- Sertraline plasma concentration had to be >223.5 ng/mL for predicted 2-sided 90% CI to exceed 10 msec (Mean 8.55 msec; 90% CI of 7.11 to 9.99 msec). This plasma concentration is at least 2.6 fold greater than therapeutic C_{max} of sertraline (86 ng/mL).

- Supratherapeutic concentration (C_{max}) of sertraline was achieved on Day 14, and the supratherapeutic C_{max} was about 3 folds higher than the therapeutic C_{max}.

12. SAFETY EVALUATION

12.1. Extent of Exposure

A total of 54 subjects received study treatment as per the randomization schedule (Table 16.1.7.2), except for 8 subjects who were discontinued due to a difference in the Randomized Sequence and Actual Sequence. A total of 9 subjects discontinued from the study (Section 10.1). The administration schedule is presented by subject in Table 16.2.5.1. A summary of administration, which includes treatment, dosing dates and duration of treatment, is provided in Table 14.4.1.

12.2. Adverse Events

12.2.1. Brief Summary of Adverse Events

All-causality and treatment-related treatment-emergent AEs (TEAEs) are presented in Table 18.

Out of 52 evaluable subjects for AEs receiving sertraline, 45 subjects reported 251 AEs (238 AEs were considered as treatment-related). One (1) subject reported a treatment-related severe AE which was also reported as an SAE. Two (2) subjects permanently discontinued due to AE. None of the subjects reduced their dose or temporarily discontinued study drug due to AEs.

Out of 50 evaluable subjects for AEs receiving moxifloxacin, 42 subjects reported 105 AEs (92 AEs were considered as treatment-related). Out of 50 evaluable subjects for AEs receiving placebo, 33 subjects reported 121 AEs (106 AEs were considered as treatment-related). There were no SAEs, severe AEs or subjects discontinued or reduced their dose or temporarily discontinued study drug due to AE during either treatment.

Table 18. All-Causalities (Treatment-Related) Treatment-Emergent Adverse Events

Number of Subjects	Sertraline	Moxifloxacin	Placebo
Subjects evaluable for adverse events	52	50	50
Number of adverse events	251 (238)	105 (92)	121 (106)
Subjects with adverse events	45 (44)	42 (41)	33 (30)
Subjects with serious adverse events	1 (1)	0	0
Subjects with severe adverse events	1 (1)	0	0
Subjects discontinued due to adverse events	2 (1)	0	0
Subjects with dose reduced or temporary discontinuation due to adverse events	0	0	0

Source: Tables 14.3.1.2.1 and 14.3.1.3.1
Included all data collected since the first dose of study drug.
Except for the number of adverse events subjects were counted only once per treatment in each row.
Serious adverse events - according to the investigator's assessment.
Severity counts were based on the maximum severity or grade of events.
MedDRA (Version 19.0) coding dictionary applied.
Abbreviation: MedDRA = Medical Dictionary for Regulatory Activities.

12.2.2. Incidence of Adverse Events

The incidence of all-causalities and treatment-related TEAEs (by system organ class and preferred term) are summarized in Table 19. The most common AEs were headache (experienced by 18, 11, and 13 subjects after receiving sertraline, moxifloxacin and placebo, respectively) insomnia (experienced by 22, 11, and 6 subjects after receiving sertraline, moxifloxacin and placebo, respectively), fatigue (experienced by 17, 7, and 7 subjects after receiving sertraline, moxifloxacin and placebo, respectively). No medication errors occurred in the study.

Table 19. All Causalities (Treatment-Related) Incidence of Treatment-Emergent Adverse Events

Number of Subjects With Adverse Events by: System Organ Class Preferred Term	Sertraline (N = 52)	Moxifloxacin (N = 50)	Placebo (N = 50)
Cardiac disorders	2 (2)	1 (1)	2 (2)
Atrioventricular block first degree	1 (1)	1 (1)	2 (2)
Palpitations	1 (1)	0	0
Ear and labyrinth disorders	1 (1)	0	2 (2)
Ear discomfort	0	0	1 (1)
Hyperacusis	0	0	1 (1)
Vertigo	1 (1)	0	0
Eye disorders	8 (8)	6 (5)	3 (3)
Dry eye	0	0	1 (1)
Ocular discomfort	1 (1)	2 (2)	0
Ocular hyperaemia	0	2 (1)	0
Photophobia	1 (1)	0	2 (2)
Vision blurred	2 (2)	0	0
Visual impairment	5 (5)	2 (2)	0
Gastrointestinal disorders	25 (25)	17 (17)	18 (17)
Abdominal discomfort	2 (2)	2 (2)	4 (4)
Abdominal distension	1 (1)	1 (1)	1 (1)
Abdominal pain	3 (3)	3 (3)	4 (4)
Abdominal pain lower	1 (1)	0	1 (0)
Abdominal pain upper	2 (2)	0	0
Change of bowel habit	3 (3)	1 (1)	0
Chapped lips	0	0	1 (1)
Cheilitis	0	0	1 (1)
Constipation	2 (2)	3 (3)	0
Diarrhoea	8 (8)	4 (4)	6 (6)
Dry mouth	5 (5)	1 (1)	0
Dyspepsia	1 (1)	3 (3)	0
Dysphagia	2 (2)	0	0
Flatulence	0	2 (2)	1 (1)
Functional gastrointestinal disorder	0	1 (1)	0
Gastrointestinal sounds abnormal	2 (2)	1 (1)	0
Gastrooesophageal reflux disease	0	0	1 (1)
Gingival bleeding	1 (1)	1 (1)	0
Gingival pain	1 (1)	0	1 (1)
Glossodynia	0	0	1 (1)
Haematochezia	2 (1)	0	0
Nausea	8 (8)	2 (2)	2 (2)
Oral disorder	1 (1)	0	0
Paraesthesia oral	1 (1)	0	0
Toothache	1 (1)	0	0
Vomiting	2 (2)	0	1 (1)
General disorders and administration site conditions	27 (25)	11 (8)	13 (11)
Application site erythema	0	2 (0)	0
Application site irritation	1 (0)	0	0
Asthenia	4 (4)	1 (1)	0
Chest discomfort	3 (3)	0	3 (3)
Fatigue	17 (17)	7 (7)	7 (7)

Table 19. All Causalities (Treatment-Related) Incidence of Treatment-Emergent Adverse Events

Number of Subjects With Adverse Events by: System Organ Class Preferred Term	Sertraline (N = 52)	Moxifloxacin (N = 50)	Placebo (N = 50)
Feeling cold	1 (1)	0	0
Feeling drunk	1 (1)	0	1 (1)
Feeling hot	2 (2)	0	1 (1)
Hangover	0	0	1 (1)
Hunger	0	1 (1)	0
Vessel puncture site erythema	3 (0)	1 (0)	0
Vessel puncture site haematoma	0	0	1 (0)
Vessel puncture site pain	0	1 (0)	2 (0)
Immune system disorders	0	0	1 (0)
Seasonal allergy	0	0	1 (0)
Infections and infestations	1 (0)	7 (2)	3 (0)
Asymptomatic bacteriuria	0	1 (0)	0
Folliculitis	0	1 (1)	0
Fungal infection	0	1 (0)	2 (0)
Gastroenteritis	1 (0)	0	0
Gingivitis	0	1 (1)	0
Hordeolum	0	1 (0)	0
Nasopharyngitis	0	2 (0)	1 (0)
Injury, poisoning and procedural complications	1 (0)	0	0
Arthropod bite	1 (0)	0	0
Investigations	2 (2)	1 (1)	0
Weight decreased	2 (2)	1 (1)	0
Metabolism and nutrition disorders	3 (3)	1 (1)	2 (2)
Decreased appetite	3 (3)	1 (1)	2 (2)
Musculoskeletal and connective tissue disorders	20 (20)	7 (7)	9 (9)
Arthralgia	0	0	1 (1)
Back pain	1 (1)	1 (1)	1 (0)
Limb discomfort	1 (1)	0	1 (1)
Muscle spasms	13 (13)	1 (1)	2 (2)
Muscular weakness	2 (2)	1 (1)	1 (1)
Musculoskeletal stiffness	2 (2)	1 (1)	1 (1)
Myalgia	1 (1)	1 (1)	0
Neck pain	1 (1)	1 (1)	1 (1)
Pain in extremity	0	1 (1)	2 (2)
Pain in jaw	2 (2)	0	1 (1)
Synovial cyst	0	0	1 (0)
Torticollis	0	0	1 (1)
Trismus	2 (2)	0	0
Nervous system disorders	32 (32)	13 (13)	17 (17)
Disturbance in attention	1 (1)	2 (2)	1 (1)
Dizziness	11 (11)	0	1 (1)
Freezing phenomenon	1 (1)	0	0
Head discomfort	2 (2)	0	1 (1)
Headache	18 (18)	11 (11)	13 (13)
Hypogeusia	0	0	1 (1)
Muscle contractions involuntary	1 (1)	0	0
Paraesthesia	4 (4)	0	1 (1)

Table 19. All Causalities (Treatment-Related) Incidence of Treatment-Emergent Adverse Events

Number of Subjects With Adverse Events by: System Organ Class Preferred Term	Sertraline (N = 52)	Moxifloxacin (N = 50)	Placebo (N = 50)
Poor quality sleep	0	1 (1)	0
Presyncope	1 (1)	0	0
Restless legs syndrome	0	1 (1)	0
Somnolence	2 (2)	1 (1)	4 (4)
Tremor	12 (12)	1 (1)	1 (1)
Psychiatric disorders	25 (25)	11 (11)	8 (8)
Abnormal behavior	1 (1)	0	0
Affect lability	1 (1)	0	1 (1)
Emotional disorder	0	1 (1)	0
Insomnia	22 (22)	11 (11)	6 (6)
Libido decreased	4 (4)	0	0
Libido increased	0	0	1 (1)
Nervousness	2 (2)	1 (1)	0
Nightmare	0	1 (1)	0
Psychiatric decompensation	1 (1)	0	0
Restlessness	1 (1)	0	0
Renal and urinary disorders	3 (3)	0	0
Dysuria	2 (2)	0	0
Polyuria	1 (1)	0	0
Reproductive system and breast disorders	1 (1)	1 (1)	3 (3)
Ejaculation failure	1 (1)	0	0
Erectile dysfunction	0	1 (1)	0
Gynaecomastia	0	0	1 (1)
Menstruation irregular	0	0	1 (1)
Testicular pain	0	0	1 (1)
Vaginal haemorrhage	0	0	1 (1)
Respiratory, thoracic and mediastinal disorders	9 (4)	4 (2)	6 (2)
Asthma	1 (0)	0	0
Cough	4 (0)	0	1 (0)
Dry throat	0	1 (1)	0
Dysphonia	1 (1)	0	0
Dyspnoea	1 (1)	0	0
Epistaxis	1 (1)	0	0
Nasal congestion	0	0	1 (1)
Oropharyngeal pain	1 (0)	3 (1)	3 (0)
Rhinorrhoea	1 (1)	0	0
Throat irritation	0	0	1 (1)
Skin and subcutaneous tissue disorders	19 (19)	5 (5)	9 (8)
Acne	2 (2)	1 (1)	1 (1)
Dry skin	1 (1)	1 (1)	3 (3)
Eczema	1 (1)	0	1 (1)
Erythema	1 (1)	2 (2)	1 (1)
Hyperhidrosis	12 (12)	0	1 (1)
Intertrigo	0	1 (0)	1 (0)
Night sweats	2 (2)	0	0
Pruritus	1 (1)	0	1 (1)
Rash macular	1 (1)	0	1 (1)

Table 19. All Causalities (Treatment-Related) Incidence of Treatment-Emergent Adverse Events

Number of Subjects With Adverse Events by: System Organ Class Preferred Term	Sertraline (N = 52)	Moxifloxacin (N = 50)	Placebo (N = 50)
Seborrhoea	0	0	2 (2)
Skin haemorrhage	1 (1)	0	0
Skin irritation	1 (1)	1 (1)	0
Vascular disorders	4 (4)	2 (2)	1 (1)
Hot flush	4 (4)	2 (2)	1 (1)
Total preferred term events	251 (238)	105 (92)	121 (106)

Source: Tables 14.3.1.2.2 and 14.3.1.3.2
Subjects were counted only once per treatment in each row.
Included all data collected since the first dose of study drug.
MedDRA (Version 19.0) coding dictionary applied.
Abbreviation: MedDRA = Medical Dictionary for Regulatory Activities.

12.2.3. Analysis of Adverse Events

Safety data were presented in tabular and/or graphical format and summarized descriptively, where appropriate. Majority of AEs were mild (429/477 = 89.9%) to moderate (47/477 = 9.9%) in severity (Tables 14.3.1.2.2 and 14.3.1.3.2). One (1) subject (Subject 10011044) receiving sertraline, reported a treatment-related severe AE of psychiatric decompensation that was considered as an SAE. There were no deaths reported in this study.

12.2.3.1. Permanent Discontinuations Due to Adverse Events

Two (2) subjects were discontinued from the study due to AEs. One (1) severe AE of psychiatric decompensation was reported by Subject 10011044 receiving sertraline which was considered serious by the investigators and discontinued from the study. [redacted] was discontinued from the study due to asthma. Details of permanent discontinuations due to AEs is provided in Table 20.

[redacted]

Table 20. Permanent Discontinuations Due to Adverse Events

Subject ID (Gender/Age)	Study Treatment at Onset	System Organ Class	Preferred Term	Severity/ Outcome	Adverse Event Study Start Day/ Study Stop Day[a]	Action/ Causality	SAE
[redacted]	Sertraline	Respiratory, thoracic and mediastinal disorders	Asthma[b]	Moderate/ Resolved	32/ 39	Permanently discontinued/ other-pre existing condition	No
[redacted]	Sertraline	Psychiatric disorders	Psychiatric decompensation[b]	Severe/ Resolved	45/ 47	Permanently discontinued/ study drug	Yes

Source: Table 14.3.1.1.1
Age at Screening.
Study treatment column gives study treatment at time of adverse event.
MedDRA (Version 19.0) coding dictionary applied.
Abbreviations: ID = identification; MedDRA = Medical Dictionary for Regulatory Activities; SAE = serious adverse event.
a. Day relative to start of study treatment. First day of study treatment = Day 1.
b. Treatment-emergent.

[redacted]

12.2.3.2. Dose Reductions or Temporary Discontinuations Due to Adverse Events (None)

There were no dose reductions or temporary discontinuations due to AEs during the study.

12.2.4. Listing of Adverse Events by Subject

A listing of AEs by subject is provided in [redacted]

12.3. Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

12.3.1. Listing of Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

12.3.1.1. Deaths (None)

There were no deaths reported in this study.

12.3.1.2. Other Serious Adverse Events

One (1) SAE (also accounted as a severe AE) was reported by [redacted] receiving sertraline and discontinued from the study due to the AE; see Section 12.3.2.2 for details.

12.3.1.3. Other Significant Adverse Events

Two (2) subjects permanently discontinued due to AE. AEs leading to permanent discontinuation are detailed in Section 12.3.2.3.

12.3.2. Narratives of Deaths, Other Serious Adverse Events, and Certain Other Significant Adverse Events

12.3.2.1. Death Narratives (Not Applicable)

12.3.2.2. Other Serious Adverse Event Narratives

One (1) SAE was reported in this study. A [redacted] experienced a TEAE of psychiatric decompensation on Study Day 45 after administration of 200 mg of sertraline which was considered as an SAE. The subject was withdrawn from the study due to the SAE on Study Day 47. The SAE resolved on 05 August 2016 (Study Day 47). The SAE listing for Subject 10011044 is presented in Section 14.3.2.

12.3.2.3. Other Significant Adverse Events Narratives

Two (2) subjects permanently discontinued the study due to TEAEs (Tables 14.1.1.2, 14.3.1.1.1, 16.2.1.2 and 16.2.7.1).

- [redacted] experienced an AE of asthma after receiving sertraline 200 mg. The AE was considered not related to study drug by the investigator and was moderate in severity. The study drug was permanently discontinued on 05 May 2016 (Day 14 of Period 2) (Table 16.2.5.1) in response to the event and the subject was withdrawn from the study on 30 May 2016.

[redacted]

- [redacted] receiving sertraline reported psychiatric decompensation which was considered serious by the investigators and discontinued from the study due to AE, see Section 12.3.2.2 for details.

12.3.3. Analysis and Discussion of Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

There were no deaths reported in this study. One (1) SAE (also accounted as a severe AE) was reported 1 SAE (also accounted as a severe AE) was reported. Two (2) subjects permanently discontinued due to AE.

12.4. Clinical Laboratory Evaluation

12.4.1. Listing of Individual Laboratory Values

Laboratory data are listed by subject in Table 16.2.8.1.1. Laboratory test abnormalities are listed in Table 16.2.8.1.2 (by subject) and Table 16.2.8.1.3 (by test).

12.4.2. Evaluation of Each Laboratory Parameter

The incidence of laboratory test abnormalities (without regard to baseline abnormality) is provided in Table 21. None of the findings were considered to be clinically significant nor reported as AEs.

[redacted]

Table 21. Incidence of Laboratory Test Abnormalities (Without Regard to Baseline Abnormality)

		Sertraline		Moxifloxacin		Placebo	
Number (%) With Laboratory Abnormalities		**26 (50%)**		**23 (46%)**		**16 (32%)**	
Parameters (Units)	**Criteria**	**N**	**n (%)**	**N**	**n (%)**	**N**	**n (%)**
Hematology							
Lymphocytes (abs) ($10^3/mm^3$)	>1.2 × ULN	52	0	50	1 (2.0)	50	0
Lymphocytes (%)	<0.8 × LLN	52	3 (5.8)	50	1 (2.0)	50	0
	>1.2 × ULN	52	0	50	1 (2.0)	50	1 (2.0)
Total neutrophils (abs) ($10^3/mm^3$)	<0.8 × LLN	52	1 (1.9)	50	1 (2.0)	50	2 (4.0)
	>1.2 × ULN	52	1 (1.9)	50	0	50	0
Neutrophils (%)	<0.8 × LLN	52	1 (1.9)	50	1 (2.0)	50	1 (2.0)
Eosinophils (abs) ($10^3/mm^3$)	>1.2 × ULN	52	3 (5.8)	50	3 (6.0)	50	4 (8.0)
Eosinophils (%)	>1.2 × ULN	52	2 (3.8)	50	2 (4.0)	50	1 (2.0)
Monocytes (abs) ($10^3/mm^3$)	>1.2 × ULN	52	8 (15.4)	50	3 (6.0)	50	3 (6.0)
Monocytes (%)	>1.2 × ULN	52	2 (3.8)	50	1 (2.0)	50	0
Liver function							
Total bilirubin (mg/dL)	>1.5 × ULN	52	0	50	1 (2.0)	50	0
Direct bilirubin (mg/dL)	>1.5 × ULN	52	2 (3.8)	50	4 (8.0)	50	3 (6.0)
Alanine aminotransferase (ALT) (IU/L)	>3.0 × ULN	52	1 (1.9)	50	0	50	0
Renal function							
Blood urea nitrogen (BUN) (mg/dL)	>1.3 × ULN	52	1 (1.9)	50	0	50	0
Electrolytes							
Bicarbonate (venous) (mEq/L)	>1.1 × ULN	52	1 (1.9)	50	1 (2.0)	50	0
Clinical chemistry (other)							
Glucose (mg/dL)	>1.5 × ULN	52	0	50	1 (2.0)	50	0
Urinalysis (dipstick)							
Urine ketones (qual)	≥1	52	3 (5.8)	50	0	50	0
Urine protein (qual)	≥1	52	0	50	1 (2.0)	50	0
Urine blood/Hgb (qual)	≥1	52	7 (13.5)	50	7 (14.0)	50	5 (10.0)
Urine urobilinogen	≥1	52	4 (7.7)	50	5 (10.0)	50	4 (8.0)
Urine bilirubin (qual)	≥1	52	1 (1.9)	50	2 (4.0)	50	0
Urine leukocyte esterase	≥1	4	0	5	1	4	2
Urinalysis (microscopy)							
Urine RBC (/HPF)	≥20	4	0	5	1	4	0
Urine WBC (/HPF)	≥20	4	0	5	1	4	2

Source: Table 14.3.4.1

Percentages were displayed for the laboratory tests having a category with ≥50 evaluable subjects.
Abbreviations: abs = absolute; ALT = alanine aminotransferase; BUN = blood urea nitrogen; Hgb = hemoglobin; HPF = high power field; N = total number of subjects with at least 1 observation of the given laboratory test while on study treatment or during lag time; n = number of subjects with a laboratory abnormality meeting specified criteria while on study treatment or during lag time; LLN = lower limit of normal; qual = qualitative; RBC = red blood cell; ULN = upper limit of normal; WBC = white blood cell.

12.5. Vital Signs, Electrocardiogram, Physical Findings, and Other Observations Related to Safety

12.5.1. Vital Signs

No clinically significant changes were observed in vital signs data nor reported as AEs during the study. Vital signs data absolute values and mean baseline and change from Baseline for vital signs data are presented in Tables 14.3.4.2.1 and 14.3.4.2.2, respectively. Vital signs maximum increase and decrease change from Baseline are presented in Tables 14.3.4.2.3.1 and 14.3.4.2.3.2, respectively.

12.5.2. Electrocardiogram

Please refer to Section 11.4.2.

12.5.3. Physical Findings

Physical examination results are listed by subject in Table 16.2.8.4. Three (3) subjects reported weight decreased [redacted] which were considered as AEs. All the 3 AEs were mild in intensity and considered not related to treatment (Table 16.2.7.1).

12.5.4. Suicidality Assessment Columbia – Suicide Severity Rating Scale

Summary of C-SSRS and C-SSRS mapped to Columbia Classification Algorithm of Suicide Assessment data are presented in Table 16.2.8.5.1 and Table 16.2.8.5.2, respectively. None of the subjects had suicidal ideation during this study.

12.6. Safety Conclusions

There were no deaths, or dose reductions due to AEs reported in the study. One (1) subject receiving sertraline reported a severe treatment-related AE that was also reported as an SAE. Majority of AEs were mild (429/477 = 89.9%) to moderate (47/477 = 9.9%) in severity. Two (2) subjects permanently discontinued due to AEs. The most common AEs were headache (experienced by 18, 11, and 13 subjects after receiving sertraline, moxifloxacin and placebo, respectively) insomnia (experienced by 22, 11, and 6 subjects after receiving sertraline, moxifloxacin and placebo, respectively), fatigue (experienced by 17, 7, and 7 subjects after receiving sertraline, moxifloxacin and placebo, respectively). No medication errors occurred in the study.

13. DISCUSSION AND OVERALL CONCLUSIONS

- In the primary analysis, at 4-hours postdose time point, the supratherapeutic dose of 400 mg/day was shown to exceed the threshold (ie, the time-matched LS mean difference of QTcF between sertraline and placebo was greater than the predefined threshold of 10 msec) for a positive thorough QT/QTc study in healthy subjects.

- Moxifloxacin demonstrated assay sensitivity, suggesting that the study was adequately sensitive to assess the effect of sertraline on QTcF interval.

[redacted]

- Exposure-response analysis indicated a slightly positive relationship between QTcF and sertraline/N-desmethylsertraline concentrations.
    - At therapeutic C_{max} of sertraline (86 ng/mL), predicted QTcF prolongation was not clinically significant (Mean 3.57 msec; 90% CI of 2.92 to 4.23 msec).
    - At supratherapeutic C_{max} of sertraline on Day 14 (234 ng/mL), predicted 2-sided 90% CI of QTcF prolongation exceeds 10 msec (Mean 8.93 msec; 90% CI of 7.42 to 10.45 msec).
    - Sertraline plasma concentration had to be >223.5 ng/mL for predicted 90% CI to exceed 10 msec (Mean 8.55 msec; 90% CI of 7.11 to 9.99 msec). This is at least 2.6 fold greater than therapeutic C_{max} of sertraline (86 ng/mL).
- Supratherapeutic concentration (C_{max}) of sertraline was achieved on Day 14, and the supratherapeutic C_{max} was about 3 folds higher than the therapeutic C_{max}.
- The 14-day multiple titrations up to supratherapeutic dose of 400 mg/day (200 mg BID) sertraline were well tolerated.

[redacted]

[redacted]

14. TABLES AND FIGURES REFERRED TO BUT NOT INCLUDED IN THE TEXT

SERTRALINE Protocol A0501104
Subject Evaluation Groups

	Sertraline	Moxifloxacin	Placebo
Number (%) of Subjects			
Assigned to Study Treatment 54			
Treated	52	50	50
Completed	47 (90.4)	49 (98.0)	47 (94.0)
Discontinued	5 (9.6)	1 (2.0)	3 (6.0)
Analyzed for Pharmacokinetics:			
Concentration	52 (100.0)	0	0
Parameter	52 (100.0)	0	0
Analyzed for ECG:			
Completer ECG Analysis Population	46 (88.5)	46 (92.0)	46 (92.0)
Primary ECG Analysis Population	52 (100.0)	50 (100.0)	50 (100.0)
Analyzed for Safety:			
Adverse events	52 (100.0)	50 (100.0)	50 (100.0)
Laboratory data	52 (100.0)	50 (100.0)	50 (100.0)

Discontinuations have been attributed to the last study treatment received.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 29JAN2017 (22:05)

Table 14.1.1.2
SERTRALINE Protocol A0501104
Discontinuations from Study

Number (%) of Subjects	Sertraline 52		Moxifloxacin 50		Placebo 50	
Discontinuations						
Relation to Study Drug not Defined	3	(5.8)	1	(2.0)	3	(6.0)
No longer willing to participate in study	2	(3.8)	1	(2.0)	3	(6.0)
Other	1	(1.9)	0		0	
Related to Study Drug	1	(1.9)	0		0	
Adverse event	1	(1.9)	0		0	
Not Related to Study Drug	1	(1.9)	0		0	
Adverse event	1	(1.9)	0		0	
Total	5	(9.6)	1	(2.0)	3	(6.0)

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:24)

	All Subjects					
	MALE		FEMALE		TOTAL	
Number (%) of Subjects	43		11		54	
Hormonal Status:						
PREMENOPAUSAL			10	(90.9)		
POSTMENOPAUSAL			1	(9.1)		
Age (years):						
< 18	0		0		0	
18-25	7	(16.3)	1	(9.1)	8	(14.8)
26-35	16	(37.2)	2	(18.2)	18	(33.3)
36-45	11	(25.6)	5	(45.5)	16	(29.6)
> 45	9	(20.9)	3	(27.3)	12	(22.2)
Mean	36.0		38.5		36.5	
SD	9.7		9.9		9.7	
Range	22-53		20-54		20-54	
Race:						
WHITE	36	(83.7)	10	(90.9)	46	(85.2)
BLACK	3	(7.0)	0		3	(5.6)
ASIAN	1	(2.3)	0		1	(1.9)
OTHER	3	(7.0)	1	(9.1)	4	(7.4)
Weight (kg):						
Mean	75.9		68.7		74.4	
SD	10.0		10.1		10.3	
Range	56.4-96.0		54.3-87.4		54.3-96.0	
N	43	(100.0)	11	(100.0)	54	(100.0)
Body Mass Index(kg/m**2):						
Mean	24.7		25.1		24.8	
SD	2.8		3.6		3.0	
Range	18.1-30.1		19.9-30.5		18.1-30.5	
N	43	(100.0)	11	(100.0)	54	(100.0)
Height (cm):						
Mean	175.3		165.5		173.3	
SD	6.5		6.8		7.6	
Range	163-193		156-179		156-193	
N	43	(100.0)	11	(100.0)	54	(100.0)

Body Mass Index is defined as wt/(ht*.01)**2.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:15)

SERTRALINE Protocol A0501104
Discontinuations Due to Adverse Events

Treatment Group: A=Sertraline, B=Moxifloxacin, C=Placebo

System Organ Class	MedDRA (v19.0) Preferred Term/ INVESTIGATOR ENTRY	Treatment: Trt	Treatment: Trt Phase	Treatment: Treatment At Onset	Adverse Event: Study Start Day+/ Study Stop Day+	Adverse Event: Period Start Day++/ Stop Day++	Adverse Event: Time Post Dose (Hrs)	Adverse Event: Duration (Hrs)	Adverse Event: SEVERITY/ Outcome	Adverse Event: ACTION/ Causality	SAE
[redacted]											
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	Asthma*/ ASTHMA EXACERBATION	A	Active	Sertraline	32/ 39	32/ 39	430.83	168.00	MODERATE/ Resolved (30MAY2016)	STUDY DRUG ACTION: (PERMANENTLY DISCONTINUED) SUBJECT ACTION: (TREATMENT GIVEN,D/C STUDY) / Other-pre existing condition	NO
[redacted]											
PSYCHIATRIC DISORDERS	Psychiatric decompensation*/ PSYCHOTIC DECOMPENSATION	A	Active	Sertraline	45/ 47	15/ 17	22.92	48.00	SEVERE/ Resolved (05AUG2016)	STUDY DRUG ACTION: (PERMANENTLY DISCONTINUED) SUBJECT ACTION: (D/C STUDY)/ Study Drug	YES

Age and weight are at Screening
* Treatment-emergent
+ Day relative to start of study treatment. First day of study treatment = day 1
++ Day relative to first day of each treatment period. First day of each treatment period = day 1
[] Values in brackets are imputed from incomplete dates and times.
SAE = Serious Adverse Event (according to Investigators assessment).
Treatment (Trt) column gives study treatment at time of adverse event.
MedDRA (v19.0) coding dictionary applied.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:23)

Table 14.3.1.2.1
SERTRALINE Protocol A0501104
Treatment-Emergent Adverse Events (All Causalities)

	Sertraline		Moxifloxacin		Placebo	
	n	(%)	n	(%)	n	(%)
Number (%) of subjects:						
Subjects evaluable for adverse events	52		50		50	
Number of adverse events	251		105		121	
Subjects with adverse events	45	(86.5)	42	(84.0)	33	(66.0)
Subjects with serious adverse events	1	(1.9)	0		0	
Subjects with severe adverse events	1	(1.9)	0		0	
Subjects discontinued due to adverse events	2	(3.8)	0		0	
Subjects with dose reduced or temporary discontinuation due to adverse events	0		0		0	

Includes all data collected since the first dose of study drug.
Except for the Number of Adverse Events subjects are counted only once per treatment in each row.
Serious Adverse Events - according to the investigator’s assessment.
Severity counts are based on the maximum severity or grade of events
MedDRA (v19.0) coding dictionary applied.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:20)

SERTRALINE Protocol A0501104
Incidence and Severity of Treatment-Emergent Adverse Events (All Causalities)

Number of Subjects evaluable for adverse events	Sertraline (n=52)					Moxifloxacin (n=50)					Placebo (n=50)				
			Severity*					Severity*					Severity*		
	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.
Number (%) of Subjects with Adverse Events by: System Organ Class and MedDRA (v19.0) preferred term															
CARDIAC DISORDERS	2	(3.8)	2	0	0	1	(2.0)	1	0	0	2	(4.0)	2	0	0
Atrioventricular block first degree	1	(1.9)	1	0	0	1	(2.0)	1	0	0	2	(4.0)	2	0	0
Palpitations	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
EAR AND LABYRINTH DISORDERS	1	(1.9)	0	1	0	0		0	0	0	2	(4.0)	2	0	0
Ear discomfort	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Hyperacusis	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Vertigo	1	(1.9)	0	1	0	0		0	0	0	0		0	0	0
EYE DISORDERS	8	(15.4)	7	1	0	6	(12.0)	3	3	0	3	(6.0)	3	0	0
Dry eye	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Ocular discomfort	1	(1.9)	0	1	0	2	(4.0)	0	2	0	0		0	0	0
Ocular hyperaemia	0		0	0	0	2	(4.0)	1	1	0	0		0	0	0
Photophobia	1	(1.9)	1	0	0	0		0	0	0	2	(4.0)	2	0	0
Vision blurred	2	(3.8)	2	0	0	0		0	0	0	0		0	0	0
Visual impairment	5	(9.6)	5	0	0	2	(4.0)	2	0	0	0		0	0	0
GASTROINTESTINAL DISORDERS	25	(48.1)	22	3	0	17	(34.0)	14	3	0	18	(36.0)	17	1	0
Abdominal discomfort	2	(3.8)	2	0	0	2	(4.0)	2	0	0	4	(8.0)	4	0	0
Abdominal distension	1	(1.9)	1	0	0	1	(2.0)	1	0	0	1	(2.0)	1	0	0
Abdominal pain	3	(5.8)	3	0	0	3	(6.0)	2	1	0	4	(8.0)	4	0	0
Abdominal pain lower	1	(1.9)	1	0	0	0		0	0	0	1	(2.0)	1	0	0
Abdominal pain upper	2	(3.8)	1	1	0	0		0	0	0	0		0	0	0

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Includes all data collected since the first dose of study drug.
Percentages of gender specific events are calculated using the corresponding gender count as denominator.
MedDRA (v19.0) coding dictionary applied.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:21)

SERTRALINE Protocol A0501104
Incidence and Severity of Treatment-Emergent Adverse Events (All Causalities)

Number of Subjects evaluable for adverse events	Sertraline (n=52)					Moxifloxacin (n=50)					Placebo (n=50)				
			Severity*					Severity*					Severity*		
	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.
Number (%) of Subjects with Adverse Events by: System Organ Class and MedDRA (v19.0) preferred term															
Change of bowel habit	3	(5.8)	3	0	0	1	(2.0)	1	0	0	0		0	0	0
Chapped lips	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Cheilitis	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Constipation	2	(3.8)	2	0	0	3	(6.0)	3	0	0	0		0	0	0
Diarrhoea	8	(15.4)	8	0	0	4	(8.0)	3	1	0	6	(12.0)	6	0	0
Dry mouth	5	(9.6)	5	0	0	1	(2.0)	1	0	0	0		0	0	0
Dyspepsia	1	(1.9)	1	0	0	3	(6.0)	3	0	0	0		0	0	0
Dysphagia	2	(3.8)	2	0	0	0		0	0	0	0		0	0	0
Flatulence	0		0	0	0	2	(4.0)	2	0	0	1	(2.0)	1	0	0
Functional gastrointestinal disorder	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Gastrointestinal sounds abnormal	2	(3.8)	2	0	0	1	(2.0)	1	0	0	0		0	0	0
Gastrooesophageal reflux disease	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Gingival bleeding	1	(1.9)	1	0	0	1	(2.0)	1	0	0	0		0	0	0
Gingival pain	1	(1.9)	1	0	0	0		0	0	0	1	(2.0)	1	0	0
Glossodynia	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Haematochezia	2	(3.8)	2	0	0	0		0	0	0	0		0	0	0
Nausea	8	(15.4)	6	2	0	2	(4.0)	1	1	0	2	(4.0)	2	0	0
Oral disorder	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Paraesthesia oral	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Toothache	1	(1.9)	0	1	0	0		0	0	0	0		0	0	0
Vomiting	2	(3.8)	0	2	0	0		0	0	0	1	(2.0)	0	1	0
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	27	(51.9)	27	0	0	11	(22.0)	11	0	0	13	(26.0)	13	0	0
Application site erythema	0		0	0	0	2	(4.0)	2	0	0	0		0	0	0
Application site irritation	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Asthenia	4	(7.7)	4	0	0	1	(2.0)	1	0	0	0		0	0	0
Chest discomfort	3	(5.8)	3	0	0	0		0	0	0	3	(6.0)	3	0	0

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SERTRALINE Protocol A0501104
Incidence and Severity of Treatment-Emergent Adverse Events (All Causalities)

Number of Subjects evaluable for adverse events	Sertraline (n=52)					Moxifloxacin (n=50)					Placebo (n=50)				
			Severity*					Severity*					Severity*		
	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.
Number (%) of Subjects with Adverse Events by: System Organ Class and MedDRA (v19.0) preferred term															
Fatigue	17	(32.7)	17	0	0	7	(14.0)	7	0	0	7	(14.0)	7	0	0
Feeling cold	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Feeling drunk	1	(1.9)	1	0	0	0		0	0	0	1	(2.0)	1	0	0
Feeling hot	2	(3.8)	2	0	0	0		0	0	0	1	(2.0)	1	0	0
Hangover	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Hunger	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Vessel puncture site erythema	3	(5.8)	3	0	0	1	(2.0)	1	0	0	0		0	0	0
Vessel puncture site haematoma	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Vessel puncture site pain	0		0	0	0	1	(2.0)	1	0	0	2	(4.0)	2	0	0
IMMUNE SYSTEM DISORDERS	0		0	0	0	0		0	0	0	1	(2.0)	0	1	0
Seasonal allergy	0		0	0	0	0		0	0	0	1	(2.0)	0	1	0
INFECTIONS AND INFESTATIONS	1	(1.9)	1	0	0	7	(14.0)	6	1	0	3	(6.0)	1	2	0
Asymptomatic bacteriuria	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Folliculitis	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Fungal infection	0		0	0	0	1	(2.0)	0	1	0	2	(4.0)	0	2	0
Gastroenteritis	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Gingivitis	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Hordeolum	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Nasopharyngitis	0		0	0	0	2	(4.0)	2	0	0	1	(2.0)	1	0	0
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1	(1.9)	0	1	0	0		0	0	0	0		0	0	0
Arthropod bite	1	(1.9)	0	1	0	0		0	0	0	0		0	0	0
INVESTIGATIONS	2	(3.8)	2	0	0	1	(2.0)	1	0	0	0		0	0	0

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Incidence and Severity of Treatment-Emergent Adverse Events (All Causalities)

Number of Subjects evaluable for adverse events	Sertraline (n=52)					Moxifloxacin (n=50)					Placebo (n=50)				
			Severity*					Severity*					Severity*		
	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.
Number (%) of Subjects with Adverse Events by: System Organ Class and MedDRA (v19.0) preferred term															
Weight decreased	2	(3.8)	2	0	0	1	(2.0)	1	0	0	0		0	0	0
METABOLISM AND NUTRITION DISORDERS	3	(5.8)	3	0	0	1	(2.0)	1	0	0	2	(4.0)	2	0	0
Decreased appetite	3	(5.8)	3	0	0	1	(2.0)	1	0	0	2	(4.0)	2	0	0
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	20	(38.5)	20	0	0	7	(14.0)	6	1	0	9	(18.0)	9	0	0
Arthralgia	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Back pain	1	(1.9)	1	0	0	1	(2.0)	1	0	0	1	(2.0)	1	0	0
Limb discomfort	1	(1.9)	1	0	0	0		0	0	0	1	(2.0)	1	0	0
Muscle spasms	13	(25.0)	13	0	0	1	(2.0)	1	0	0	2	(4.0)	2	0	0
Muscular weakness	2	(3.8)	2	0	0	1	(2.0)	1	0	0	1	(2.0)	1	0	0
Musculoskeletal stiffness	2	(3.8)	2	0	0	1	(2.0)	1	0	0	1	(2.0)	1	0	0
Myalgia	1	(1.9)	1	0	0	1	(2.0)	0	1	0	0		0	0	0
Neck pain	1	(1.9)	1	0	0	1	(2.0)	1	0	0	1	(2.0)	1	0	0
Pain in extremity	0		0	0	0	1	(2.0)	1	0	0	2	(4.0)	2	0	0
Pain in jaw	2	(3.8)	2	0	0	0		0	0	0	1	(2.0)	1	0	0
Synovial cyst	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Torticollis	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Trismus	2	(3.8)	2	0	0	0		0	0	0	0		0	0	0
NERVOUS SYSTEM DISORDERS	32	(61.5)	24	8	0	13	(26.0)	10	3	0	17	(34.0)	12	5	0
Disturbance in attention	1	(1.9)	1	0	0	2	(4.0)	2	0	0	1	(2.0)	1	0	0
Dizziness	11	(21.2)	10	1	0	0		0	0	0	1	(2.0)	1	0	0

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SERTRALINE Protocol A0501104
Incidence and Severity of Treatment-Emergent Adverse Events (All Causalities)

Number of Subjects evaluable for adverse events	Sertraline (n=52)					Moxifloxacin (n=50)					Placebo (n=50)				
			Severity*					Severity*					Severity*		
	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.
Number (%) of Subjects with Adverse Events by:															
System Organ Class and MedDRA (v19.0) preferred term															
Freezing phenomenon	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Head discomfort	2	(3.8)	2	0	0	0		0	0	0	1	(2.0)	1	0	0
Headache	18	(34.6)	12	6	0	11	(22.0)	8	3	0	13	(26.0)	8	5	0
Hypogeusia	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Muscle contractions involuntary	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Paraesthesia	4	(7.7)	3	1	0	0		0	0	0	1	(2.0)	1	0	0
Poor quality sleep	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Presyncope	1	(1.9)	0	1	0	0		0	0	0	0		0	0	0
Restless legs syndrome	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Somnolence	2	(3.8)	2	0	0	1	(2.0)	1	0	0	4	(8.0)	4	0	0
Tremor	12	(23.1)	12	0	0	1	(2.0)	1	0	0	1	(2.0)	1	0	0
PSYCHIATRIC DISORDERS	25	(48.1)	24	0	1	11	(22.0)	10	1	0	8	(16.0)	7	1	0
Abnormal behaviour	1	(1.9)	0	1	0	0		0	0	0	0		0	0	0
Affect lability	1	(1.9)	1	0	0	0		0	0	0	1	(2.0)	1	0	0
Emotional disorder	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Insomnia	22	(42.3)	22	0	0	11	(22.0)	10	1	0	6	(12.0)	5	1	0
Libido decreased	4	(7.7)	4	0	0	0		0	0	0	0		0	0	0
Libido increased	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Nervousness	2	(3.8)	2	0	0	1	(2.0)	1	0	0	0		0	0	0
Nightmare	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Psychiatric decompensation	1	(1.9)	0	0	1	0		0	0	0	0		0	0	0
Restlessness	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
RENAL AND URINARY DISORDERS	3	(5.8)	3	0	0	0		0	0	0	0		0	0	0
Dysuria	2	(3.8)	2	0	0	0		0	0	0	0		0	0	0

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Number of Subjects evaluable for adverse events	Sertraline (n=52)					Moxifloxacin (n=50)					Placebo (n=50)				
			Severity*					Severity*					Severity*		
	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.
Number (%) of Subjects with Adverse Events by: System Organ Class and MedDRA (v19.0) preferred term															
Polyuria	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1	(2.4)	1	0	0	1	(2.6)	1	0	0	3	(6.0)	3	0	0
Ejaculation failure	1	(2.4)	1	0	0	0		0	0	0	0		0	0	0
Erectile dysfunction	0		0	0	0	1	(2.6)	1	0	0	0		0	0	0
Gynaecomastia	0		0	0	0	0		0	0	0	1	(2.6)	1	0	0
Menstruation irregular	0		0	0	0	0		0	0	0	1	(9.1)	1	0	0
Testicular pain	0		0	0	0	0		0	0	0	1	(2.6)	1	0	0
Vaginal haemorrhage	0		0	0	0	0		0	0	0	1	(9.1)	1	0	0
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	9	(17.3)	8	1	0	4	(8.0)	4	0	0	6	(12.0)	6	0	0
Asthma	1	(1.9)	0	1	0	0		0	0	0	0		0	0	0
Cough	4	(7.7)	4	0	0	0		0	0	0	1	(2.0)	1	0	0
Dry throat	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Dysphonia	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Dyspnoea	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Epistaxis	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Nasal congestion	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Oropharyngeal pain	1	(1.9)	1	0	0	3	(6.0)	3	0	0	3	(6.0)	3	0	0
Rhinorrhoea	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Throat irritation	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	19	(36.5)	17	2	0	5	(10.0)	4	1	0	9	(18.0)	7	2	0
Acne	2	(3.8)	2	0	0	1	(2.0)	1	0	0	1	(2.0)	1	0	0
Dry skin	1	(1.9)	1	0	0	1	(2.0)	1	0	0	3	(6.0)	3	0	0

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			Severity*					Severity*					Severity*		
	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.
Number (%) of Subjects with Adverse Events by: System Organ Class and MedDRA (v19.0) preferred term															
Eczema	1	(1.9)	0	1	0	0		0	0	0	1	(2.0)	0	1	0
Erythema	1	(1.9)	1	0	0	2	(4.0)	2	0	0	1	(2.0)	1	0	0
Hyperhidrosis	12	(23.1)	12	0	0	0		0	0	0	1	(2.0)	1	0	0
Intertrigo	0		0	0	0	1	(2.0)	0	1	0	1	(2.0)	0	1	0
Night sweats	2	(3.8)	2	0	0	0		0	0	0	0		0	0	0
Pruritus	1	(1.9)	1	0	0	0		0	0	0	1	(2.0)	1	0	0
Rash macular	1	(1.9)	1	0	0	0		0	0	0	1	(2.0)	1	0	0
Seborrhoea	0		0	0	0	0		0	0	0	2	(4.0)	2	0	0
Skin haemorrhage	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Skin irritation	1	(1.9)	0	1	0	1	(2.0)	1	0	0	0		0	0	0
VASCULAR DISORDERS	4	(7.7)	4	0	0	2	(4.0)	2	0	0	1	(2.0)	1	0	0
Hot flush	4	(7.7)	4	0	0	2	(4.0)	2	0	0	1	(2.0)	1	0	0
Total preferred term events	251		228	22	1	105		92	13	0	121		109	12	0

* If the same subject in a given treatment had more than one occurrence in the same preferred term event category, only the most severe occurrence is taken. Subjects are counted only once per treatment in each row. For the TESS algorithm any missing severities have been imputed as severe unless the subject experienced another occurrence of the same event in a given treatment for which severity was recorded.
In this case, the reported severity is summarized. Missing baseline severities are imputed as mild.
Includes all data collected since the first dose of study drug.
Percentages of gender specific events are calculated using the corresponding gender count as denominator.
MedDRA (v19.0) coding dictionary applied.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:21)

SERTRALINE Protocol A0501104
Treatment-Emergent Adverse Events (Treatment Related)

	Sertraline		Moxifloxacin		Placebo	
	n	(%)	n	(%)	n	(%)
Number (%) of subjects:						
Subjects evaluable for adverse events	52		50		50	
Number of adverse events	238		92		106	
Subjects with adverse events	44	(84.6)	41	(82.0)	30	(60.0)
Subjects with serious adverse events	1	(1.9)	0		0	
Subjects with severe adverse events	1	(1.9)	0		0	
Subjects discontinued due to adverse events	1	(1.9)	0		0	
Subjects with dose reduced or temporary discontinuation due to adverse events	0		0		0	

Includes all data collected since the first dose of study drug.
Except for the Number of Adverse Events subjects are counted only once per treatment in each row.
Serious Adverse Events - according to the investigator’s assessment.
Severity counts are based on the maximum severity or grade of events
MedDRA (v19.0) coding dictionary applied.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:21)

SERTRALINE Protocol A0501104
Incidence and Severity of Treatment-Emergent Adverse Events (Treatment Related)

Number of Subjects evaluable for adverse events	Sertraline (n=52)					Moxifloxacin (n=50)					Placebo (n=50)				
			Severity*					Severity*					Severity*		
	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.
Number (%) of Subjects with Adverse Events by: System Organ Class and MedDRA (v19.0) preferred term															
CARDIAC DISORDERS	2	(3.8)	2	0	0	1	(2.0)	1	0	0	2	(4.0)	2	0	0
Atrioventricular block first degree	1	(1.9)	1	0	0	1	(2.0)	1	0	0	2	(4.0)	2	0	0
Palpitations	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
EAR AND LABYRINTH DISORDERS	1	(1.9)	0	1	0	0		0	0	0	2	(4.0)	2	0	0
Ear discomfort	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Hyperacusis	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Vertigo	1	(1.9)	0	1	0	0		0	0	0	0		0	0	0
EYE DISORDERS	8	(15.4)	7	1	0	5	(10.0)	3	2	0	3	(6.0)	3	0	0
Dry eye	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Ocular discomfort	1	(1.9)	0	1	0	2	(4.0)	0	2	0	0		0	0	0
Ocular hyperaemia	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Photophobia	1	(1.9)	1	0	0	0		0	0	0	2	(4.0)	2	0	0
Vision blurred	2	(3.8)	2	0	0	0		0	0	0	0		0	0	0
Visual impairment	5	(9.6)	5	0	0	2	(4.0)	2	0	0	0		0	0	0
GASTROINTESTINAL DISORDERS	25	(48.1)	22	3	0	17	(34.0)	14	3	0	17	(34.0)	16	1	0
Abdominal discomfort	2	(3.8)	2	0	0	2	(4.0)	2	0	0	4	(8.0)	4	0	0
Abdominal distension	1	(1.9)	1	0	0	1	(2.0)	1	0	0	1	(2.0)	1	0	0
Abdominal pain	3	(5.8)	3	0	0	3	(6.0)	2	1	0	4	(8.0)	4	0	0
Abdominal pain lower	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Abdominal pain upper	2	(3.8)	1	1	0	0		0	0	0	0		0	0	0
Change of bowel habit	3	(5.8)	3	0	0	1	(2.0)	1	0	0	0		0	0	0
Chapped lips	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Cheilitis	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Constipation	2	(3.8)	2	0	0	3	(6.0)	3	0	0	0		0	0	0
Diarrhoea	8	(15.4)	8	0	0	4	(8.0)	3	1	0	6	(12.0)	6	0	0

* If the same subject in a given treatment had more than one occurrence in the same preferred term event category, only the most severe occurrence is taken. Subjects are counted only once per treatment in each row. For the TESS algorithm any missing severities have been imputed as severe unless the subject experienced another occurrence of the same event in a given treatment for which severity was recorded.
In this case, the reported severity is summarized. Missing baseline severities are imputed as mild.
Includes all data collected since the first dose of study drug.
Percentages of gender specific events are calculated using the corresponding gender count as denominator.
MedDRA (v19.0) coding dictionary applied.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:22)

SERTRALINE Protocol A0501104
Incidence and Severity of Treatment-Emergent Adverse Events (Treatment Related)

Number of Subjects evaluable for adverse events	Sertraline (n=52)					Moxifloxacin (n=50)					Placebo (n=50)				
			Severity*					Severity*					Severity*		
	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.
Number (%) of Subjects with Adverse Events by: System Organ Class and MedDRA (v19.0) preferred term															
Dry mouth	5	(9.6)	5	0	0	1	(2.0)	1	0	0	0		0	0	0
Dyspepsia	1	(1.9)	1	0	0	3	(6.0)	3	0	0	0		0	0	0
Dysphagia	2	(3.8)	2	0	0	0		0	0	0	0		0	0	0
Flatulence	0		0	0	0	2	(4.0)	2	0	0	1	(2.0)	1	0	0
Functional gastrointestinal disorder	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Gastrointestinal sounds abnormal	2	(3.8)	2	0	0	1	(2.0)	1	0	0	0		0	0	0
Gastrooesophageal reflux disease	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Gingival bleeding	1	(1.9)	1	0	0	1	(2.0)	1	0	0	0		0	0	0
Gingival pain	1	(1.9)	1	0	0	0		0	0	0	1	(2.0)	1	0	0
Glossodynia	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Haematochezia	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Nausea	8	(15.4)	6	2	0	2	(4.0)	1	1	0	2	(4.0)	2	0	0
Oral disorder	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Paraesthesia oral	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Toothache	1	(1.9)	0	1	0	0		0	0	0	0		0	0	0
Vomiting	2	(3.8)	0	2	0	0		0	0	0	1	(2.0)	0	1	0
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	25	(48.1)	25	0	0	8	(16.0)	8	0	0	11	(22.0)	11	0	0
Asthenia	4	(7.7)	4	0	0	1	(2.0)	1	0	0	0		0	0	0
Chest discomfort	3	(5.8)	3	0	0	0		0	0	0	3	(6.0)	3	0	0
Fatigue	17	(32.7)	17	0	0	7	(14.0)	7	0	0	7	(14.0)	7	0	0
Feeling cold	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Feeling drunk	1	(1.9)	1	0	0	0		0	0	0	1	(2.0)	1	0	0
Feeling hot	2	(3.8)	2	0	0	0		0	0	0	1	(2.0)	1	0	0
Hangover	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Hunger	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
INFECTIONS AND INFESTATIONS	0		0	0	0	2	(4.0)	2	0	0	0		0	0	0
Folliculitis	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Gingivitis	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
INVESTIGATIONS	2	(3.8)	2	0	0	1	(2.0)	1	0	0	0		0	0	0

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In this case, the reported severity is summarized. Missing baseline severities are imputed as mild.
Includes all data collected since the first dose of study drug.
Percentages of gender specific events are calculated using the corresponding gender count as denominator.
MedDRA (v19.0) coding dictionary applied.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:22)

SERTRALINE Protocol A0501104
Incidence and Severity of Treatment-Emergent Adverse Events (Treatment Related)

Number of Subjects evaluable for adverse events	Sertraline (n=52)					Moxifloxacin (n=50)					Placebo (n=50)				
			Severity*					Severity*					Severity*		
	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.
Number (%) of Subjects with Adverse Events by: System Organ Class and MedDRA (v19.0) preferred term															
Weight decreased	2	(3.8)	2	0	0	1	(2.0)	1	0	0	0		0	0	0
METABOLISM AND NUTRITION DISORDERS	3	(5.8)	3	0	0	1	(2.0)	1	0	0	2	(4.0)	2	0	0
Decreased appetite	3	(5.8)	3	0	0	1	(2.0)	1	0	0	2	(4.0)	2	0	0
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	20	(38.5)	20	0	0	7	(14.0)	6	1	0	9	(18.0)	9	0	0
Arthralgia	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Back pain	1	(1.9)	1	0	0	1	(2.0)	1	0	0	0		0	0	0
Limb discomfort	1	(1.9)	1	0	0	0		0	0	0	1	(2.0)	1	0	0
Muscle spasms	13	(25.0)	13	0	0	1	(2.0)	1	0	0	2	(4.0)	2	0	0
Muscular weakness	2	(3.8)	2	0	0	1	(2.0)	1	0	0	1	(2.0)	1	0	0
Musculoskeletal stiffness	2	(3.8)	2	0	0	1	(2.0)	1	0	0	1	(2.0)	1	0	0
Myalgia	1	(1.9)	1	0	0	1	(2.0)	0	1	0	0		0	0	0
Neck pain	1	(1.9)	1	0	0	1	(2.0)	1	0	0	1	(2.0)	1	0	0
Pain in extremity	0		0	0	0	1	(2.0)	1	0	0	2	(4.0)	2	0	0
Pain in jaw	2	(3.8)	2	0	0	0		0	0	0	1	(2.0)	1	0	0
Torticollis	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Trismus	2	(3.8)	2	0	0	0		0	0	0	0		0	0	0
NERVOUS SYSTEM DISORDERS	32	(61.5)	24	8	0	13	(26.0)	10	3	0	17	(34.0)	12	5	0
Disturbance in attention	1	(1.9)	1	0	0	2	(4.0)	2	0	0	1	(2.0)	1	0	0
Dizziness	11	(21.2)	10	1	0	0		0	0	0	1	(2.0)	1	0	0
Freezing phenomenon	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Head discomfort	2	(3.8)	2	0	0	0		0	0	0	1	(2.0)	1	0	0
Headache	18	(34.6)	12	6	0	11	(22.0)	8	3	0	13	(26.0)	8	5	0
Hypogeusia	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Muscle contractions involuntary	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Paraesthesia	4	(7.7)	3	1	0	0		0	0	0	1	(2.0)	1	0	0

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In this case, the reported severity is summarized. Missing baseline severities are imputed as mild.
Includes all data collected since the first dose of study drug.
Percentages of gender specific events are calculated using the corresponding gender count as denominator.
MedDRA (v19.0) coding dictionary applied.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:22)

SERTRALINE Protocol A0501104
Incidence and Severity of Treatment-Emergent Adverse Events (Treatment Related)

Number of Subjects evaluable for adverse events	Sertraline (n=52)					Moxifloxacin (n=50)					Placebo (n=50)				
			Severity*					Severity*					Severity*		
	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.
Number (%) of Subjects with Adverse Events by:															
System Organ Class and MedDRA (v19.0) preferred term															
Poor quality sleep	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Presyncope	1	(1.9)	0	1	0	0		0	0	0	0		0	0	0
Restless legs syndrome	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Somnolence	2	(3.8)	2	0	0	1	(2.0)	1	0	0	4	(8.0)	4	0	0
Tremor	12	(23.1)	12	0	0	1	(2.0)	1	0	0	1	(2.0)	1	0	0
PSYCHIATRIC DISORDERS	25	(48.1)	24	0	1	11	(22.0)	10	1	0	8	(16.0)	7	1	0
Abnormal behaviour	1	(1.9)	0	1	0	0		0	0	0	0		0	0	0
Affect lability	1	(1.9)	1	0	0	0		0	0	0	1	(2.0)	1	0	0
Emotional disorder	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Insomnia	22	(42.3)	22	0	0	11	(22.0)	10	1	0	6	(12.0)	5	1	0
Libido decreased	4	(7.7)	4	0	0	0		0	0	0	0		0	0	0
Libido increased	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Nervousness	2	(3.8)	2	0	0	1	(2.0)	1	0	0	0		0	0	0
Nightmare	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Psychiatric decompensation	1	(1.9)	0	0	1	0		0	0	0	0		0	0	0
Restlessness	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
RENAL AND URINARY DISORDERS	3	(5.8)	3	0	0	0		0	0	0	0		0	0	0
Dysuria	2	(3.8)	2	0	0	0		0	0	0	0		0	0	0
Polyuria	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1	(2.4)	1	0	0	1	(2.6)	1	0	0	3	(6.0)	3	0	0
Ejaculation failure	1	(2.4)	1	0	0	0		0	0	0	0		0	0	0
Erectile dysfunction	0		0	0	0	1	(2.6)	1	0	0	0		0	0	0
Gynaecomastia	0		0	0	0	0		0	0	0	1	(2.6)	1	0	0
Menstruation irregular	0		0	0	0	0		0	0	0	1	(9.1)	1	0	0
Testicular pain	0		0	0	0	0		0	0	0	1	(2.6)	1	0	0
Vaginal haemorrhage	0		0	0	0	0		0	0	0	1	(9.1)	1	0	0
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	4	(7.7)	4	0	0	2	(4.0)	2	0	0	2	(4.0)	2	0	0

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In this case, the reported severity is summarized. Missing baseline severities are imputed as mild.
Includes all data collected since the first dose of study drug.
Percentages of gender specific events are calculated using the corresponding gender count as denominator.
MedDRA (v19.0) coding dictionary applied.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:22)

SERTRALINE Protocol A0501104
Incidence and Severity of Treatment-Emergent Adverse Events (Treatment Related)

Number of Subjects evaluable for adverse events	Sertraline (n=52)					Moxifloxacin (n=50)					Placebo (n=50)				
			Severity*					Severity*					Severity*		
	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.	N	(%)	Mild	Mod.	Sev.
Number (%) of Subjects with Adverse Events by: System Organ Class and MedDRA (v19.0) preferred term															
Dry throat	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Dysphonia	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Dyspnoea	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Epistaxis	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Nasal congestion	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
Oropharyngeal pain	0		0	0	0	1	(2.0)	1	0	0	0		0	0	0
Rhinorrhoea	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Throat irritation	0		0	0	0	0		0	0	0	1	(2.0)	1	0	0
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	19	(36.5)	17	2	0	5	(10.0)	5	0	0	8	(16.0)	7	1	0
Acne	2	(3.8)	2	0	0	1	(2.0)	1	0	0	1	(2.0)	1	0	0
Dry skin	1	(1.9)	1	0	0	1	(2.0)	1	0	0	3	(6.0)	3	0	0
Eczema	1	(1.9)	0	1	0	0		0	0	0	1	(2.0)	0	1	0
Erythema	1	(1.9)	1	0	0	2	(4.0)	2	0	0	1	(2.0)	1	0	0
Hyperhidrosis	12	(23.1)	12	0	0	0		0	0	0	1	(2.0)	1	0	0
Night sweats	2	(3.8)	2	0	0	0		0	0	0	0		0	0	0
Pruritus	1	(1.9)	1	0	0	0		0	0	0	1	(2.0)	1	0	0
Rash macular	1	(1.9)	1	0	0	0		0	0	0	1	(2.0)	1	0	0
Seborrhoea	0		0	0	0	0		0	0	0	2	(4.0)	2	0	0
Skin haemorrhage	1	(1.9)	1	0	0	0		0	0	0	0		0	0	0
Skin irritation	1	(1.9)	0	1	0	1	(2.0)	1	0	0	0		0	0	0
VASCULAR DISORDERS	4	(7.7)	4	0	0	2	(4.0)	2	0	0	1	(2.0)	1	0	0
Hot flush	4	(7.7)	4	0	0	2	(4.0)	2	0	0	1	(2.0)	1	0	0
Total preferred term events	238		217	20	1	92		82	10	0	106		98	8	0

* If the same subject in a given treatment had more than one occurrence in the same preferred term event category, only the most severe occurrence is taken. Subjects are counted only once per treatment in each row. For the TESS algorithm any missing severities have been imputed as severe unless the subject experienced another occurrence of the same event in a given treatment for which severity was recorded.
In this case, the reported severity is summarized. Missing baseline severities are imputed as mild.
Includes all data collected since the first dose of study drug.
Percentages of gender specific events are calculated using the corresponding gender count as denominator.
MedDRA (v19.0) coding dictionary applied.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:22)

SERTRALINE Protocol A0501104
SAE Listing
Reporting Period: Cumulative Through - 28Sep2016
Actual Treatment Sequence: Moxifloxacin-->Sertraline

AER Number	Actual Treatment Group/ Total Daily Dose (b)	Suspect Drug(s)/ Dose (b)	Action Taken (Drug level)	Therapy Stop Day (c)	Event Onset Day (d)	Event Stop Day (e)	Event Onset Period Day (f)	Verbatim Term/ MedDRA Preferred Term	Investigator Causality/ Sponsor Causality	Clinical Outcome/ Seriousness
[redacted]										
[redacted]	Sertraline/200 MG	MOXIFLOXACIN HCL/ 400.00 mg	NOT APPLICABLE	44	45	47	15	Psychotic Decompensation/ PSYCHIATRIC DECOMPENSATION	UNRELATED/ UNRELATED	RECOVERED/RESOLVED/ Hospitalization; IMP MED EVENT
		SERTRALINE HCL/ 200.00	PERMANENTLY WITHDRAWN	44	45	47	15	Psychotic Decompensation/ PSYCHIATRIC DECOMPENSATION	RELATED/ RELATED	RECOVERED/RESOLVED/ Hospitalization; IMP MED EVENT

Patient Identifier(Country/Sex/Age at Onset(a)/Race/Weight(Kg))

Number of Cases: 1 Number of Events: 1

Total Number of Cases: 1 Total Number of Events: 1

(a) Age at date of SAE onset.
(b) Source of Actual treatment Group or Sequence is OC(Oracle Clinical) or PIMS(Phase I Management System).
Source of Suspect Drug is from SDW(Safety Data Warehouse). Dose for treatment(s) at the earliest ONSET date.
(c) Therapy stop day is calculated as OC last active therapy date minus OC first active therapy date plus one.
(d) Onset study day is calculated as SDW onset date minus OC first active therapy date plus one.
(e) Event stop day is calculated as SDW SAE stop date minus OC first active therapy date plus one.
(f) Onset period day is calculated as SDW onset date minus OC treatment period start date plus one.
N/A = Not Available or Not Applicable UNK = Unknown
MedDRA v.19.0 coding dictionary applied
[redacted] Date of Reporting Dataset Creation: 28SEP2016 Date of Table Generation: 28SEP2016 (21:04)

SERTRALINE Protocol A0501104
Incidence of Laboratory Test Abnormalities (Without Regard to Baseline Abnormality)

	Sertraline	Moxifloxacin	Placebo
Number of Subjects Evaluable for Laboratory Abnormalities	52	50	50
Number (%) with Laboratory Abnormalities	26 (50%)	23 (46%)	16 (32%)

GROUP	PARAMETER	UNITS	CRITERIA	N	n	(%)	N	n	(%)	N	n	(%)
HEMATOLOGY	Hemoglobin (HGB)	G/DL	<0.8x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Hematocrit (HCT)	%	<0.8x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Red Blood Cell Count	10**6/MM**3	<0.8x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	MCV	10**-15L	<0.9x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.1x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	MCH	PG	<0.9x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.1x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	MCHC	G/DL	<0.9x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.1x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Platelets	10**3/MM**3	<0.5x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.75x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	White Blood Cell Count	10**3/MM**3	<0.6x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.5x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Lymphocytes (Abs)	10**3/MM**3	<0.8x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.2x ULN	52	0	(0.0)	50	1	(2.0)	50	0	(0.0)
	Lymphocytes (%)	%	<0.8x LLN	52	3	(5.8)	50	1	(2.0)	50	0	(0.0)
			>1.2x ULN	52	0	(0.0)	50	1	(2.0)	50	1	(2.0)
	Total Neutrophils (Abs)	10**3/MM**3	<0.8x LLN	52	1	(1.9)	50	1	(2.0)	50	2	(4.0)
			>1.2x ULN	52	1	(1.9)	50	0	(0.0)	50	0	(0.0)
	Neutrophils (%)	%	<0.8x LLN	52	1	(1.9)	50	1	(2.0)	50	1	(2.0)
			>1.2x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Basophils (Abs)	10**3/MM**3	>1.2x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Basophils (%)	%	>1.2x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Eosinophils (Abs)	10**3/MM**3	>1.2x ULN	52	3	(5.8)	50	3	(6.0)	50	4	(8.0)
	Eosinophils (%)	%	>1.2x ULN	52	2	(3.8)	50	2	(4.0)	50	1	(2.0)
	Monocytes (Abs)	10**3/MM**3	>1.2x ULN	52	8	(15.4)	50	3	(6.0)	50	3	(6.0)
	Monocytes (%)	%	>1.2x ULN	52	2	(3.8)	50	1	(2.0)	50	0	(0.0)
LIVER FUNCTION	Total Bilirubin	MG/DL	>1.5x ULN	52	0	(0.0)	50	1	(2.0)	50	0	(0.0)
	Direct Bilirubin	MG/DL	>1.5x ULN	52	2	(3.8)	50	4	(8.0)	50	3	(6.0)
	Indirect Bilirubin	MG/DL	>1.5x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Aspartate Aminotransferase (AST)	IU/L	>3.0x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Alanine Aminotransferase (ALT)	IU/L	>3.0x ULN	52	1	(1.9)	50	0	(0.0)	50	0	(0.0)

NOTE: N = total number of subjects with at least one observation of the given laboratory test while on study treatment or during lag time.
n = number of subjects with a laboratory abnormality meeting specified criteria while on study treatment or during lag time.
Percentages are displayed for the laboratory tests having a category with greater or equal to 50 evaluable subjects
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 20SEP2016 (01:27)

Incidence of Laboratory Test Abnormalities (Without Regard to Baseline Abnormality)

	Sertraline	Moxifloxacin	Placebo
Number of Subjects Evaluable for Laboratory Abnormalities	52	50	50
Number (%) with Laboratory Abnormalities	26 (50%)	23 (46%)	16 (32%)

GROUP	PARAMETER	UNITS	CRITERIA	N	n	(%)	N	n	(%)	N	n	(%)
LIVER FUNCTION	Alkaline Phosphatase	IU/L	>3.0x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Total Protein	G/DL	<0.8x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.2x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Albumin	G/DL	<0.8x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.2x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
RENAL FUNCTION	Blood Urea Nitrogen (BUN)	MG/DL	>1.3x ULN	52	1	(1.9)	50	0	(0.0)	50	0	(0.0)
	Creatinine	MG/DL	>1.3x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Uric Acid	MG/DL	>1.2x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
ELECTROLYTES	Sodium	MEQ/L	<0.95x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.05x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Potassium	MEQ/L	<0.9x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.1x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Chloride	MEQ/L	<0.9x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.1x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Calcium	MG/DL	<0.9x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.1x ULN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Bicarbonate (venous)	MEQ/L	<0.9x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.1x ULN	52	1	(1.9)	50	1	(2.0)	50	0	(0.0)
CLINICAL CHEMISTRY (OTHER)	Glucose	MG/DL	<0.6x LLN	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.5x ULN	52	0	(0.0)	50	1	(2.0)	50	0	(0.0)
URINALYSIS (DIPSTICK)	Urine Specific Gravity		<1.003	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>1.030	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Urine pH		<4.5	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
			>8	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Urine Glucose (Qual)		>=1	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Urine Ketones (Qual)		>=1	52	3	(5.8)	50	0	(0.0)	50	0	(0.0)
	Urine Protein (Qual)		>=1	52	0	(0.0)	50	1	(2.0)	50	0	(0.0)
	Urine Blood/Hgb (Qual)		>=1	52	7	(13.5)	50	7	(14.0)	50	5	(10.0)
	Urine Urobilinogen		>=1	52	4	(7.7)	50	5	(10.0)	50	4	(8.0)
	Urine Bilirubin (Qual)		>=1	52	1	(1.9)	50	2	(4.0)	50	0	(0.0)
	Urine Nitrite		>=1	52	0	(0.0)	50	0	(0.0)	50	0	(0.0)
	Urine Leukocyte Esterase		>=1	4	0		5	1		4	2	

NOTE: N = total number of subjects with at least one observation of the given laboratory test while on study treatment or during lag time.
n = number of subjects with a laboratory abnormality meeting specified criteria while on study treatment or during lag time.
Percentages are displayed for the laboratory tests having a category with greater or equal to 50 evaluable subjects
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 20SEP2016 (01:27)

SERTRALINE Protocol A0501104
Incidence of Laboratory Test Abnormalities (Without Regard to Baseline Abnormality)

	Sertraline	Moxifloxacin	Placebo
Number of Subjects Evaluable for Laboratory Abnormalities	52	50	50
Number (%) with Laboratory Abnormalities	26 (50%)	23 (46%)	16 (32%)

GROUP	PARAMETER	UNITS	CRITERIA	N	n	(%)	N	n	(%)	N	n	(%)
URINALYSIS (MICROSCOPY)	Urine RBC	/HPF	>=20	4	0		5	1		4	0	
	Urine WBC	/HPF	>=20	4	0		5	1		4	2	
	Urine Epithelial Cells	/HPF	>=6	4	0		5	0		4	0	
	Urine Granular Casts	/LPF	>1	4	0		5	0		4	0	
	Urine Hyaline Casts	/LPF	>1	4	0		5	0		4	0	
	Urine Bacteria	/HPF	>20	4	0		5	0		4	0	

NOTE: N = total number of subjects with at least one observation of the given laboratory test while on study treatment or during lag time.
n = number of subjects with a laboratory abnormality meeting specified criteria while on study treatment or during lag time.
Percentages are displayed for the laboratory tests having a category with greater or equal to 50 evaluable subjects
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 20SEP2016 (01:27)

Supine Systolic BP (mmHg)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Screening			N	18	18	18
			Mean	119.0	117.3	119.9
			Std. Dev.	9.46	6.74	12.04
			Median	118.5	117.5	121.0
			Min	102	107	100
			Max	134	128	140
Day 1	0		N	52	50	50
			Mean	109.7	109.1	108.5
			Std. Dev.	9.63	9.20	8.62
			Median	108.0	107.0	107.0
			Min	90	91	91
			Max	135	134	128
Day 2	24		N	52	50	50
			Mean	112.4	109.9	109.4
			Std. Dev.	8.95	7.80	7.95
			Median	113.0	109.0	109.5
			Min	95	94	95
			Max	132	126	130
Day 15	24		N	50	50	50
			Mean	111.7	108.5	108.2
			Std. Dev.	9.19	7.50	8.14
			Median	111.0	109.0	106.0
			Min	91	93	91
			Max	128	125	126
Day 16	48		N	50	50	50
			Mean	111.3	107.6	108.9
			Std. Dev.	9.69	6.97	8.91
			Median	110.0	108.5	109.5
			Min	94	90	88
			Max	138	125	132
Day 17	72		N	50	50	50
			Mean	112.2	110.8	110.5
			Std. Dev.	9.47	8.88	8.89
			Median	112.5	109.5	109.0
			Min	90	97	96
			Max	128	133	131

Means and Medians have been determined within a subject prior to summarizing across subjects.
The minimum and maximum values have been determined from all values recorded.
Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:19)

Supine Diastolic BP (mmHg)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Screening			N	18	18	18
			Mean	71.8	71.6	71.6
			Std. Dev.	8.40	8.42	8.75
			Median	72.5	71.0	71.5
			Min	54	57	57
			Max	87	86	86
Day 1	0		N	52	50	50
			Mean	62.7	63.8	62.4
			Std. Dev.	6.62	7.46	7.15
			Median	61.0	63.5	60.0
			Min	53	50	52
			Max	76	86	78
Day 2	24		N	52	50	50
			Mean	62.0	60.2	60.6
			Std. Dev.	6.35	5.89	7.13
			Median	59.5	58.5	59.0
			Min	53	52	50
			Max	77	76	77
Day 15	24		N	50	50	50
			Mean	65.9	62.5	61.5
			Std. Dev.	7.44	6.62	7.69
			Median	66.5	61.5	59.0
			Min	51	53	51
			Max	84	78	83
Day 16	48		N	50	50	50
			Mean	65.2	62.7	63.0
			Std. Dev.	6.76	6.64	7.44
			Median	65.0	62.0	62.0
			Min	53	51	50
			Max	83	77	84
Day 17	72		N	50	50	50
			Mean	66.1	65.4	63.9
			Std. Dev.	7.34	6.51	6.72
			Median	65.5	64.0	63.0
			Min	54	56	53
			Max	82	79	79

Means and Medians have been determined within a subject prior to summarizing across subjects.
The minimum and maximum values have been determined from all values recorded.
Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:19)

Supine Pulse Rate (BPM)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Screening		N	18	18	18
		Mean	68.3	64.1	65.9
		Std. Dev.	6.88	10.50	6.75
		Median	68.0	60.5	66.0
		Min	52	48	56
		Max	81	84	83
Day 1	0	N	52	50	50
		Mean	61.5	63.0	63.2
		Std. Dev.	7.39	7.50	8.64
		Median	62.0	62.5	63.0
		Min	41	46	48
		Max	78	85	96
Day 2	24	N	52	50	50
		Mean	69.7	69.3	69.8
		Std. Dev.	7.55	6.24	7.77
		Median	69.0	68.0	69.0
		Min	56	56	54
		Max	91	82	94
Day 15	24	N	50	50	50
		Mean	60.2	62.4	60.9
		Std. Dev.	6.63	8.29	8.77
		Median	60.0	63.0	60.5
		Min	47	44	44
		Max	76	86	85
Day 16	48	N	50	50	50
		Mean	62.1	62.9	60.3
		Std. Dev.	9.15	9.44	7.84
		Median	60.5	63.0	60.5
		Min	49	43	44
		Max	95	87	75
Day 17	72	N	50	50	50
		Mean	65.7	67.5	65.9
		Std. Dev.	7.26	8.19	7.53
		Median	66.0	66.5	65.0
		Min	52	51	46
		Max	83	84	82

Means and Medians have been determined within a subject prior to summarizing across subjects.
The minimum and maximum values have been determined from all values recorded.
Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:19)

Table 14.3.4.2.2
SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for Vital Signs Data

Supine Systolic BP (mmHg)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Baseline			N	52	50	50
			Mean	109.7	109.1	108.5
			Std. Dev.	9.63	9.20	8.62
			Median	108.0	107.0	107.0
			Min	90	91	91
			Max	135	134	128
Day 2		24	N	52	50	50
			Mean	2.7	0.7	0.9
			Std. Dev.	7.18	7.20	6.65
			Median	3.0	1.0	2.0
			Min	-16	-18	-17
			Max	17	14	14
Day 15		24	N	50	50	50
			Mean	1.7	-0.7	-0.3
			Std. Dev.	7.03	7.62	6.32
			Median	3.0	-0.5	-0.5
			Min	-17	-19	-14
			Max	16	22	11
Day 16		48	N	50	50	50
			Mean	1.3	-1.5	0.4
			Std. Dev.	8.40	7.97	7.65
			Median	1.5	0.0	-0.5
			Min	-16	-22	-17
			Max	27	16	16
Day 17		72	N	50	50	50
			Mean	2.2	1.6	2.1
			Std. Dev.	7.85	7.58	7.58
			Median	2.0	1.5	2.5
			Min	-16	-13	-17
			Max	25	25	23

Baseline is defined as the last predose measurement on Day 1 in each period.
Unplanned readings have been excluded from the presentation.
The minimum and maximum values have been determined from all values recorded.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:40)

SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for Vital Signs Data

Supine Diastolic BP (mmHg)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Baseline		N	52	50	50
		Mean	62.7	63.8	62.4
		Std. Dev.	6.62	7.46	7.15
		Median	61.0	63.5	60.0
		Min	53	50	52
		Max	76	86	78
Day 2	24	N	52	50	50
		Mean	-0.8	-3.6	-1.8
		Std. Dev.	5.68	4.64	5.58
		Median	-0.5	-3.0	-2.0
		Min	-17	-16	-14
		Max	11	6	14
Day 15	24	N	50	50	50
		Mean	3.1	-1.3	-0.9
		Std. Dev.	5.84	5.34	4.49
		Median	2.0	-1.0	0.0
		Min	-8	-12	-13
		Max	16	10	7
Day 16	48	N	50	50	50
		Mean	2.4	-1.2	0.6
		Std. Dev.	5.90	5.76	5.44
		Median	3.0	0.0	0.5
		Min	-11	-13	-11
		Max	13	8	14
Day 17	72	N	50	50	50
		Mean	3.3	1.6	1.5
		Std. Dev.	6.82	5.93	4.58
		Median	4.0	1.0	2.0
		Min	-11	-11	-7
		Max	19	14	12

Baseline is defined as the last predose measurement on Day 1 in each period.
Unplanned readings have been excluded from the presentation.
The minimum and maximum values have been determined from all values recorded.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:40)

SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for Vital Signs Data

Supine Pulse Rate (BPM)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Baseline		N	52	50	50
		Mean	61.5	63.0	63.2
		Std. Dev.	7.39	7.50	8.64
		Median	62.0	62.5	63.0
		Min	41	46	48
		Max	78	85	96
Day 2	24	N	52	50	50
		Mean	8.1	6.3	6.5
		Std. Dev.	7.49	6.69	6.37
		Median	7.5	6.0	5.0
		Min	-12	-7	-12
		Max	30	29	23
Day 15	24	N	50	50	50
		Mean	-1.2	-0.6	-2.3
		Std. Dev.	7.34	5.55	8.48
		Median	-1.0	0.0	-3.0
		Min	-25	-11	-29
		Max	22	14	24
Day 16	48	N	50	50	50
		Mean	0.7	-0.1	-2.9
		Std. Dev.	9.50	7.89	7.28
		Median	-0.5	0.5	-2.0
		Min	-23	-21	-28
		Max	37	22	7
Day 17	72	N	50	50	50
		Mean	4.4	4.5	2.7
		Std. Dev.	8.58	8.16	7.48
		Median	4.0	3.0	3.0
		Min	-18	-16	-17
		Max	32	30	27

Baseline is defined as the last predose measurement on Day 1 in each period.
Unplanned readings have been excluded from the presentation.
The minimum and maximum values have been determined from all values recorded.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:40)

SERTRALINE Protocol A0501104
Vital Signs Maximum Increase Change from Baseline

Supine Systolic BP (mmHg)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	6.7	4.7	5.4
Std.Dev.	7.62	7.48	6.77
Median	7.0	4.0	6.0
Min	-16	-12	-10
Max	27	25	23

Baseline is defined as the last predose measurement on Day 1 in each period.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:40)

Supine Diastolic BP (mmHg)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	6.3	2.5	4.0
Std.Dev.	5.44	5.46	4.41
Median	6.0	2.0	3.5
Min	-6	-9	-5
Max	19	14	14

Baseline is defined as the last predose measurement on Day 1 in each period.
Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:40)

Supine Pulse Rate (BPM)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	9.8	9.2	8.0
Std.Dev.	8.45	6.94	7.20
Median	8.0	9.0	8.5
Min	-12	-4	-12
Max	37	30	27

Baseline is defined as the last predose measurement on Day 1 in each period.
Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:40)

SERTRALINE Protocol A0501104
Vital Signs Maximum Decrease Change from Baseline

Supine Systolic BP (mmHg)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	-1.9	-4.5	-4.1
Std.Dev.	7.00	6.78	6.36
Median	-2.0	-3.5	-2.5
Min	-17	-22	-17
Max	16	6	9

Baseline is defined as the last predose measurement on Day 1 in each period.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:41)

Supine Diastolic BP (mmHg)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	-2.0	-5.0	-4.3
Std.Dev.	5.65	4.72	4.15
Median	-1.5	-4.5	-4.0
Min	-17	-16	-14
Max	11	5	3

Baseline is defined as the last predose measurement on Day 1 in each period.
Unplanned readings have been excluded from the presentation.

SERTRALINE Protocol A0501104
Vital Signs Maximum Decrease Change from Baseline

Supine Pulse Rate (BPM)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	-2.1	-3.4	-4.8
Std.Dev.	6.83	5.94	7.00
Median	-2.0	-3.0	-4.0
Min	-25	-21	-29
Max	17	9	7

Baseline is defined as the last predose measurement on Day 1 in each period.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:41)

SERTRALINE Protocol A0501104
ECG Data Absolute Values

RR INTERVAL (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Screening			N	18	18	18
			Mean	925.1	981.4	938.9
			Std. Dev.	86.29	128.99	91.03
			Median	923.0	1025.5	930.5
			Min	779	750	723
			Max	1091	1176	1132
Day 1	-1		N	52	50	50
			Mean	1014.6	995.8	988.0
			Std. Dev.	125.00	113.14	109.83
			Median	1019.8	995.2	974.0
			Min	778	710	634
			Max	1442	1365	1234
	-0.5		N	52	50	50
			Mean	1030.8	1022.9	1022.0
			Std. Dev.	119.75	118.85	110.60
			Median	1028.8	1023.5	1029.8
			Min	767	712	669
			Max	1429	1344	1208
	0		N	52	50	50
			Mean	1028.7	1017.5	1019.2
			Std. Dev.	133.31	115.93	118.64
			Median	1024.7	1005.5	1006.5
			Min	788	726	679
			Max	1440	1396	1288
	1		N	52	50	50
			Mean	1059.9	1033.3	1038.2
			Std. Dev.	122.35	119.84	122.68
			Median	1075.8	1035.7	1038.3
			Min	819	760	714
			Max	1465	1389	1268
	2		N	52	50	50
			Mean	1059.2	1051.0	1044.9
			Std. Dev.	122.33	132.03	124.84
			Median	1065.2	1061.0	1051.8
			Min	800	786	738
			Max	1380	1478	1397

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Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

RR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	3	N	52	50	50
		Mean	1058.8	1053.7	1042.0
		Std. Dev.	126.97	137.65	125.58
		Median	1068.2	1050.0	1048.8
		Min	808	753	687
		Max	1442	1386	1395
	4	N	52	50	50
		Mean	1033.9	1031.7	1037.6
		Std. Dev.	138.09	145.22	115.01
		Median	1028.5	1036.3	1063.8
		Min	757	704	686
		Max	1453	1429	1224
	5	N	52	50	50
		Mean	906.3	898.7	885.5
		Std. Dev.	103.25	110.96	93.15
		Median	918.3	891.8	893.0
		Min	682	667	636
		Max	1115	1085	1118
	6	N	52	50	50
		Mean	922.4	892.1	915.2
		Std. Dev.	107.97	98.89	92.30
		Median	934.2	918.7	921.7
		Min	715	660	662
		Max	1125	1072	1127
	8	N	52	50	50
		Mean	953.9	966.3	961.2
		Std. Dev.	101.93	117.27	103.35
		Median	948.7	981.0	959.3
		Min	751	625	630
		Max	1148	1208	1162
	12	N	52	50	50
		Mean	932.7	904.3	918.4
		Std. Dev.	97.66	104.85	102.02
		Median	933.7	900.3	918.7
		Min	744	617	650
		Max	1182	1121	1251

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

RR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 2	24	N	52	50	50
		Mean	906.4	885.8	900.0
		Std. Dev.	89.61	88.33	100.41
		Median	912.5	877.8	909.2
		Min	738	687	638
		Max	1201	1063	1169
Day 14	0	N	50	50	50
		Mean	1000.4	965.8	988.9
		Std. Dev.	101.65	101.78	115.23
		Median	992.3	971.5	989.5
		Min	776	706	712
		Max	1225	1225	1253
	1	N	50	50	50
		Mean	1034.3	967.9	1047.5
		Std. Dev.	104.37	108.95	110.45
		Median	1052.8	963.3	1047.7
		Min	829	687	763
		Max	1268	1192	1316
	2	N	50	50	50
		Mean	1029.0	1012.2	1055.6
		Std. Dev.	111.88	125.99	116.30
		Median	1034.7	1017.7	1052.8
		Min	756	701	747
		Max	1305	1296	1354
	3	N	50	50	50
		Mean	1028.8	1024.1	1040.5
		Std. Dev.	106.56	127.41	120.88
		Median	1046.8	1033.8	1032.8
		Min	712	695	741
		Max	1217	1334	1304
	4	N	50	50	50
		Mean	1024.8	1003.6	1038.0
		Std. Dev.	112.52	125.97	115.48
		Median	1036.7	1014.3	1047.0
		Min	680	693	800
		Max	1217	1326	1333

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

RR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	5	N	50	50	50
		Mean	889.1	891.7	908.6
		Std. Dev.	98.98	108.49	100.25
		Median	895.7	870.2	897.5
		Min	608	598	677
		Max	1078	1161	1139
	6	N	50	50	50
		Mean	903.2	889.3	921.1
		Std. Dev.	94.95	93.75	93.65
		Median	913.8	910.0	914.3
		Min	625	621	726
		Max	1112	1218	1126
	8	N	50	50	50
		Mean	962.8	932.5	965.0
		Std. Dev.	108.61	107.78	109.88
		Median	960.3	912.2	950.2
		Min	651	674	747
		Max	1208	1277	1234
	12	N	50	50	50
		Mean	929.7	891.2	906.5
		Std. Dev.	97.83	98.75	79.23
		Median	943.0	892.5	903.2
		Min	650	657	726
		Max	1154	1084	1072
Day 15	24	N	51	50	50
		Mean	989.4	963.5	991.1
		Std. Dev.	117.18	120.59	127.72
		Median	984.0	941.2	977.2
		Min	667	695	701
		Max	1250	1307	1387
Day 16	48	N	50	50	50
		Mean	991.1	948.4	980.1
		Std. Dev.	105.59	121.85	126.63
		Median	993.0	938.0	956.8
		Min	760	704	706
		Max	1217	1305	1343

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

SERTRALINE Protocol A0501104
ECG Data Absolute Values

RR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 17	72	N	50	50	50
		Mean	951.1	935.4	933.9
		Std. Dev.	106.25	113.15	116.21
		Median	948.0	910.2	928.5
		Min	744	737	675
		Max	1176	1259	1314

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

HEART RATE (bpm)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Screening		N	18	18	18
		Mean	65.4	62.2	64.5
		Std. Dev.	6.03	8.82	6.62
		Median	65.0	58.5	64.5
		Min	55	51	53
		Max	77	80	83
Day 1	-1	N	52	50	50
		Mean	60.1	61.1	61.6
		Std. Dev.	7.21	7.03	7.53
		Median	58.8	60.3	61.7
		Min	42	44	49
		Max	78	85	95
	-0.5	N	52	50	50
		Mean	59.1	59.5	59.5
		Std. Dev.	6.68	7.33	7.18
		Median	58.7	58.7	58.3
		Min	42	45	50
		Max	78	84	90
	0	N	52	50	50
		Mean	59.4	59.8	59.8
		Std. Dev.	7.56	6.98	7.43
		Median	58.8	59.8	59.7
		Min	42	43	47
		Max	76	83	88
	1	N	52	50	50
		Mean	57.5	59.0	58.7
		Std. Dev.	6.73	7.15	7.40
		Median	55.8	58.0	57.8
		Min	41	43	47
		Max	74	79	84
	2	N	52	50	50
		Mean	57.5	58.1	58.4
		Std. Dev.	6.85	7.23	7.36
		Median	56.3	56.7	57.2
		Min	44	41	43
		Max	75	76	81

Means and Medians have been determined within a subject prior to summarizing across subjects.
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HEART RATE (bpm)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	3	N	52	50	50
		Mean	57.6	58.0	58.5
		Std. Dev.	7.00	7.76	7.53
		Median	56.3	57.3	57.3
		Min	42	43	43
		Max	74	80	87
	4	N	52	50	50
		Mean	59.2	59.4	58.7
		Std. Dev.	7.99	8.70	7.51
		Median	58.7	58.0	56.5
		Min	41	42	49
		Max	79	85	88
	5	N	52	50	50
		Mean	67.1	67.8	68.7
		Std. Dev.	7.79	8.63	7.73
		Median	65.3	67.3	67.7
		Min	54	55	54
		Max	88	90	94
	6	N	52	50	50
		Mean	66.0	68.3	66.3
		Std. Dev.	8.06	8.04	7.14
		Median	64.3	65.3	65.2
		Min	54	56	53
		Max	84	91	91
	8	N	52	50	50
		Mean	63.7	63.1	63.3
		Std. Dev.	6.87	8.37	7.63
		Median	63.7	61.3	62.7
		Min	52	50	52
		Max	80	96	95
	12	N	52	50	50
		Mean	65.1	67.4	66.2
		Std. Dev.	6.92	8.43	7.63
		Median	64.3	66.7	65.3
		Min	51	54	48
		Max	81	97	92

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The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

HEART RATE (bpm)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 2	24	N	52	50	50
		Mean	66.9	68.5	67.6
		Std. Dev.	6.63	6.82	7.93
		Median	65.8	68.5	66.0
		Min	50	57	51
		Max	81	87	94
Day 14	0	N	50	50	50
		Mean	60.6	62.9	61.6
		Std. Dev.	6.27	6.86	7.49
		Median	60.5	62.0	60.7
		Min	49	49	48
		Max	77	85	84
	1	N	50	50	50
		Mean	58.7	62.9	58.0
		Std. Dev.	6.11	7.71	6.44
		Median	57.0	62.3	57.3
		Min	47	50	46
		Max	72	87	79
	2	N	50	50	50
		Mean	59.1	60.3	57.6
		Std. Dev.	6.57	8.16	6.58
		Median	58.0	59.0	57.2
		Min	46	46	44
		Max	79	86	80
	3	N	50	50	50
		Mean	59.0	59.6	58.6
		Std. Dev.	6.80	7.73	7.09
		Median	57.3	58.2	58.2
		Min	49	45	46
		Max	84	86	81
	4	N	50	50	50
		Mean	59.4	60.8	58.6
		Std. Dev.	7.26	7.72	6.66
		Median	58.0	59.3	57.3
		Min	49	46	45
		Max	88	87	75

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

HEART RATE (bpm)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	5	N	50	50	50
		Mean	68.4	68.4	66.9
		Std. Dev.	8.33	8.68	7.34
		Median	67.0	69.0	67.0
		Min	56	52	53
		Max	99	100	89
	6	N	50	50	50
		Mean	67.2	68.3	65.9
		Std. Dev.	7.66	7.45	6.84
		Median	65.7	66.0	65.7
		Min	54	49	53
		Max	96	97	83
	8	N	50	50	50
		Mean	63.2	65.2	63.0
		Std. Dev.	7.68	7.41	7.16
		Median	62.5	66.0	63.2
		Min	50	47	49
		Max	92	89	80
	12	N	50	50	50
		Mean	65.4	68.2	66.8
		Std. Dev.	7.57	8.09	5.98
		Median	63.7	67.5	66.5
		Min	52	55	56
		Max	92	91	83
Day 15	24	N	51	50	50
		Mean	61.6	63.3	61.5
		Std. Dev.	7.75	7.89	7.72
		Median	61.0	63.8	61.5
		Min	48	46	43
		Max	90	86	86
Day 16	48	N	50	50	50
		Mean	61.3	64.4	62.3
		Std. Dev.	6.74	8.21	7.80
		Median	60.5	64.2	62.8
		Min	49	46	45
		Max	79	85	85

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

SERTRALINE Protocol A0501104
ECG Data Absolute Values

HEART RATE (bpm)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 17		72	N	50	50	50
			Mean	63.9	65.1	65.3
			Std. Dev.	7.23	7.55	7.99
			Median	63.3	66.0	64.7
			Min	51	48	46
			Max	81	82	89

Means and Medians have been determined within a subject prior to summarizing across subjects.
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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

PR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Screening		N	18	18	18
		Mean	161.1	163.8	163.7
		Std. Dev.	16.28	17.86	19.81
		Median	158.0	164.0	164.0
		Min	136	140	132
		Max	196	204	204
Day 1	-1	N	52	50	50
		Mean	166.2	168.4	167.5
		Std. Dev.	16.22	17.70	16.51
		Median	165.3	166.7	166.7
		Min	125	128	131
		Max	204	208	203
	-0.5	N	52	50	50
		Mean	165.7	167.0	167.5
		Std. Dev.	18.05	17.43	17.93
		Median	166.0	168.0	166.0
		Min	125	125	132
		Max	205	204	208
	0	N	52	50	50
		Mean	167.2	167.8	167.4
		Std. Dev.	18.74	18.41	18.53
		Median	168.0	168.0	166.7
		Min	124	128	135
		Max	211	213	205
	1	N	52	50	50
		Mean	167.6	167.1	168.2
		Std. Dev.	18.36	19.31	19.01
		Median	167.3	166.7	166.0
		Min	128	121	124
		Max	215	215	208
	2	N	52	50	50
		Mean	166.1	167.1	166.4
		Std. Dev.	18.39	19.21	20.05
		Median	165.3	167.3	165.3
		Min	131	126	123
		Max	220	215	207

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

PR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	3	N	52	50	50
		Mean	163.9	165.9	167.8
		Std. Dev.	18.48	18.25	18.03
		Median	164.0	165.3	166.0
		Min	125	124	129
		Max	211	217	203
	4	N	52	50	50
		Mean	163.3	166.5	166.8
		Std. Dev.	16.94	19.35	18.95
		Median	161.3	166.0	166.7
		Min	128	126	128
		Max	205	215	204
	5	N	52	50	50
		Mean	160.1	162.8	162.3
		Std. Dev.	15.01	17.64	16.64
		Median	160.0	162.7	161.3
		Min	127	131	128
		Max	193	203	199
	6	N	52	50	50
		Mean	157.1	160.9	160.3
		Std. Dev.	15.13	17.11	16.51
		Median	156.7	160.0	161.3
		Min	127	131	125
		Max	195	209	191
	8	N	52	50	50
		Mean	157.7	160.5	160.0
		Std. Dev.	16.02	16.33	17.15
		Median	156.0	159.3	160.0
		Min	125	128	128
		Max	196	201	203
	12	N	52	50	50
		Mean	159.6	161.6	160.5
		Std. Dev.	14.71	17.79	15.89
		Median	158.0	160.0	160.0
		Min	127	123	128
		Max	193	200	197

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PR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 2	24	N	52	50	50
		Mean	163.5	164.5	164.7
		Std. Dev.	15.25	14.80	17.10
		Median	163.3	164.0	165.3
		Min	129	129	131
		Max	197	199	203
Day 14	0	N	50	50	50
		Mean	163.7	168.3	170.8
		Std. Dev.	16.23	17.09	17.58
		Median	163.3	168.0	169.3
		Min	124	127	128
		Max	196	208	207
	1	N	50	50	50
		Mean	164.3	170.5	171.5
		Std. Dev.	15.28	18.50	19.02
		Median	163.3	168.7	169.3
		Min	131	124	133
		Max	195	216	217
	2	N	50	50	50
		Mean	164.4	170.1	171.9
		Std. Dev.	15.60	18.86	18.41
		Median	165.3	169.3	171.3
		Min	128	123	129
		Max	197	215	211
	3	N	50	50	50
		Mean	163.7	168.9	170.8
		Std. Dev.	16.12	17.97	18.61
		Median	164.0	169.3	169.3
		Min	124	121	127
		Max	199	219	215
	4	N	50	50	50
		Mean	163.7	169.4	170.8
		Std. Dev.	16.60	18.34	18.59
		Median	164.0	167.3	170.7
		Min	123	127	128
		Max	193	215	216

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

PR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	5	N	50	50	50
		Mean	158.1	162.6	165.7
		Std. Dev.	14.86	16.60	16.93
		Median	157.3	162.0	166.7
		Min	126	125	128
		Max	189	199	199
	6	N	50	50	50
		Mean	157.7	162.3	163.2
		Std. Dev.	15.93	16.58	16.18
		Median	160.0	161.3	164.0
		Min	121	124	125
		Max	191	197	197
	8	N	50	50	50
		Mean	158.9	161.9	162.8
		Std. Dev.	15.45	16.06	17.49
		Median	159.3	162.0	161.3
		Min	124	123	127
		Max	191	201	207
	12	N	50	50	50
		Mean	159.5	164.0	164.4
		Std. Dev.	15.85	16.38	17.52
		Median	158.7	164.7	164.0
		Min	124	128	127
		Max	196	200	205
Day 15	24	N	51	50	50
		Mean	163.8	168.6	168.3
		Std. Dev.	15.43	17.44	16.39
		Median	164.0	168.0	169.3
		Min	124	124	131
		Max	192	205	209
Day 16	48	N	50	50	50
		Mean	164.6	171.6	169.3
		Std. Dev.	16.03	17.05	17.30
		Median	164.0	169.3	168.7
		Min	127	131	129
		Max	199	204	207

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

SERTRALINE Protocol A0501104
ECG Data Absolute Values

PR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 17	72	N	50	50	50
		Mean	164.7	169.9	168.5
		Std. Dev.	15.94	17.34	17.43
		Median	166.7	168.0	166.7
		Min	125	131	131
		Max	200	211	211

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QRS COMPLEX (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Screening			N	18	18	18
			Mean	91.6	90.1	92.9
			Std. Dev.	7.37	6.42	6.80
			Median	90.0	90.0	92.0
			Min	78	78	80
			Max	104	100	108
Day 1	-1		N	52	50	50
			Mean	92.1	91.9	91.8
			Std. Dev.	7.53	7.68	7.81
			Median	92.0	91.3	93.0
			Min	76	76	77
			Max	107	109	109
	-0.5		N	52	50	50
			Mean	92.2	92.1	92.7
			Std. Dev.	7.58	8.12	7.81
			Median	92.0	92.0	92.3
			Min	77	77	78
			Max	109	113	109
	0		N	52	50	50
			Mean	92.2	91.6	92.3
			Std. Dev.	7.55	7.43	8.87
			Median	91.3	90.0	91.7
			Min	78	76	75
			Max	107	108	116
	1		N	52	50	50
			Mean	92.4	91.6	92.4
			Std. Dev.	7.67	7.81	7.40
			Median	92.3	91.3	92.7
			Min	77	77	78
			Max	113	109	109
	2		N	52	50	50
			Mean	92.0	91.7	92.2
			Std. Dev.	8.45	7.55	7.22
			Median	90.7	91.0	92.3
			Min	74	75	77
			Max	117	107	107

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QRS COMPLEX (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	3	N	52	50	50
		Mean	91.2	90.8	91.7
		Std. Dev.	8.35	7.68	7.81
		Median	89.3	89.3	91.7
		Min	73	73	77
		Max	109	108	107
	4	N	52	50	50
		Mean	91.8	91.7	91.8
		Std. Dev.	7.92	7.65	7.67
		Median	90.3	91.7	91.3
		Min	75	76	77
		Max	108	108	112
	5	N	52	50	50
		Mean	91.5	91.5	91.6
		Std. Dev.	8.19	8.12	8.44
		Median	90.0	91.0	91.7
		Min	77	75	72
		Max	111	112	112
	6	N	52	50	50
		Mean	90.6	90.3	90.4
		Std. Dev.	8.10	7.89	8.00
		Median	89.7	90.3	89.7
		Min	73	75	72
		Max	111	107	108
	8	N	52	50	50
		Mean	90.6	89.8	90.4
		Std. Dev.	7.78	7.99	8.37
		Median	89.3	89.0	89.7
		Min	77	73	75
		Max	107	109	111
	12	N	52	50	50
		Mean	91.1	91.1	90.9
		Std. Dev.	8.00	8.17	8.44
		Median	91.0	90.0	91.0
		Min	76	75	70
		Max	105	108	108

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QRS COMPLEX (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 2	24	N	52	50	50
		Mean	92.7	92.2	93.3
		Std. Dev.	7.83	8.22	7.77
		Median	93.0	91.3	93.3
		Min	79	77	77
		Max	111	108	107
Day 14	0	N	50	50	50
		Mean	90.1	90.8	91.2
		Std. Dev.	7.46	7.30	8.13
		Median	89.3	90.3	90.0
		Min	71	75	72
		Max	107	105	107
	1	N	50	50	50
		Mean	90.4	90.9	92.0
		Std. Dev.	7.84	7.60	8.02
		Median	90.0	89.3	91.0
		Min	74	75	76
		Max	110	107	108
	2	N	50	50	50
		Mean	90.2	91.0	91.8
		Std. Dev.	7.25	7.54	8.16
		Median	89.7	90.0	90.7
		Min	75	73	75
		Max	107	106	107
	3	N	50	50	50
		Mean	90.6	91.0	91.4
		Std. Dev.	7.27	7.68	8.12
		Median	90.0	90.7	90.0
		Min	78	75	72
		Max	107	108	109
	4	N	50	50	50
		Mean	90.4	91.0	91.1
		Std. Dev.	7.68	8.01	8.10
		Median	89.3	91.0	90.0
		Min	71	75	73
		Max	108	109	108

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QRS COMPLEX (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	5	N	50	50	50
		Mean	90.6	90.3	91.7
		Std. Dev.	8.51	8.86	8.52
		Median	89.3	89.7	91.0
		Min	71	74	76
		Max	112	111	110
	6	N	50	50	50
		Mean	89.6	89.0	90.3
		Std. Dev.	8.22	8.05	8.16
		Median	88.7	88.0	90.0
		Min	69	73	73
		Max	108	106	108
	8	N	50	50	50
		Mean	89.9	89.5	90.9
		Std. Dev.	8.08	8.22	8.26
		Median	89.3	88.3	90.0
		Min	73	73	71
		Max	110	111	109
	12	N	50	50	50
		Mean	89.9	89.9	90.6
		Std. Dev.	7.52	8.64	8.05
		Median	88.7	88.7	89.7
		Min	76	73	73
		Max	105	110	109
Day 15	24	N	51	50	50
		Mean	90.3	90.4	90.5
		Std. Dev.	7.34	7.36	7.50
		Median	90.7	89.3	90.3
		Min	77	71	75
		Max	109	108	105
Day 16	48	N	50	50	50
		Mean	90.2	91.3	91.1
		Std. Dev.	7.45	8.22	7.90
		Median	90.0	90.0	90.7
		Min	75	75	75
		Max	107	108	107

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

SERTRALINE Protocol A0501104
ECG Data Absolute Values

QRS COMPLEX (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 17	72	N	50	50	50
		Mean	90.8	91.5	91.4
		Std. Dev.	7.63	8.28	8.17
		Median	90.0	90.7	90.0
		Min	78	75	75
		Max	106	108	108

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QT INTERVAL (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Screening			N	18	18	18
			Mean	401.3	407.3	404.2
			Std. Dev.	22.79	26.89	16.55
			Median	398.0	402.0	406.0
			Min	360	356	380
			Max	456	452	436
Day 1	-1		N	52	50	50
			Mean	413.4	410.6	410.0
			Std. Dev.	24.59	23.43	21.26
			Median	409.3	407.3	410.7
			Min	356	373	359
			Max	503	489	477
	-0.5		N	52	50	50
			Mean	418.6	416.1	416.6
			Std. Dev.	24.24	24.13	22.55
			Median	416.7	416.0	414.0
			Min	364	373	363
			Max	505	493	477
	0		N	52	50	50
			Mean	417.7	415.1	416.3
			Std. Dev.	25.25	25.30	23.17
			Median	418.0	414.7	411.3
			Min	367	379	361
			Max	501	501	477
	1		N	52	50	50
			Mean	419.5	415.8	418.5
			Std. Dev.	23.24	24.99	24.27
			Median	419.3	414.7	411.3
			Min	375	359	372
			Max	499	488	485
	2		N	52	50	50
			Mean	419.8	418.9	419.4
			Std. Dev.	23.42	24.49	24.37
			Median	421.3	416.0	416.0
			Min	377	369	369
			Max	500	489	480

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QT INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	3	N	52	50	50
		Mean	420.0	418.3	417.8
		Std. Dev.	23.61	26.85	22.90
		Median	417.3	414.7	414.0
		Min	379	364	368
		Max	487	493	479
	4	N	52	50	50
		Mean	417.8	415.6	418.0
		Std. Dev.	24.87	28.53	23.21
		Median	419.3	413.3	416.0
		Min	375	356	368
		Max	488	493	469
	5	N	52	50	50
		Mean	396.1	392.1	392.8
		Std. Dev.	20.22	22.01	20.79
		Median	397.3	389.3	389.3
		Min	359	345	351
		Max	439	451	461
	6	N	52	50	50
		Mean	395.5	389.6	393.9
		Std. Dev.	20.61	21.45	21.77
		Median	392.7	387.3	393.3
		Min	360	348	344
		Max	439	441	437
	8	N	52	50	50
		Mean	399.2	399.1	399.3
		Std. Dev.	20.17	22.54	21.42
		Median	394.7	396.7	396.0
		Min	367	347	347
		Max	444	447	461
	12	N	52	50	50
		Mean	400.7	394.5	396.3
		Std. Dev.	19.06	21.54	21.30
		Median	396.7	391.3	396.0
		Min	356	351	349
		Max	440	460	461

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QT INTERVAL (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 2		24	N	52	50	50
			Mean	395.2	391.5	394.3
			Std. Dev.	17.53	19.51	17.63
			Median	392.7	388.7	390.7
			Min	353	356	359
			Max	439	441	445
Day 14		0	N	50	50	50
			Mean	414.4	402.3	405.0
			Std. Dev.	20.25	20.62	22.11
			Median	417.3	402.7	401.3
			Min	361	364	360
			Max	465	444	471
		1	N	50	50	50
			Mean	419.7	413.7	413.1
			Std. Dev.	20.69	21.18	20.95
			Median	422.0	416.7	412.0
			Min	367	365	377
			Max	463	455	465
		2	N	50	50	50
			Mean	420.1	421.0	414.5
			Std. Dev.	21.82	24.40	21.02
			Median	420.0	423.3	416.0
			Min	376	355	368
			Max	460	469	457
		3	N	50	50	50
			Mean	421.1	423.1	413.4
			Std. Dev.	22.03	24.04	21.31
			Median	421.3	421.3	412.7
			Min	376	367	372
			Max	464	467	456
		4	N	50	50	50
			Mean	422.2	421.6	413.1
			Std. Dev.	22.84	24.42	22.57
			Median	422.7	418.7	412.0
			Min	373	363	360
			Max	476	472	457

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QT INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	5	N	50	50	50
		Mean	396.0	397.2	390.7
		Std. Dev.	20.38	20.67	20.45
		Median	393.3	395.3	390.7
		Min	355	344	343
		Max	448	441	435
	6	N	50	50	50
		Mean	395.9	395.3	391.2
		Std. Dev.	20.69	20.03	17.78
		Median	393.3	392.7	388.7
		Min	348	359	348
		Max	443	441	427
	8	N	50	50	50
		Mean	404.1	400.6	397.8
		Std. Dev.	21.60	20.69	20.12
		Median	400.7	398.7	397.3
		Min	356	353	361
		Max	459	447	443
	12	N	50	50	50
		Mean	401.7	395.5	392.1
		Std. Dev.	20.75	19.77	19.54
		Median	401.3	396.0	390.7
		Min	353	341	347
		Max	435	431	427
Day 15	24	N	51	50	50
		Mean	412.7	406.7	405.1
		Std. Dev.	21.31	21.59	22.61
		Median	413.3	404.0	403.3
		Min	367	356	357
		Max	452	455	471
Day 16	48	N	50	50	50
		Mean	413.1	401.4	404.9
		Std. Dev.	20.92	20.98	22.33
		Median	418.0	399.3	401.3
		Min	367	359	369
		Max	453	457	471

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SERTRALINE Protocol A0501104
ECG Data Absolute Values

QT INTERVAL (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 17		72	N	50	50	50
			Mean	405.7	396.1	396.0
			Std. Dev.	20.92	21.28	21.33
			Median	406.7	394.0	394.7
			Min	364	357	349
			Max	464	448	448

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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QTCB INTERVAL (BAZETT'S CORRECTION) (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Screening			N	18	18	18
			Mean	418.0	412.5	418.3
			Std. Dev.	18.28	19.34	18.03
			Median	423.0	415.5	421.0
			Min	375	378	389
			Max	440	449	452
Day 1	-1		N	52	50	50
			Mean	411.9	412.7	413.8
			Std. Dev.	18.89	19.17	19.86
			Median	416.5	412.0	412.3
			Min	368	374	375
			Max	453	454	456
	-0.5		N	52	50	50
			Mean	413.6	412.7	413.4
			Std. Dev.	17.48	18.73	19.57
			Median	416.0	414.3	415.3
			Min	376	365	373
			Max	449	455	451
	0		N	52	50	50
			Mean	413.5	412.7	413.8
			Std. Dev.	18.46	18.20	18.65
			Median	416.3	413.5	415.7
			Min	367	373	376
			Max	453	455	452
	1		N	52	50	50
			Mean	408.9	410.5	412.1
			Std. Dev.	19.37	19.81	19.95
			Median	409.8	410.0	412.3
			Min	371	369	376
			Max	458	448	447
	2		N	52	50	50
			Mean	409.3	410.2	411.8
			Std. Dev.	18.79	19.77	20.13
			Median	408.3	410.5	414.2
			Min	368	368	365
			Max	448	448	448

Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.

QTCB INTERVAL (BAZETT'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	3	N	52	50	50
		Mean	409.7	409.1	410.9
		Std. Dev.	19.84	18.60	20.66
		Median	409.2	409.5	409.7
		Min	366	365	371
		Max	459	452	453
	4	N	52	50	50
		Mean	412.8	411.0	411.7
		Std. Dev.	20.14	20.52	19.82
		Median	411.7	412.5	411.2
		Min	371	363	363
		Max	465	456	449
	5	N	52	50	50
		Mean	417.4	415.0	418.6
		Std. Dev.	18.64	17.93	18.72
		Median	420.0	413.8	416.7
		Min	374	380	381
		Max	457	450	458
	6	N	52	50	50
		Mean	413.2	413.8	412.7
		Std. Dev.	17.57	18.07	18.09
		Median	412.8	416.2	412.3
		Min	379	379	374
		Max	461	447	454
	8	N	52	50	50
		Mean	409.9	407.5	408.4
		Std. Dev.	18.15	18.30	19.21
		Median	411.7	405.8	409.3
		Min	368	373	368
		Max	451	445	446
	12	N	52	50	50
		Mean	416.1	416.1	414.8
		Std. Dev.	17.63	17.91	17.60
		Median	416.5	416.5	414.5
		Min	378	384	377
		Max	452	450	456

Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QTCB INTERVAL (BAZETT'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 2	24	N	52	50	50
		Mean	416.2	416.9	417.1
		Std. Dev.	16.47	15.43	18.67
		Median	418.3	417.5	417.0
		Min	388	381	381
		Max	455	453	451
Day 14	0	N	50	50	50
		Mean	415.3	410.5	408.7
		Std. Dev.	16.58	17.13	19.56
		Median	413.7	412.7	410.5
		Min	377	376	366
		Max	450	451	452
	1	N	50	50	50
		Mean	413.6	421.9	404.9
		Std. Dev.	16.02	18.92	19.28
		Median	413.3	424.7	406.3
		Min	384	379	364
		Max	443	463	452
	2	N	50	50	50
		Mean	415.4	419.9	404.9
		Std. Dev.	18.40	19.07	20.02
		Median	416.7	420.2	406.5
		Min	371	380	361
		Max	449	465	463
	3	N	50	50	50
		Mean	416.2	419.7	406.8
		Std. Dev.	17.05	19.53	20.75
		Median	416.5	419.8	406.5
		Min	386	376	359
		Max	455	466	459
	4	N	50	50	50
		Mean	418.3	422.5	406.8
		Std. Dev.	17.41	20.16	20.05
		Median	416.5	420.3	403.5
		Min	378	382	363
		Max	453	468	456

Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QTCB INTERVAL (BAZETT'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	5	N	50	50	50
		Mean	421.2	422.3	411.1
		Std. Dev.	17.08	18.67	19.30
		Median	421.0	424.7	408.8
		Min	388	382	366
		Max	463	469	457
	6	N	50	50	50
		Mean	417.7	420.2	408.7
		Std. Dev.	17.78	17.64	18.05
		Median	417.3	416.3	408.7
		Min	388	387	379
		Max	457	461	455
	8	N	50	50	50
		Mean	413.1	416.2	406.3
		Std. Dev.	18.52	19.43	17.98
		Median	413.0	414.0	407.0
		Min	373	368	375
		Max	452	456	452
	12	N	50	50	50
		Mean	417.8	420.2	412.5
		Std. Dev.	18.40	17.47	17.59
		Median	419.5	417.0	410.5
		Min	379	387	385
		Max	460	457	447
Day 15	24	N	51	50	50
		Mean	416.3	416.0	408.5
		Std. Dev.	18.35	20.66	18.59
		Median	418.0	415.3	407.5
		Min	372	378	367
		Max	451	459	453
Day 16	48	N	50	50	50
		Mean	416.1	413.8	410.6
		Std. Dev.	17.06	18.16	19.57
		Median	418.5	414.3	414.2
		Min	380	375	372
		Max	454	455	454

Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QTCB INTERVAL (BAZETT'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 17	72	N	50	50	50
		Mean	417.1	410.9	411.3
		Std. Dev.	16.05	17.54	18.64
		Median	415.7	411.3	411.2
		Min	376	377	373
		Max	447	460	451

Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Screening		N	18	18	18
		Mean	412.2	410.8	413.2
		Std. Dev.	17.90	17.80	14.59
		Median	415.0	417.0	413.5
		Min	379	381	390
		Max	443	433	438
Day 1	-1	N	52	50	50
		Mean	412.2	411.8	412.4
		Std. Dev.	17.10	17.33	16.93
		Median	414.0	411.3	411.8
		Min	373	377	378
		Max	448	441	448
	-0.5	N	52	50	50
		Mean	415.1	413.7	414.2
		Std. Dev.	16.44	16.92	17.37
		Median	415.2	415.7	416.8
		Min	381	371	377
		Max	449	447	448
	0	N	52	50	50
		Mean	414.7	413.3	414.5
		Std. Dev.	16.79	17.30	16.51
		Median	416.0	415.5	414.3
		Min	376	376	380
		Max	445	448	451
	1	N	52	50	50
		Mean	412.2	412.1	414.1
		Std. Dev.	17.20	18.33	17.79
		Median	413.8	414.2	416.5
		Min	379	373	377
		Max	449	461	450
	2	N	52	50	50
		Mean	412.7	412.9	414.1
		Std. Dev.	16.87	17.52	17.81
		Median	412.8	417.5	417.3
		Min	373	376	372
		Max	450	442	452

Means and Medians have been determined within a subject prior to summarizing across subjects.
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Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	3	N	52	50	50
		Mean	412.9	412.0	413.0
		Std. Dev.	17.45	17.21	17.63
		Median	413.2	415.8	414.2
		Min	370	369	376
		Max	447	447	451
	4	N	52	50	50
		Mean	414.2	412.3	413.6
		Std. Dev.	17.33	18.72	17.43
		Median	414.7	416.5	416.0
		Min	373	367	368
		Max	448	448	450
	5	N	52	50	50
		Mean	410.1	407.0	409.6
		Std. Dev.	15.61	15.32	16.41
		Median	411.0	408.0	409.8
		Min	371	372	372
		Max	441	439	444
	6	N	52	50	50
		Mean	407.0	405.4	406.3
		Std. Dev.	14.72	15.98	16.77
		Median	404.8	405.5	405.7
		Min	373	372	364
		Max	436	439	447
	8	N	52	50	50
		Mean	406.1	404.5	405.2
		Std. Dev.	15.82	15.81	16.76
		Median	405.7	405.7	405.3
		Min	367	375	366
		Max	438	438	440
	12	N	52	50	50
		Mean	410.7	408.6	408.3
		Std. Dev.	15.00	15.38	15.56
		Median	411.5	409.2	406.7
		Min	381	378	372
		Max	441	443	440

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Means of Replicates have been used in the calculations.
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Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 2	24	N	52	50	50
		Mean	408.9	408.2	409.2
		Std. Dev.	13.91	14.02	14.58
		Median	409.2	407.7	410.2
		Min	386	383	381
		Max	438	440	438
Day 14	0	N	50	50	50
		Mean	414.9	407.6	407.2
		Std. Dev.	14.89	15.20	16.85
		Median	416.0	409.8	411.7
		Min	381	373	367
		Max	446	439	439
	1	N	50	50	50
		Mean	415.5	419.0	407.5
		Std. Dev.	14.60	15.90	16.76
		Median	416.3	423.2	410.3
		Min	381	379	372
		Max	447	443	444
	2	N	50	50	50
		Mean	416.8	420.0	407.9
		Std. Dev.	16.42	16.66	17.14
		Median	417.3	422.5	410.7
		Min	383	382	367
		Max	453	451	441
	3	N	50	50	50
		Mean	417.6	420.6	408.8
		Std. Dev.	15.37	16.96	17.42
		Median	419.8	422.0	410.7
		Min	385	380	366
		Max	444	454	440
	4	N	50	50	50
		Mean	419.4	421.9	408.8
		Std. Dev.	15.65	17.58	17.89
		Median	420.0	425.0	408.0
		Min	383	383	369
		Max	453	453	448

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Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	5		N	50	50	50
			Mean	412.5	413.5	404.1
			Std. Dev.	14.41	15.24	16.73
			Median	414.5	414.8	404.3
			Min	387	377	369
			Max	448	452	432
	6		N	50	50	50
			Mean	410.2	411.6	402.6
			Std. Dev.	15.65	15.36	15.03
			Median	411.8	412.2	406.0
			Min	376	381	375
			Max	446	447	432
	8		N	50	50	50
			Mean	409.9	410.8	403.3
			Std. Dev.	16.12	16.59	15.33
			Median	411.5	410.5	404.0
			Min	380	373	373
			Max	451	445	431
	12		N	50	50	50
			Mean	412.2	411.6	405.5
			Std. Dev.	16.01	14.64	16.25
			Median	414.3	415.3	405.7
			Min	379	385	375
			Max	442	443	434
Day 15	24		N	51	50	50
			Mean	414.9	412.7	407.1
			Std. Dev.	15.45	17.11	15.73
			Median	418.3	415.3	406.7
			Min	383	380	368
			Max	448	443	438
Day 16	48		N	50	50	50
			Mean	414.9	409.5	408.5
			Std. Dev.	15.27	14.69	16.35
			Median	417.2	409.5	410.3
			Min	386	378	381
			Max	443	436	438

Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.

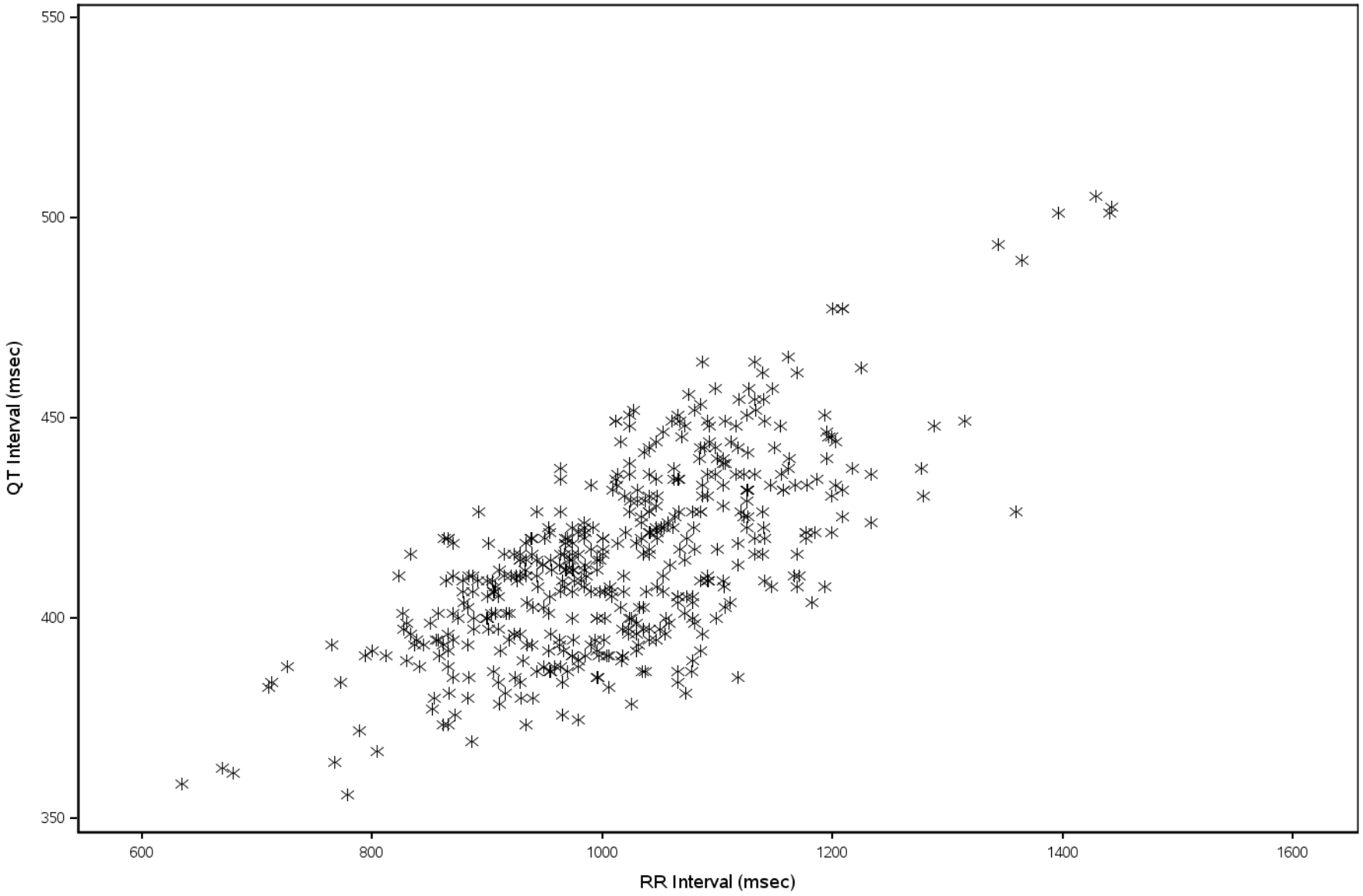
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)

SERTRALINE Protocol A0501104
ECG Data Absolute Values

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

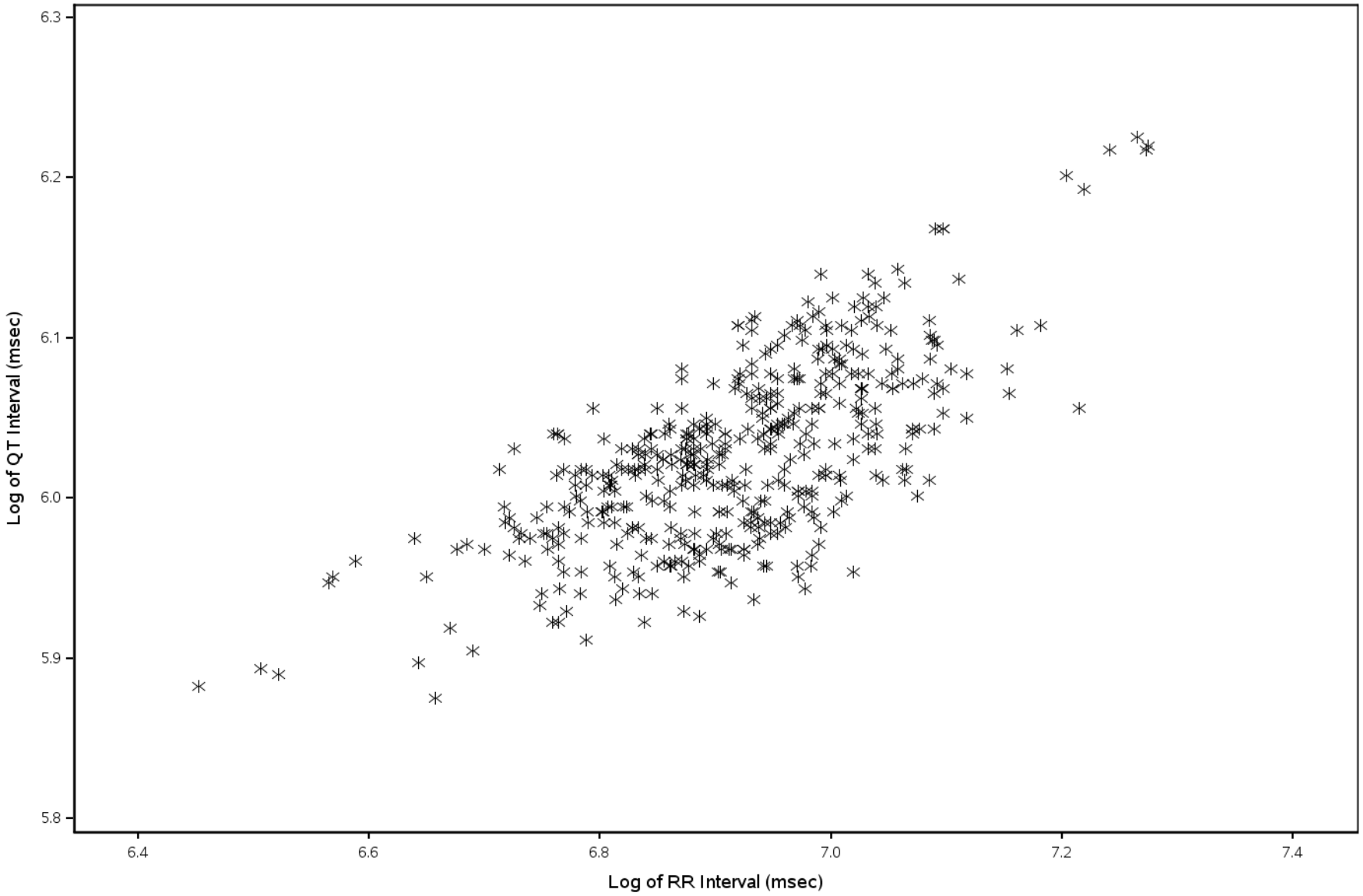
Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 17	72	N	50	50	50
		Mean	413.1	405.8	406.0
		Std. Dev.	14.20	15.04	15.72
		Median	413.5	405.8	407.0
		Min	387	372	374
		Max	445	440	433

Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:45)



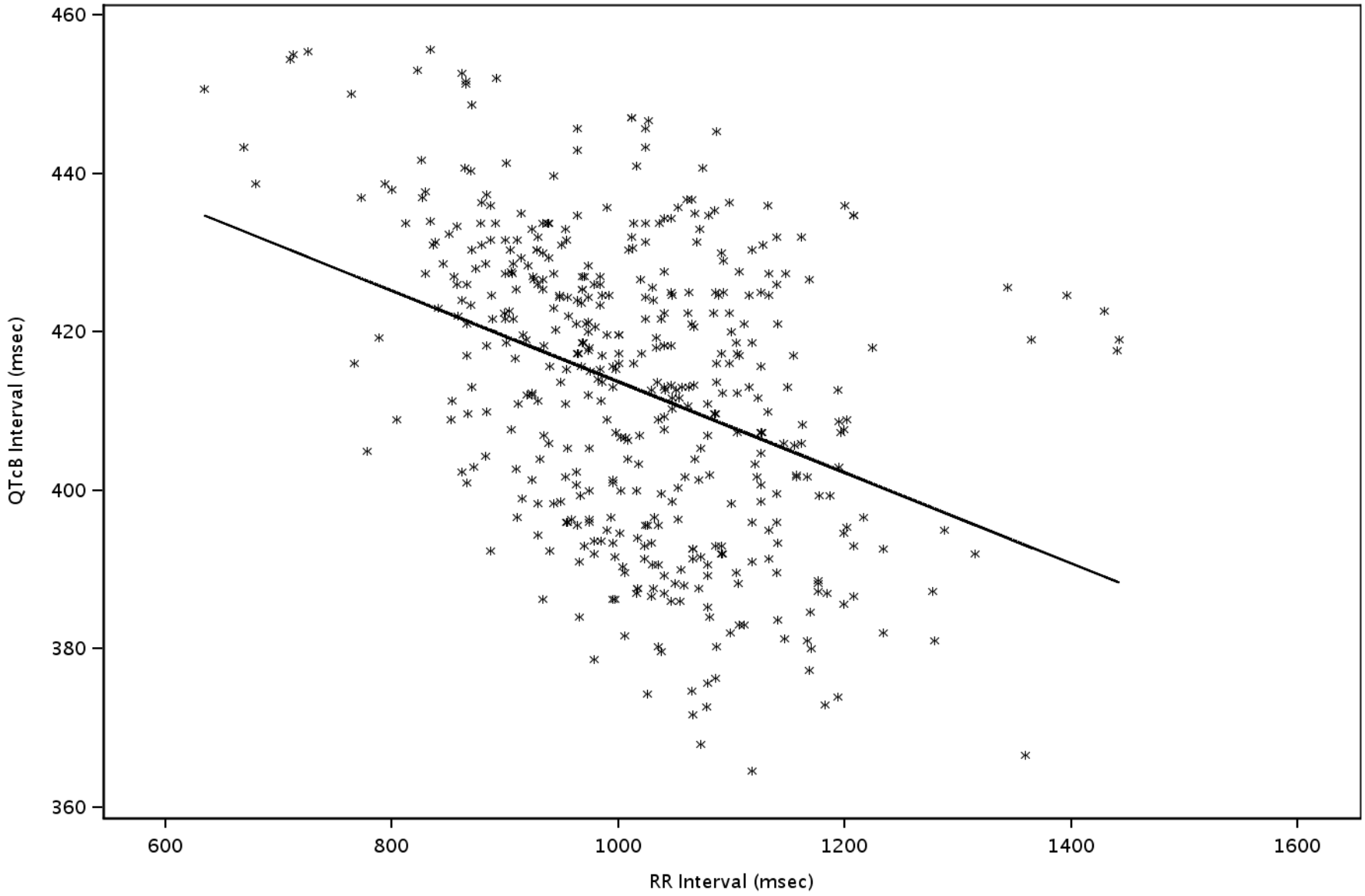
Screening and unplanned readings have been excluded from the presentation.
Pre-dose records are defined as the measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.

[redacted] [redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:18)



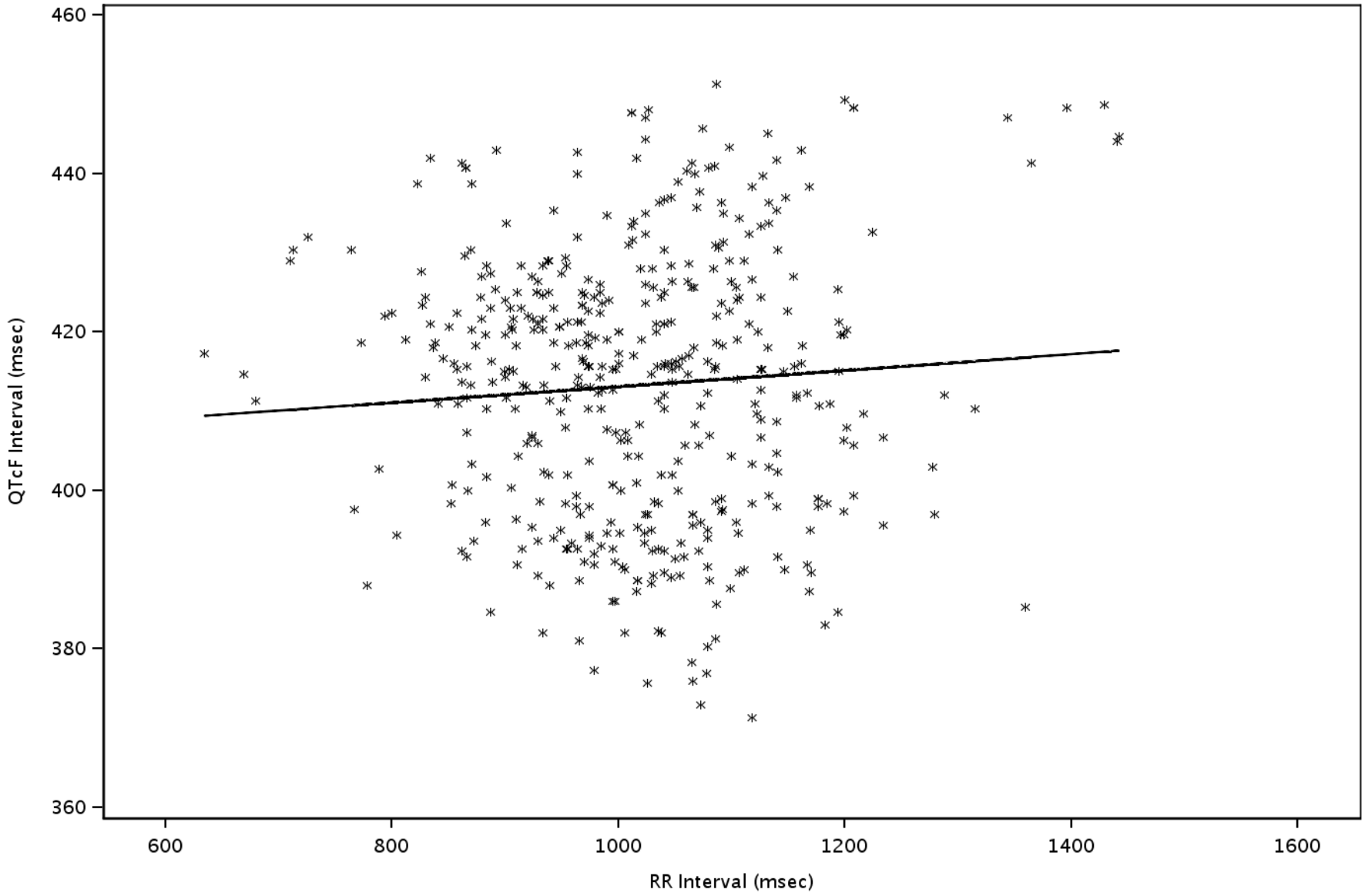
Screening and unplanned readings have been excluded from the presentation.
Pre-dose records are defined as the measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.

[redacted] [redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:18)



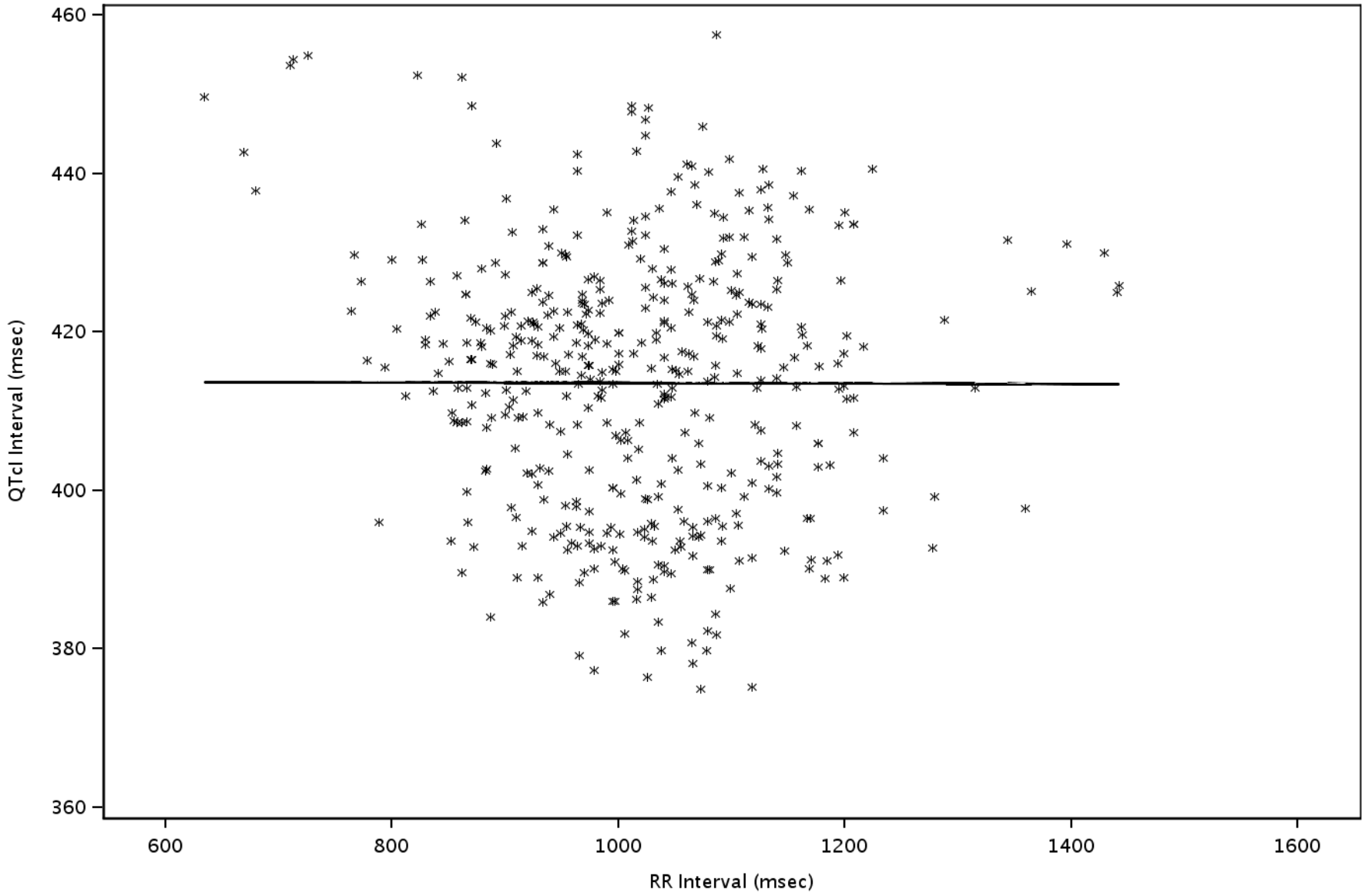
Screening and Unplanned readings have been excluded.
Pre-dose records are defined as the measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.

[redacted] [redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:35)



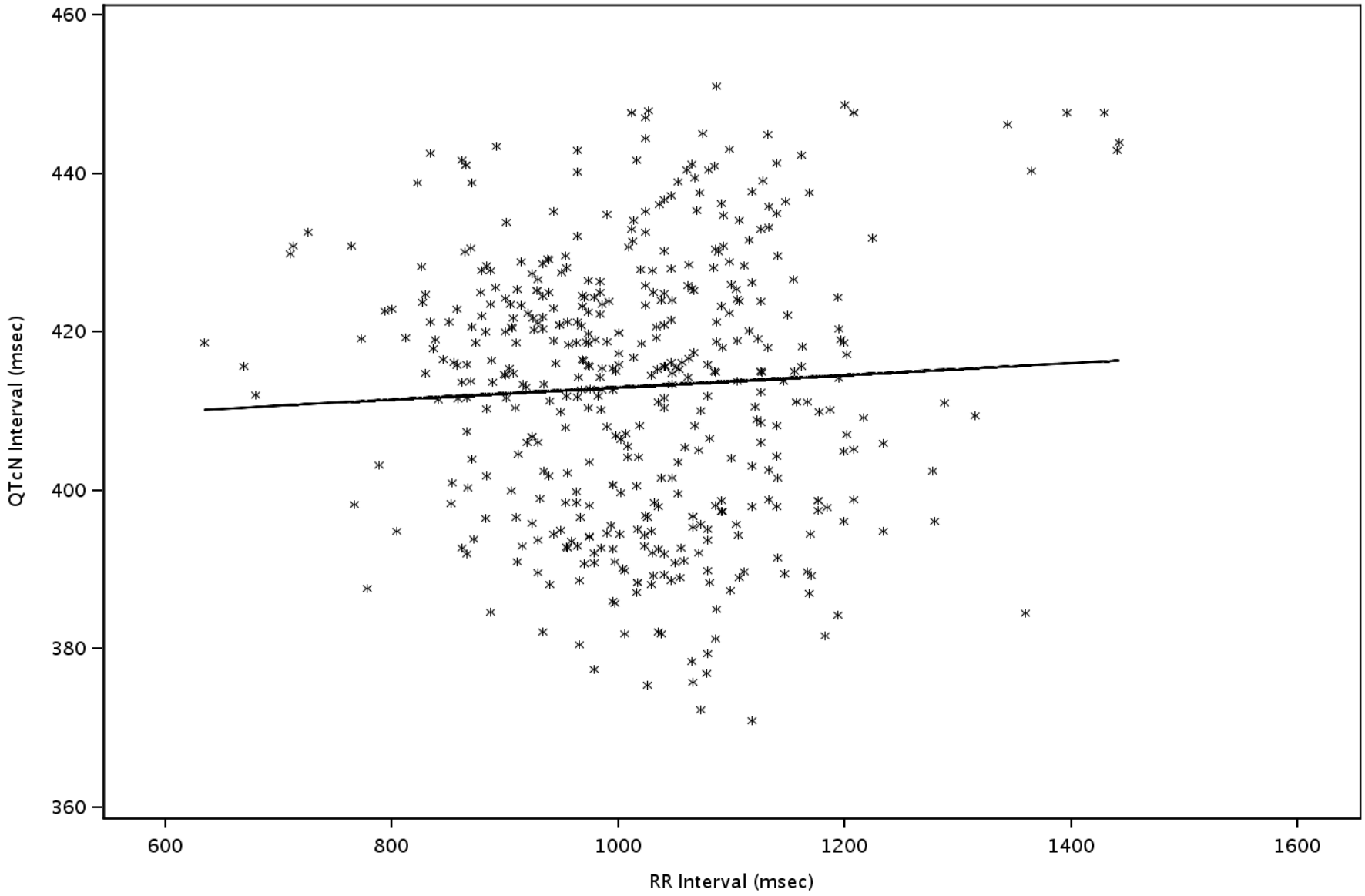
Screening and Unplanned readings have been excluded.
Pre-dose records are defined as the measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.

[redacted] [redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:36)



Screening and Unplanned readings have been excluded.
Pre-dose records are defined as the measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.

[redacted] [redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:36)



Screening and Unplanned readings have been excluded.
Pre-dose records are defined as the measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.

[redacted] [redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:37)

SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

RR INTERVAL (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Baseline			N	52	50	50
			Mean	1024.7	1012.1	1009.7
			Std. Dev.	121.21	111.73	108.94
			Median	1023.1	1015.5	1010.4
			Min	783	716	661
			Max	1437	1368	1206
Day 1		1	N	52	50	50
			Mean	35.2	21.2	28.5
			Std. Dev.	63.21	66.38	64.80
			Median	31.8	34.2	36.9
			Min	-64	-178	-98
			Max	245	179	159
		2	N	52	50	50
			Mean	34.5	38.9	35.1
			Std. Dev.	80.25	63.27	68.73
			Median	24.6	41.5	35.5
			Min	-116	-118	-120
			Max	343	182	300
		3	N	52	50	50
			Mean	34.0	41.7	32.3
			Std. Dev.	89.41	64.20	78.79
			Median	29.3	35.9	18.3
			Min	-179	-84	-115
			Max	349	190	298
		4	N	52	50	50
			Mean	9.2	19.6	27.9
			Std. Dev.	102.46	80.46	74.56
			Median	-7.5	18.3	19.2
			Min	-207	-178	-128
			Max	334	195	197
		5	N	52	50	50
			Mean	-118.4	-113.4	-124.2
			Std. Dev.	107.22	75.11	77.79
			Median	-117.7	-110.3	-122.8
			Min	-643	-361	-295
			Max	114	98	56

Means and Medians have been determined within a subject prior to summarizing across subjects.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:46)

SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

RR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	6	N	52	50	50
		Mean	-102.3	-120.0	-94.5
		Std. Dev.	94.16	75.23	87.59
		Median	-106.7	-121.8	-100.2
		Min	-474	-369	-265
		Max	98	29	73
	8	N	52	50	50
		Mean	-70.8	-45.8	-48.5
		Std. Dev.	107.81	77.71	76.63
		Median	-80.6	-30.3	-51.3
		Min	-396	-282	-222
		Max	182	149	175
	12	N	52	50	50
		Mean	-92.0	-107.8	-91.3
		Std. Dev.	103.48	69.93	91.30
		Median	-96.9	-111.8	-105.5
		Min	-325	-258	-243
		Max	187	71	155
Day 2	24	N	52	50	50
		Mean	-118.3	-126.3	-109.7
		Std. Dev.	104.16	74.19	60.72
		Median	-112.9	-128.4	-124.8
		Min	-489	-327	-221
		Max	182	8	27
Day 14	0	N	50	50	50
		Mean	-25.7	-46.3	-20.8
		Std. Dev.	116.12	95.43	80.34
		Median	-11.8	-36.6	-26.1
		Min	-267	-331	-217
		Max	350	142	156
	1	N	50	50	50
		Mean	8.2	-44.2	37.8
		Std. Dev.	114.87	98.34	89.51
		Median	4.8	-29.7	37.7
		Min	-245	-489	-148
		Max	279	111	224

Means and Medians have been determined within a subject prior to summarizing across subjects.
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Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:46)

SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

RR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	2	N	50	50	50
		Mean	2.9	0.1	45.9
		Std. Dev.	119.18	91.15	89.87
		Median	14.1	14.7	35.4
		Min	-257	-216	-158
		Max	282	135	310
	3	N	50	50	50
		Mean	2.7	12.0	30.8
		Std. Dev.	124.05	90.51	93.61
		Median	10.5	17.2	27.5
		Min	-279	-174	-149
		Max	262	196	224
	4	N	50	50	50
		Mean	-1.3	-8.5	28.2
		Std. Dev.	112.77	92.25	95.10
		Median	5.3	-11.4	29.3
		Min	-253	-180	-182
		Max	211	226	202
	5	N	50	50	50
		Mean	-137.0	-120.4	-101.2
		Std. Dev.	117.55	92.57	101.31
		Median	-137.1	-107.8	-93.1
		Min	-415	-522	-278
		Max	125	33	136
	6	N	50	50	50
		Mean	-122.9	-122.8	-88.6
		Std. Dev.	122.78	87.81	83.28
		Median	-112.3	-128.5	-93.2
		Min	-495	-338	-291
		Max	206	57	124
	8	N	50	50	50
		Mean	-63.3	-79.6	-44.8
		Std. Dev.	122.83	90.01	93.85
		Median	-58.2	-88.0	-51.5
		Min	-326	-227	-247
		Max	270	116	141

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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

RR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	12	N	50	50	50
		Mean	-96.4	-120.9	-103.2
		Std. Dev.	127.85	95.39	80.83
		Median	-90.3	-107.7	-104.7
		Min	-472	-444	-263
		Max	234	72	65
Day 15	24	N	51	50	50
		Mean	-34.8	-48.6	-18.6
		Std. Dev.	115.08	98.35	96.83
		Median	-32.2	-35.0	-8.6
		Min	-412	-493	-234
		Max	290	146	291
Day 16	48	N	50	50	50
		Mean	-36.4	-63.6	-29.6
		Std. Dev.	127.69	119.53	89.13
		Median	-33.5	-62.3	-38.3
		Min	-447	-488	-214
		Max	356	216	219
Day 17	72	N	50	50	50
		Mean	-76.4	-76.7	-75.8
		Std. Dev.	138.61	87.09	91.64
		Median	-96.3	-77.9	-80.8
		Min	-509	-251	-289
		Max	364	98	131

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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

HEART RATE (bpm)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Baseline			N	52	50	50
			Mean	59.5	60.1	60.3
			Std. Dev.	6.84	6.88	7.17
			Median	59.1	59.2	59.7
			Min	42	44	50
			Max	77	84	91
Day 1	1		N	52	50	50
			Mean	-2.1	-1.2	-1.6
			Std. Dev.	3.84	3.74	3.77
			Median	-1.8	-1.7	-1.9
			Min	-16	-10	-8
			Max	4	8	6
	2		N	52	50	50
			Mean	-2.0	-2.0	-1.9
			Std. Dev.	4.67	3.57	3.82
			Median	-1.6	-2.4	-1.9
			Min	-21	-9	-12
			Max	8	8	7
	3		N	52	50	50
			Mean	-2.0	-2.1	-1.8
			Std. Dev.	5.39	3.42	4.31
			Median	-1.5	-2.2	-0.9
			Min	-21	-10	-12
			Max	10	5	7
	4		N	52	50	50
			Mean	-0.3	-0.7	-1.6
			Std. Dev.	5.89	4.83	4.39
			Median	0.5	-1.2	-1.3
			Min	-21	-11	-12
			Max	11	12	9
	5		N	52	50	50
			Mean	7.6	7.7	8.3
			Std. Dev.	6.54	5.04	5.12
			Median	7.4	7.7	8.1
			Min	-9	-6	-4
			Max	34	19	19

Means and Medians have been determined within a subject prior to summarizing across subjects.
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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

HEART RATE (bpm)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	6	N	52	50	50
		Mean	6.5	8.1	6.0
		Std. Dev.	5.74	5.33	5.63
		Median	7.2	7.7	6.1
		Min	-8	-2	-5
		Max	21	31	19
	8	N	52	50	50
		Mean	4.2	3.0	3.0
		Std. Dev.	6.35	5.16	4.48
		Median	4.4	1.9	3.3
		Min	-13	-8	-9
		Max	17	21	13
	12	N	52	50	50
		Mean	5.6	7.2	5.9
		Std. Dev.	6.56	4.76	5.65
		Median	5.8	6.9	6.6
		Min	-13	-4	-8
		Max	17	17	16
Day 2	24	N	52	50	50
		Mean	7.4	8.3	7.3
		Std. Dev.	6.51	4.59	4.16
		Median	7.8	8.3	7.6
		Min	-15	-1	-1
		Max	22	17	16
Day 14	0	N	50	50	50
		Mean	1.2	2.8	1.3
		Std. Dev.	6.99	6.04	4.97
		Median	0.4	2.6	1.6
		Min	-24	-9	-7
		Max	15	16	11
	1	N	50	50	50
		Mean	-0.8	2.8	-2.3
		Std. Dev.	6.79	5.92	5.13
		Median	-0.6	1.9	-2.2
		Min	-20	-6	-12
		Max	14	24	8

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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

HEART RATE (bpm)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	2	N	50	50	50
		Mean	-0.4	0.2	-2.7
		Std. Dev.	7.15	5.84	4.89
		Median	-0.8	-0.8	-2.3
		Min	-21	-9	-13
		Max	15	17	8
	3	N	50	50	50
		Mean	-0.4	-0.6	-1.8
		Std. Dev.	7.49	5.30	5.35
		Median	-0.9	-1.1	-1.6
		Min	-17	-9	-12
		Max	17	11	9
	4	N	50	50	50
		Mean	-0.1	0.7	-1.7
		Std. Dev.	6.96	5.62	5.77
		Median	-0.6	0.5	-1.9
		Min	-16	-10	-16
		Max	18	13	13
	5	N	50	50	50
		Mean	9.0	8.2	6.6
		Std. Dev.	8.19	6.24	7.01
		Median	8.9	7.1	6.1
		Min	-11	-1	-15
		Max	29	27	21
	6	N	50	50	50
		Mean	7.8	8.2	5.6
		Std. Dev.	8.09	6.05	5.52
		Median	7.3	7.3	6.4
		Min	-16	-5	-8
		Max	26	22	20
	8	N	50	50	50
		Mean	3.7	5.1	2.7
		Std. Dev.	7.80	5.69	5.98
		Median	3.8	5.3	2.6
		Min	-20	-7	-11
		Max	22	14	16

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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

HEART RATE (bpm)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	12	N	50	50	50
		Mean	5.9	8.1	6.5
		Std. Dev.	8.25	6.37	5.35
		Median	5.5	7.3	7.4
		Min	-18	-4	-8
		Max	28	24	18
Day 15	24	N	51	50	50
		Mean	2.0	3.2	1.2
		Std. Dev.	7.03	5.64	5.51
		Median	1.6	2.3	0.4
		Min	-21	-6	-12
		Max	20	25	14
Day 16	48	N	50	50	50
		Mean	1.9	4.2	2.0
		Std. Dev.	7.56	7.41	5.16
		Median	1.9	4.3	2.6
		Min	-24	-10	-10
		Max	19	24	14
Day 17	72	N	50	50	50
		Mean	4.5	5.0	5.0
		Std. Dev.	8.49	5.73	5.83
		Median	5.6	5.1	5.1
		Min	-25	-6	-8
		Max	23	20	18

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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

PR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Baseline		N	52	50	50
		Mean	166.4	167.7	167.5
		Std. Dev.	17.44	17.65	17.39
		Median	166.2	165.3	167.1
		Min	125	127	133
		Max	204	208	204
Day 1	1	N	52	50	50
		Mean	1.2	-0.6	0.7
		Std. Dev.	4.73	5.42	5.09
		Median	0.9	-0.9	0.7
		Min	-9	-22	-19
		Max	14	12	13
	2	N	52	50	50
		Mean	-0.3	-0.6	-1.0
		Std. Dev.	5.95	4.92	6.11
		Median	-0.7	-1.6	-1.6
		Min	-17	-12	-20
		Max	16	10	15
	3	N	52	50	50
		Mean	-2.4	-1.8	0.3
		Std. Dev.	5.63	5.60	5.44
		Median	-2.9	-2.7	-0.4
		Min	-17	-14	-11
		Max	8	11	14
	4	N	52	50	50
		Mean	-3.1	-1.2	-0.7
		Std. Dev.	6.38	7.00	5.36
		Median	-3.2	-1.8	-0.7
		Min	-21	-16	-10
		Max	15	15	13
	5	N	52	50	50
		Mean	-6.3	-4.9	-5.1
		Std. Dev.	8.29	6.70	7.09
		Median	-7.6	-5.8	-5.1
		Min	-23	-25	-20
		Max	14	10	20

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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

PR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	6	N	52	50	50
		Mean	-9.3	-6.9	-7.1
		Std. Dev.	7.54	8.57	8.37
		Median	-9.8	-7.3	-8.4
		Min	-27	-29	-21
		Max	12	19	26
	8	N	52	50	50
		Mean	-8.7	-7.2	-7.4
		Std. Dev.	7.86	7.71	7.23
		Median	-9.1	-6.9	-7.1
		Min	-26	-20	-26
		Max	13	18	14
	12	N	52	50	50
		Mean	-6.8	-6.2	-6.9
		Std. Dev.	8.41	9.10	7.79
		Median	-6.7	-6.6	-6.7
		Min	-23	-23	-22
		Max	14	28	18
Day 2	24	N	52	50	50
		Mean	-2.8	-3.2	-2.7
		Std. Dev.	8.62	8.40	6.56
		Median	-2.7	-3.1	-3.1
		Min	-22	-24	-14
		Max	29	20	18
Day 14	0	N	50	50	50
		Mean	-2.8	0.6	3.3
		Std. Dev.	9.47	6.02	8.74
		Median	-2.4	0.9	1.8
		Min	-20	-13	-13
		Max	20	16	41
	1	N	50	50	50
		Mean	-2.3	2.7	4.0
		Std. Dev.	8.29	8.47	8.21
		Median	-2.2	3.6	3.6
		Min	-19	-14	-13
		Max	16	19	33

Means and Medians have been determined within a subject prior to summarizing across subjects.
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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

PR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	2	N	50	50	50
		Mean	-2.2	2.4	4.4
		Std. Dev.	9.52	9.51	8.63
		Median	-2.0	3.1	5.3
		Min	-18	-17	-13
		Max	20	36	33
	3	N	50	50	50
		Mean	-2.9	1.2	3.3
		Std. Dev.	8.27	8.61	7.92
		Median	-2.9	0.7	2.7
		Min	-20	-17	-11
		Max	14	28	26
	4	N	50	50	50
		Mean	-2.8	1.6	3.3
		Std. Dev.	8.61	9.23	8.43
		Median	-3.1	0.4	2.2
		Min	-20	-18	-13
		Max	16	38	32
	5	N	50	50	50
		Mean	-8.5	-5.2	-1.8
		Std. Dev.	10.89	9.85	9.15
		Median	-8.9	-4.9	-2.4
		Min	-39	-30	-23
		Max	14	32	24
	6	N	50	50	50
		Mean	-8.9	-5.4	-4.3
		Std. Dev.	10.60	10.86	9.72
		Median	-10.0	-5.1	-6.2
		Min	-39	-30	-19
		Max	16	35	28
	8	N	50	50	50
		Mean	-7.7	-5.8	-4.7
		Std. Dev.	11.04	8.79	10.62
		Median	-8.4	-6.2	-5.8
		Min	-33	-28	-25
		Max	18	24	36

Means and Medians have been determined within a subject prior to summarizing across subjects.
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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

PR INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	12	N	50	50	50
		Mean	-7.0	-3.8	-3.1
		Std. Dev.	10.92	10.20	10.67
		Median	-8.9	-4.2	-4.4
		Min	-27	-26	-22
		Max	23	38	33
Day 15	24	N	51	50	50
		Mean	-2.7	0.8	0.8
		Std. Dev.	8.79	8.33	8.13
		Median	-3.6	-0.7	0.4
		Min	-22	-11	-15
		Max	16	35	22
Day 16	48	N	50	50	50
		Mean	-2.2	3.8	1.8
		Std. Dev.	9.13	7.94	8.78
		Median	-2.4	2.9	0.7
		Min	-19	-10	-14
		Max	22	25	40
Day 17	72	N	50	50	50
		Mean	-2.0	2.2	1.0
		Std. Dev.	9.12	6.11	8.81
		Median	-2.9	1.8	0.4
		Min	-24	-8	-20
		Max	19	16	24

Means and Medians have been determined within a subject prior to summarizing across subjects.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of Replicates have been used in the calculations.
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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:46)

SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QRS COMPLEX (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Baseline			N	52	50	50
			Mean	92.1	91.8	92.3
			Std. Dev.	7.45	7.59	7.93
			Median	91.1	90.4	92.7
			Min	77	76	77
			Max	107	108	110
Day 1	1		N	52	50	50
			Mean	0.2	-0.2	0.1
			Std. Dev.	2.14	2.29	2.61
			Median	0.2	-0.3	-0.2
			Min	-3	-7	-6
			Max	7	7	8
	2		N	52	50	50
			Mean	-0.2	-0.1	-0.1
			Std. Dev.	2.88	2.70	2.26
			Median	0.4	-0.1	-0.1
			Min	-14	-7	-8
			Max	10	11	6
	3		N	52	50	50
			Mean	-1.0	-1.0	-0.6
			Std. Dev.	3.27	2.25	2.65
			Median	-0.8	-0.8	-0.4
			Min	-14	-10	-14
			Max	9	3	4
	4		N	52	50	50
			Mean	-0.4	-0.1	-0.5
			Std. Dev.	2.61	3.35	3.00
			Median	-0.1	-0.3	-0.4
			Min	-11	-5	-11
			Max	6	19	4
	5		N	52	50	50
			Mean	-0.6	-0.4	-0.6
			Std. Dev.	4.44	3.41	3.78
			Median	-0.2	-0.6	0.3
			Min	-22	-14	-16
			Max	8	6	5

Means and Medians have been determined within a subject prior to summarizing across subjects.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:46)

SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QRS COMPLEX (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	6	N	52	50	50
		Mean	-1.6	-1.5	-1.9
		Std. Dev.	2.99	3.64	3.35
		Median	-1.3	-1.2	-1.7
		Min	-9	-18	-15
		Max	5	6	4
	8	N	52	50	50
		Mean	-1.6	-2.1	-1.9
		Std. Dev.	3.45	2.93	3.88
		Median	-0.8	-1.9	-1.7
		Min	-12	-14	-14
		Max	7	4	7
	12	N	52	50	50
		Mean	-1.0	-0.8	-1.4
		Std. Dev.	3.95	2.90	4.16
		Median	0.0	-0.8	-0.8
		Min	-13	-12	-13
		Max	5	4	8
Day 2	24	N	52	50	50
		Mean	0.5	0.4	1.1
		Std. Dev.	3.55	3.20	3.42
		Median	1.3	0.6	1.2
		Min	-16	-9	-9
		Max	6	11	12
Day 14	0	N	50	50	50
		Mean	-2.1	-1.1	-1.1
		Std. Dev.	5.24	3.19	3.68
		Median	-1.3	-0.8	-1.7
		Min	-22	-11	-8
		Max	6	6	10
	1	N	50	50	50
		Mean	-1.8	-0.9	-0.3
		Std. Dev.	5.13	3.43	3.57
		Median	-0.8	-0.4	-0.1
		Min	-22	-9	-9
		Max	8	8	9

Means and Medians have been determined within a subject prior to summarizing across subjects.
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Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QRS COMPLEX (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	2	N	50	50	50
		Mean	-2.0	-0.9	-0.5
		Std. Dev.	5.29	3.70	3.86
		Median	-1.3	-1.2	-0.7
		Min	-22	-10	-8
		Max	5	10	14
	3	N	50	50	50
		Mean	-1.5	-0.9	-0.8
		Std. Dev.	5.21	3.68	3.90
		Median	-1.0	-0.8	-0.4
		Min	-23	-12	-12
		Max	7	7	8
	4	N	50	50	50
		Mean	-1.8	-0.9	-1.2
		Std. Dev.	5.32	3.51	4.42
		Median	-0.8	-0.8	-0.7
		Min	-22	-10	-16
		Max	7	12	6
	5	N	50	50	50
		Mean	-1.5	-1.6	-0.6
		Std. Dev.	6.11	4.39	4.61
		Median	-0.9	-1.6	-0.4
		Min	-21	-16	-15
		Max	10	14	9
	6	N	50	50	50
		Mean	-2.5	-2.8	-2.0
		Std. Dev.	5.36	3.61	4.35
		Median	-1.2	-2.4	-1.3
		Min	-22	-11	-14
		Max	8	7	6
	8	N	50	50	50
		Mean	-2.2	-2.3	-1.4
		Std. Dev.	5.22	4.30	3.99
		Median	-1.8	-2.1	-1.2
		Min	-22	-10	-12
		Max	8	14	8

Means and Medians have been determined within a subject prior to summarizing across subjects.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QRS COMPLEX (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	12	N	50	50	50
		Mean	-2.2	-2.0	-1.6
		Std. Dev.	5.97	4.60	4.40
		Median	-1.2	-2.0	-0.4
		Min	-23	-18	-16
		Max	8	13	5
Day 15	24	N	51	50	50
		Mean	-2.0	-1.4	-1.8
		Std. Dev.	4.70	3.21	3.85
		Median	-0.7	-1.4	-1.3
		Min	-18	-8	-11
		Max	4	7	4
Day 16	48	N	50	50	50
		Mean	-2.0	-0.6	-1.2
		Std. Dev.	5.00	3.62	4.09
		Median	-0.8	0.0	-0.7
		Min	-22	-10	-13
		Max	6	10	6
Day 17	72	N	50	50	50
		Mean	-1.4	-0.3	-0.9
		Std. Dev.	5.87	3.60	4.44
		Median	-0.1	-0.4	0.0
		Min	-23	-12	-17
		Max	6	6	7

Means and Medians have been determined within a subject prior to summarizing across subjects.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:46)

SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QT INTERVAL (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Baseline			N	52	50	50
			Mean	416.6	413.9	414.3
			Std. Dev.	24.33	23.89	21.92
			Median	413.1	414.4	412.2
			Min	362	377	361
			Max	503	495	477
Day 1		1	N	52	50	50
			Mean	2.9	1.9	4.2
			Std. Dev.	9.16	9.56	9.48
			Median	1.8	0.9	4.7
			Min	-12	-22	-16
			Max	40	27	25
		2	N	52	50	50
			Mean	3.3	4.9	5.1
			Std. Dev.	11.25	9.68	9.82
			Median	1.8	6.0	4.9
			Min	-20	-20	-14
			Max	38	28	36
		3	N	52	50	50
			Mean	3.4	4.4	3.5
			Std. Dev.	12.66	9.54	11.67
			Median	2.0	5.6	4.9
			Min	-20	-14	-20
			Max	36	25	36
		4	N	52	50	50
			Mean	1.3	1.7	3.7
			Std. Dev.	13.80	12.86	11.75
			Median	-2.2	0.9	2.4
			Min	-23	-33	-18
			Max	32	32	35
		5	N	52	50	50
			Mean	-20.5	-21.8	-21.5
			Std. Dev.	18.11	12.71	12.73
			Median	-20.4	-20.2	-20.0
			Min	-104	-65	-55
			Max	12	8	11

Means and Medians have been determined within a subject prior to summarizing across subjects.
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Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.

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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QT INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	6	N	52	50	50
		Mean	-21.0	-24.3	-20.4
		Std. Dev.	15.96	12.66	15.10
		Median	-20.7	-25.1	-22.2
		Min	-86	-70	-52
		Max	8	4	15
	8	N	52	50	50
		Mean	-17.4	-14.8	-15.0
		Std. Dev.	16.90	12.35	12.83
		Median	-18.0	-12.9	-16.4
		Min	-59	-60	-40
		Max	18	3	14
	12	N	52	50	50
		Mean	-15.8	-19.5	-18.0
		Std. Dev.	17.07	12.31	14.55
		Median	-16.2	-20.2	-18.9
		Min	-71	-44	-53
		Max	22	16	19
Day 2	24	N	52	50	50
		Mean	-21.4	-22.4	-20.0
		Std. Dev.	15.41	13.39	10.62
		Median	-22.2	-25.6	-19.8
		Min	-84	-53	-40
		Max	20	2	10
Day 14	0	N	50	50	50
		Mean	-2.3	-11.6	-9.3
		Std. Dev.	17.44	17.39	15.31
		Median	-1.1	-10.9	-8.4
		Min	-38	-59	-51
		Max	62	30	28
	1	N	50	50	50
		Mean	3.0	-0.2	-1.1
		Std. Dev.	16.73	18.28	14.37
		Median	4.4	0.1	-1.3
		Min	-40	-71	-37
		Max	54	31	34

Means and Medians have been determined within a subject prior to summarizing across subjects.
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Means of Replicates have been used in the calculations.
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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QT INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	2	N	50	50	50
		Mean	3.4	7.0	0.2
		Std. Dev.	17.53	17.53	15.15
		Median	5.3	11.1	-0.7
		Min	-44	-33	-41
		Max	42	35	39
	3	N	50	50	50
		Mean	4.4	9.2	-0.9
		Std. Dev.	17.20	17.47	14.33
		Median	6.4	12.7	-0.9
		Min	-39	-36	-35
		Max	42	41	34
	4	N	50	50	50
		Mean	5.5	7.7	-1.2
		Std. Dev.	17.70	17.94	16.15
		Median	6.9	11.8	1.1
		Min	-48	-35	-41
		Max	36	39	47
	5	N	50	50	50
		Mean	-20.7	-16.7	-23.6
		Std. Dev.	17.77	17.93	18.83
		Median	-20.9	-16.0	-24.2
		Min	-72	-92	-63
		Max	19	12	39
	6	N	50	50	50
		Mean	-20.8	-18.7	-23.1
		Std. Dev.	17.95	17.75	16.34
		Median	-19.6	-18.7	-23.3
		Min	-86	-72	-75
		Max	27	14	27
	8	N	50	50	50
		Mean	-12.6	-13.3	-16.4
		Std. Dev.	17.87	15.73	16.48
		Median	-12.0	-15.3	-19.1
		Min	-66	-52	-51
		Max	38	18	30

Means and Medians have been determined within a subject prior to summarizing across subjects.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QT INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	12	N	50	50	50
		Mean	-15.0	-18.4	-22.2
		Std. Dev.	18.17	18.57	15.00
		Median	-13.6	-21.3	-24.2
		Min	-71	-73	-55
		Max	36	17	20
Day 15	24	N	51	50	50
		Mean	-3.4	-7.2	-9.2
		Std. Dev.	18.63	17.74	14.46
		Median	-5.3	-2.0	-9.6
		Min	-63	-79	-44
		Max	54	26	28
Day 16	48	N	50	50	50
		Mean	-3.4	-12.5	-9.4
		Std. Dev.	20.36	19.37	15.10
		Median	-5.6	-8.7	-10.4
		Min	-70	-83	-48
		Max	60	24	28
Day 17	72	N	50	50	50
		Mean	-10.8	-17.8	-18.3
		Std. Dev.	22.19	15.83	15.24
		Median	-12.0	-16.0	-17.8
		Min	-75	-52	-47
		Max	58	18	10

Means and Medians have been determined within a subject prior to summarizing across subjects.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:46)

Mean Baseline and Change from Baseline for ECG Data

QTCB INTERVAL (BAZETT'S CORRECTION) (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Baseline			N	52	50	50
			Mean	413.0	412.7	413.7
			Std. Dev.	17.48	18.17	18.88
			Median	415.5	414.0	415.3
			Min	372	374	374
			Max	451	455	453
Day 1	1		N	52	50	50
			Mean	-4.1	-2.2	-1.5
			Std. Dev.	7.43	7.34	8.16
			Median	-2.8	-1.2	-2.4
			Min	-31	-21	-20
			Max	8	25	18
	2		N	52	50	50
			Mean	-3.6	-2.5	-1.9
			Std. Dev.	7.87	7.74	7.31
			Median	-4.1	-3.6	-1.8
			Min	-30	-20	-18
			Max	12	25	18
	3		N	52	50	50
			Mean	-3.3	-3.6	-2.8
			Std. Dev.	9.44	6.89	8.41
			Median	-2.9	-3.9	-2.6
			Min	-33	-18	-27
			Max	15	14	17
	4		N	52	50	50
			Mean	-0.2	-1.7	-2.0
			Std. Dev.	10.14	8.22	7.46
			Median	0.3	-1.1	-0.9
			Min	-34	-21	-20
			Max	17	15	15
	5		N	52	50	50
			Mean	4.5	2.4	5.0
			Std. Dev.	10.22	9.21	9.06
			Median	4.8	1.1	3.6
			Min	-20	-23	-12
			Max	28	21	27

Means and Medians have been determined within a subject prior to summarizing across subjects.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QTCB INTERVAL (BAZETT'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	6	N	52	50	50
		Mean	0.2	1.1	-0.9
		Std. Dev.	9.83	9.57	9.36
		Median	-0.7	1.8	-0.9
		Min	-20	-21	-16
		Max	25	23	23
	8	N	52	50	50
		Mean	-3.1	-5.2	-5.2
		Std. Dev.	8.66	9.76	8.04
		Median	-3.4	-4.9	-5.8
		Min	-21	-33	-28
		Max	19	19	14
	12	N	52	50	50
		Mean	3.1	3.5	1.1
		Std. Dev.	9.29	9.16	10.90
		Median	2.8	3.8	2.0
		Min	-20	-14	-19
		Max	21	31	24
Day 2	24	N	52	50	50
		Mean	3.2	4.2	3.4
		Std. Dev.	10.55	9.33	9.78
		Median	4.1	4.4	4.4
		Min	-20	-25	-23
		Max	21	24	27
Day 14	0	N	50	50	50
		Mean	2.4	-2.2	-5.0
		Std. Dev.	11.00	9.92	10.68
		Median	2.4	-3.4	-3.8
		Min	-21	-25	-30
		Max	29	17	25
	1	N	50	50	50
		Mean	0.7	9.2	-8.7
		Std. Dev.	11.21	9.39	12.06
		Median	-0.6	7.4	-7.7
		Min	-23	-9	-35
		Max	31	29	13

Means and Medians have been determined within a subject prior to summarizing across subjects.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QTCB INTERVAL (BAZETT'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	2	N	50	50	50
		Mean	2.5	7.2	-8.8
		Std. Dev.	12.15	10.35	11.57
		Median	1.5	7.5	-9.7
		Min	-22	-23	-36
		Max	34	28	19
	3	N	50	50	50
		Mean	3.3	7.0	-6.8
		Std. Dev.	12.26	12.38	11.46
		Median	2.6	9.5	-7.3
		Min	-26	-22	-37
		Max	29	30	17
	4	N	50	50	50
		Mean	5.4	9.8	-6.8
		Std. Dev.	10.84	11.94	11.78
		Median	4.6	10.4	-6.1
		Min	-17	-23	-32
		Max	30	35	22
	5	N	50	50	50
		Mean	8.3	9.6	-2.6
		Std. Dev.	12.10	11.70	13.44
		Median	8.4	11.3	-2.4
		Min	-16	-18	-30
		Max	37	34	28
	6	N	50	50	50
		Mean	4.8	7.6	-4.9
		Std. Dev.	11.98	13.39	11.97
		Median	4.3	8.0	-5.5
		Min	-25	-28	-28
		Max	31	39	21
	8	N	50	50	50
		Mean	0.2	3.6	-7.4
		Std. Dev.	13.36	13.75	11.82
		Median	-0.4	4.0	-6.8
		Min	-28	-39	-50
		Max	28	30	16

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Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QTCB INTERVAL (BAZETT'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	12	N	50	50	50
		Mean	4.9	7.5	-1.1
		Std. Dev.	13.51	11.19	12.00
		Median	3.3	6.4	-1.7
		Min	-28	-16	-30
		Max	34	36	22
Day 15	24	N	51	50	50
		Mean	3.7	3.3	-5.2
		Std. Dev.	11.98	11.25	10.67
		Median	4.1	4.4	-5.4
		Min	-23	-26	-28
		Max	28	26	12
Day 16	48	N	50	50	50
		Mean	3.7	1.1	-3.0
		Std. Dev.	11.08	12.34	11.41
		Median	3.3	0.4	-4.6
		Min	-23	-25	-23
		Max	30	23	23
Day 17	72	N	50	50	50
		Mean	4.7	-1.8	-2.3
		Std. Dev.	12.41	11.42	11.40
		Median	7.1	-0.7	-0.8
		Min	-30	-35	-29
		Max	24	25	22

Means and Medians have been determined within a subject prior to summarizing across subjects.
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Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:46)

SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Baseline			N	52	50	50
			Mean	414.0	412.9	413.7
			Std. Dev.	16.36	16.87	16.64
			Median	415.5	414.7	414.3
			Min	377	376	379
			Max	446	446	449
Day 1	1		N	52	50	50
			Mean	-1.8	-0.8	0.4
			Std. Dev.	5.28	5.35	6.05
			Median	-1.7	-0.3	-0.1
			Min	-16	-15	-14
			Max	9	15	17
	2		N	52	50	50
			Mean	-1.3	-0.0	0.4
			Std. Dev.	5.29	6.12	5.08
			Median	-1.8	-0.7	0.7
			Min	-10	-16	-11
			Max	10	19	11
	3		N	52	50	50
			Mean	-1.1	-0.9	-0.7
			Std. Dev.	6.31	5.23	6.28
			Median	0.6	-1.4	-0.3
			Min	-15	-12	-16
			Max	10	16	14
	4		N	52	50	50
			Mean	0.2	-0.7	-0.1
			Std. Dev.	6.36	6.40	5.76
			Median	0.9	0.3	-0.1
			Min	-15	-15	-13
			Max	14	12	12
	5		N	52	50	50
			Mean	-3.9	-5.9	-4.0
			Std. Dev.	8.35	7.35	7.15
			Median	-4.4	-5.8	-4.8
			Min	-22	-22	-19
			Max	16	12	13

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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 1	6	N	52	50	50
		Mean	-7.0	-7.5	-7.4
		Std. Dev.	8.08	7.51	7.93
		Median	-8.1	-6.9	-8.2
		Min	-23	-23	-23
		Max	8	12	11
	8	N	52	50	50
		Mean	-7.9	-8.4	-8.5
		Std. Dev.	6.43	7.66	6.69
		Median	-7.9	-9.0	-8.7
		Min	-26	-26	-28
		Max	7	9	4
	12	N	52	50	50
		Mean	-3.3	-4.3	-5.4
		Std. Dev.	7.08	7.57	8.56
		Median	-3.2	-3.6	-5.6
		Min	-29	-20	-23
		Max	10	19	11
Day 2	24	N	52	50	50
		Mean	-5.1	-4.7	-4.5
		Std. Dev.	6.98	8.23	8.03
		Median	-5.2	-4.4	-5.2
		Min	-20	-26	-22
		Max	9	15	13
Day 14	0	N	50	50	50
		Mean	0.9	-5.3	-6.5
		Std. Dev.	7.84	8.82	9.68
		Median	1.0	-5.7	-5.7
		Min	-20	-25	-26
		Max	16	12	19
	1	N	50	50	50
		Mean	1.5	6.1	-6.2
		Std. Dev.	7.72	8.65	9.74
		Median	1.2	4.9	-6.0
		Min	-15	-12	-26
		Max	16	27	17

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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	2	N	50	50	50
		Mean	2.8	7.1	-5.7
		Std. Dev.	8.37	9.57	9.93
		Median	1.6	8.3	-5.1
		Min	-14	-16	-24
		Max	22	25	26
	3	N	50	50	50
		Mean	3.6	7.7	-4.9
		Std. Dev.	7.42	11.36	8.96
		Median	2.4	9.1	-4.3
		Min	-7	-21	-25
		Max	20	30	22
	4	N	50	50	50
		Mean	5.4	9.0	-4.9
		Std. Dev.	7.86	11.01	10.08
		Median	5.6	11.2	-5.9
		Min	-18	-15	-25
		Max	21	31	25
	5	N	50	50	50
		Mean	-1.5	0.6	-9.6
		Std. Dev.	7.85	10.56	11.78
		Median	-1.9	1.7	-10.1
		Min	-18	-24	-37
		Max	14	23	17
	6	N	50	50	50
		Mean	-3.8	-1.3	-11.0
		Std. Dev.	7.51	12.07	10.89
		Median	-3.2	0.3	-10.1
		Min	-20	-30	-34
		Max	11	32	17
	8	N	50	50	50
		Mean	-4.1	-2.1	-10.4
		Std. Dev.	9.09	11.47	10.11
		Median	-3.1	-0.7	-9.9
		Min	-24	-34	-40
		Max	19	22	16

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SERTRALINE Protocol A0501104
Mean Baseline and Change from Baseline for ECG Data

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline	Moxifloxacin	Placebo
Day 14	12	N	50	50	50
		Mean	-1.8	-1.3	-8.2
		Std. Dev.	8.62	10.30	10.39
		Median	-2.2	-1.0	-9.6
		Min	-24	-21	-28
		Max	15	25	11
Day 15	24	N	51	50	50
		Mean	1.3	-0.2	-6.6
		Std. Dev.	9.51	9.94	8.11
		Median	0.7	1.2	-5.3
		Min	-23	-23	-23
		Max	20	22	12
Day 16	48	N	50	50	50
		Mean	1.4	-3.4	-5.1
		Std. Dev.	8.54	9.54	9.59
		Median	1.5	-3.3	-5.1
		Min	-21	-24	-24
		Max	19	17	14
Day 17	72	N	50	50	50
		Mean	-0.4	-7.1	-7.7
		Std. Dev.	9.37	9.82	9.27
		Median	-0.7	-5.9	-7.4
		Min	-31	-31	-32
		Max	23	11	8

Means and Medians have been determined within a subject prior to summarizing across subjects.
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Means of Replicates have been used in the calculations.
The minimum and maximum values have been determined from the means of the values recorded at each time post dose.
Unplanned readings have been excluded from the presentation.
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SERTRALINE Protocol A0501104
Categorical Summary of Post-dose ECG Data - Absolute Values

Parameter	Criteria	Sertraline N	Sertraline n (%)	Moxifloxacin N	Moxifloxacin n (%)	Placebo N	Placebo n (%)
Maximum HEART RATE (bpm)	>120	52	0	50	0	50	0
	<40	52	0	50	0	50	0
Maximum PR INTERVAL (msec)	>=300	52	0	50	0	50	0
Maximum QRS COMPLEX (msec)	>=200	52	0	50	0	50	0
Maximum QT INTERVAL (msec)	450-<480	52	12 (23.1)	50	11 (22.0)	50	9 (18.0)
	480-<500	52	0	50	1 (2.0)	50	1 (2.0)
	>=500	52	1 (1.9)	50	0	50	0
Maximum QTCB INTERVAL (BAZETT'S CORRECTION) (msec)	450-<480	52	6 (11.5)	50	7 (14.0)	50	6 (12.0)
	480-<500	52	0	50	0	50	0
	>=500	52	0	50	0	50	0
Maximum QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)	450-<480	52	1 (1.9)	50	3 (6.0)	50	3 (6.0)
	480-<500	52	0	50	0	50	0
	>=500	52	0	50	0	50	0

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SERTRALINE Protocol A0501104
Categorical Summary of Maximum Increase from Baseline for ECG Data

Parameter	Criteria	Sertraline N	Sertraline n (%)	Moxifloxacin N	Moxifloxacin n (%)	Placebo N	Placebo n (%)
Maximum PR INTERVAL increase from baseline (msec)	PctChg>=25/50%	52	0	50	0	50	0
Maximum QRS COMPLEX increase from baseline (msec)	PctChg>=25/50%	52	0	50	0	50	0
Maximum QT INTERVAL increase from baseline (msec)	30<=Change<60	52	6 (11.5)	50	10 (20.0)	50	4 (8.0)
	Change>=60	52	1 (1.9)	50	0	50	0
Maximum QTCB INTERVAL (BAZETT'S CORRECTION) increase from baseline (msec)	30<=Change<60	52	9 (17.3)	50	5 (10.0)	50	0
	Change>=60	52	0	50	0	50	0
Maximum QTCF INTERVAL (FRIDERICIA'S CORRECTION) increase from baseline (msec)	30<=Change<60	52	0	50	1 (2.0)	50	0
	Change>=60	52	0	50	0	50	0

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:48)

SERTRALINE Protocol A0501104
Mean Difference from Placebo for ECG Data (Heart Rate, QT and QTcF)

HEART RATE (bpm)

Period Day	Time Post Dose (HOURS)		Sertraline - Placebo	Moxifloxacin - Placebo
Day 1	-1	N	48	48
		Mean	-1.6	-0.8
		90% CI	-3.3 ,0.0	-2.1 ,0.6
	-0.5	N	48	48
		Mean	-0.7	-0.3
		90% CI	-2.1 ,0.7	-1.5 ,0.8
	0	N	48	48
		Mean	-0.8	-0.4
		90% CI	-2.3 ,0.7	-1.6 ,0.8
	1	N	48	48
		Mean	-1.8	0.3
		90% CI	-2.9 ,-0.6	-1.1 ,1.7
	2	N	48	48
		Mean	-1.3	-0.6
		90% CI	-2.4 ,-0.1	-1.7 ,0.5
	3	N	48	48
		Mean	-1.4	-0.7
		90% CI	-2.7 ,-0.2	-2.2 ,0.8
	4	N	48	48
		Mean	0.0	0.6
		90% CI	-1.0 ,1.1	-0.8 ,2.0
	5	N	48	48
		Mean	-2.2	-1.0
		90% CI	-3.4 ,-0.9	-2.4 ,0.5
	6	N	48	48
		Mean	-0.8	2.1
		90% CI	-2.1 ,0.4	0.5 ,3.6
	8	N	48	48
		Mean	-0.3	-0.5
		90% CI	-1.6 ,1.0	-1.5 ,0.5

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Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
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[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:49)

SERTRALINE Protocol A0501104
Mean Difference from Placebo for ECG Data (Heart Rate, QT and QTcF)

HEART RATE (bpm)

Period	Day	Time Post Dose (HOURS)		Sertraline - Placebo	Moxifloxacin - Placebo
Day 1		12	N	48	48
			Mean	-1.5	1.5
			90% CI	-2.7 ,-0.2	0.1 ,2.9
Day 2		24	N	48	48
			Mean	-1.1	0.6
			90% CI	-2.4 ,0.2	-0.7 ,2.0
Day 14		0	N	48	48
			Mean	-1.4	0.9
			90% CI	-2.8 ,0.1	-0.3 ,2.1
		1	N	48	48
			Mean	0.2	4.3
			90% CI	-1.2 ,1.5	3.2 ,5.5
		2	N	48	48
			Mean	0.8	2.1
			90% CI	-0.6 ,2.3	0.9 ,3.3
		3	N	48	48
			Mean	-0.3	0.9
			90% CI	-1.8 ,1.2	-0.2 ,2.0
		4	N	48	48
			Mean	-0.1	2.0
			90% CI	-1.5 ,1.3	1.1 ,3.0
		5	N	48	48
			Mean	0.8	1.6
			90% CI	-0.7 ,2.3	0.2 ,2.9
		6	N	48	48
			Mean	0.7	2.3
			90% CI	-0.8 ,2.3	0.9 ,3.7
		8	N	48	48
			Mean	-0.6	2.0
			90% CI	-2.3 ,1.0	0.6 ,3.4

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SERTRALINE Protocol A0501104
Mean Difference from Placebo for ECG Data (Heart Rate, QT and QTcF)

HEART RATE (bpm)

Period	Day	Time Post Dose (HOURS)		Sertraline - Placebo	Moxifloxacin - Placebo
Day 14		12	N	48	48
			Mean	-1.9	1.5
			90% CI	-3.3 ,-0.6	0.3 ,2.6
Day 15		24	N	48	48
			Mean	-1.0	1.4
			90% CI	-2.4 ,0.3	0.2 ,2.7
Day 16		48	N	48	48
			Mean	-1.5	1.4
			90% CI	-3.0 ,-0.1	0.0 ,2.8
Day 17		72	N	48	48
			Mean	-2.1	-0.6
			90% CI	-3.6 ,-0.6	-1.8 ,0.5

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SERTRALINE Protocol A0501104
Mean Difference from Placebo for ECG Data (Heart Rate, QT and QTcF)

QT INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline - Placebo	Moxifloxacin - Placebo
Day 1	-1	N	48	48
		Mean	3.1	1.0
		90% CI	-1.7 ,7.9	-3.0 ,5.0
	-0.5	N	48	48
		Mean	2.1	-0.1
		90% CI	-2.1 ,6.4	-3.6 ,3.3
	0	N	48	48
		Mean	1.4	-0.9
		90% CI	-3.3 ,6.1	-5.3 ,3.4
	1	N	48	48
		Mean	1.8	-3.5
		90% CI	-2.3 ,5.9	-7.3 ,0.4
	2	N	48	48
		Mean	0.8	-0.7
		90% CI	-3.0 ,4.7	-4.0 ,2.6
	3	N	48	48
		Mean	2.4	0.6
		90% CI	-0.6 ,5.4	-3.1 ,4.4
	4	N	48	48
		Mean	0.3	-2.1
		90% CI	-2.9 ,3.5	-6.0 ,1.8
	5	N	48	48
		Mean	4.1	-0.4
		90% CI	1.1 ,7.1	-3.4 ,2.7
	6	N	48	48
		Mean	2.0	-4.6
		90% CI	-1.2 ,5.2	-8.0 ,-1.3
	8	N	48	48
		Mean	1.4	0.2
		90% CI	-2.0 ,4.7	-2.9 ,3.3

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SERTRALINE Protocol A0501104
Mean Difference from Placebo for ECG Data (Heart Rate, QT and QTcF)

QT INTERVAL (msec)

Period Day	Time Post Dose (HOURS)		Sertraline - Placebo	Moxifloxacin - Placebo
Day 1	12	N	48	48
		Mean	4.4	-2.9
		90% CI	1.1 ,7.8	-5.8 ,-0.1
Day 2	24	N	48	48
		Mean	1.5	-2.4
		90% CI	-1.3 ,4.2	-5.7 ,1.0
Day 14	0	N	48	48
		Mean	9.4	-1.6
		90% CI	6.1 ,12.7	-4.6 ,1.5
	1	N	48	48
		Mean	6.5	1.5
		90% CI	3.1 ,9.8	-1.4 ,4.5
	2	N	48	48
		Mean	5.8	7.5
		90% CI	2.1 ,9.5	4.3 ,10.7
	3	N	48	48
		Mean	7.8	10.0
		90% CI	4.3 ,11.2	7.4 ,12.7
	4	N	48	48
		Mean	9.5	8.7
		90% CI	6.2 ,12.8	6.1 ,11.2
	5	N	48	48
		Mean	5.4	6.6
		90% CI	1.8 ,9.0	3.2 ,10.1
	6	N	48	48
		Mean	4.8	4.5
		90% CI	1.1 ,8.6	1.4 ,7.6
	8	N	48	48
		Mean	6.3	3.3
		90% CI	2.4 ,10.3	-0.3 ,7.0

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SERTRALINE Protocol A0501104
Mean Difference from Placebo for ECG Data (Heart Rate, QT and QTcF)

QT INTERVAL (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline - Placebo	Moxifloxacin - Placebo
Day 14		12	N	48	48
			Mean	9.6	3.1
			90% CI	6.3 ,12.9	0.3 ,5.8
Day 15		24	N	48	48
			Mean	9.2	2.1
			90% CI	6.1 ,12.3	-1.1 ,5.3
Day 16		48	N	48	48
			Mean	9.2	-2.3
			90% CI	5.1 ,13.3	-5.7 ,1.2
Day 17		72	N	48	48
			Mean	10.8	0.8
			90% CI	7.2 ,14.5	-2.2 ,3.9

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SERTRALINE Protocol A0501104
Mean Difference from Placebo for ECG Data (Heart Rate, QT and QTcF)

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

Period Day	Time Post Dose (HOURS)		Sertraline - Placebo	Moxifloxacin - Placebo
Day 1	-1	N	48	48
		Mean	-0.9	-0.9
		90% CI	-3.3 ,1.6	-3.0 ,1.2
	-0.5	N	48	48
		Mean	0.3	-1.0
		90% CI	-2.3 ,3.0	-3.6 ,1.5
	0	N	48	48
		Mean	-0.7	-1.9
		90% CI	-3.2 ,1.8	-4.5 ,0.7
	1	N	48	48
		Mean	-2.2	-2.7
		90% CI	-4.8 ,0.4	-5.2 ,-0.2
	2	N	48	48
		Mean	-2.1	-2.3
		90% CI	-4.8 ,0.6	-4.9 ,0.3
	3	N	48	48
		Mean	-1.0	-1.4
		90% CI	-3.4 ,1.5	-3.6 ,0.8
	4	N	48	48
		Mean	0.2	-1.3
		90% CI	-2.0 ,2.4	-3.7 ,1.0
	5	N	48	48
		Mean	0.0	-2.6
		90% CI	-2.2 ,2.2	-4.7 ,-0.5
	6	N	48	48
		Mean	0.0	-0.9
		90% CI	-2.3 ,2.4	-3.0 ,1.2
	8	N	48	48
		Mean	0.9	-1.0
		90% CI	-1.0 ,2.8	-3.2 ,1.1

Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicates have been used in the calculations.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:49)

SERTRALINE Protocol A0501104
Mean Difference from Placebo for ECG Data (Heart Rate, QT and QTcF)

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline - Placebo	Moxifloxacin - Placebo
Day 1		12	N	48	48
			Mean	1.8	-0.1
			90% CI	-0.2 ,3.7	-1.9 ,1.8
Day 2		24	N	48	48
			Mean	-0.5	-1.1
			90% CI	-2.3 ,1.2	-3.0 ,0.8
Day 14		0	N	48	48
			Mean	6.7	0.6
			90% CI	4.8 ,8.5	-0.9 ,2.1
		1	N	48	48
			Mean	6.8	11.3
			90% CI	5.0 ,8.7	9.5 ,13.2
		2	N	48	48
			Mean	7.8	12.0
			90% CI	5.9 ,9.6	10.4 ,13.6
		3	N	48	48
			Mean	7.2	11.8
			90% CI	5.5 ,8.9	10.0 ,13.5
		4	N	48	48
			Mean	9.2	13.0
			90% CI	7.4 ,11.0	11.4 ,14.6
		5	N	48	48
			Mean	7.2	9.6
			90% CI	5.1 ,9.2	7.5 ,11.7
		6	N	48	48
			Mean	6.5	9.2
			90% CI	4.4 ,8.6	7.2 ,11.2
		8	N	48	48
			Mean	5.2	7.5
			90% CI	3.0 ,7.5	5.6 ,9.5

Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicates have been used in the calculations.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:49)

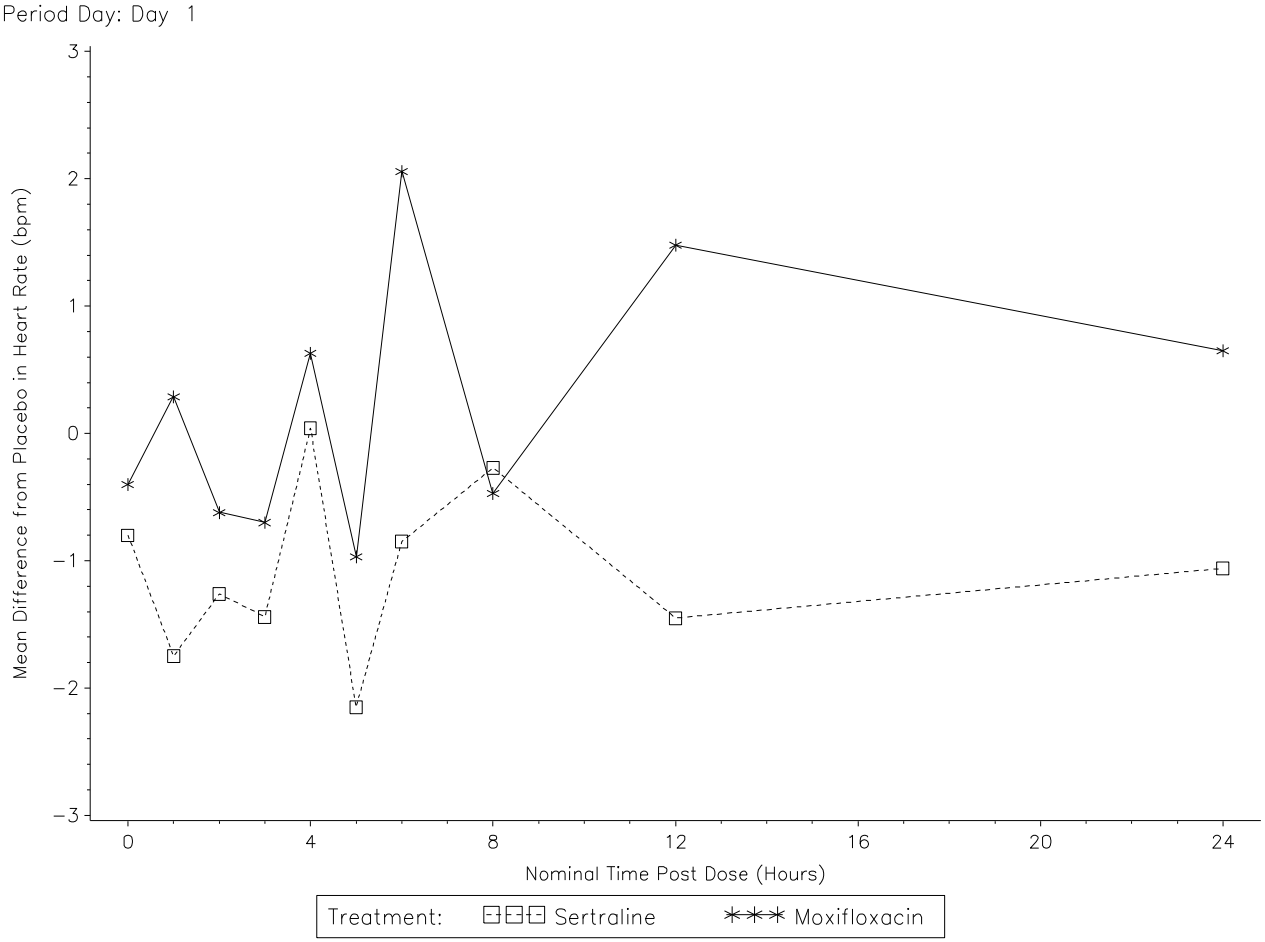
SERTRALINE Protocol A0501104
Mean Difference from Placebo for ECG Data (Heart Rate, QT and QTcF)

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

Period	Day	Time Post Dose (HOURS)		Sertraline - Placebo	Moxifloxacin - Placebo
Day 14		12	N	48	48
			Mean	5.7	5.7
			90% CI	3.9 ,7.6	3.9 ,7.6
Day 15		24	N	48	48
			Mean	7.2	5.4
			90% CI	5.4 ,9.0	3.7 ,7.0
Day 16		48	N	48	48
			Mean	6.2	0.9
			90% CI	4.0 ,8.3	-0.9 ,2.7
Day 17		72	N	48	48
			Mean	6.7	-0.3
			90% CI	4.5 ,8.9	-2.1 ,1.6

Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicates have been used in the calculations.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:49)

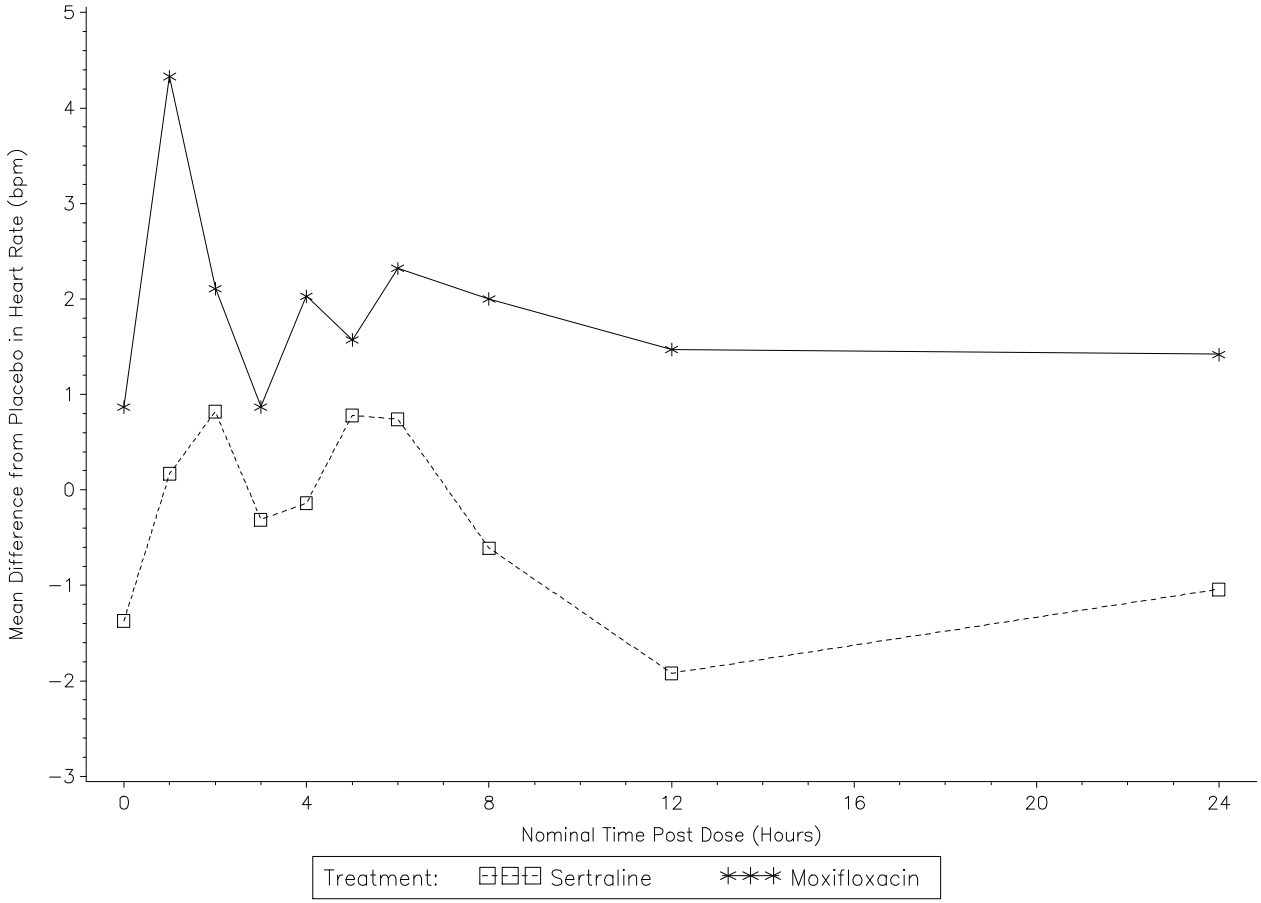
Figure 14.3.4.3.3.2.1
SERTRALINE Protocol A0501104
Mean Difference from Placebo of ECG Value in Heart Rate versus Time



Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicate have been used in the calculations.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (−1 hours, −0.5 hours, 0 hours) before dosing within each period.
Unplanned readings have been excluded from the presentation.
[redacted] Source Data: Table 14.3.4.3.3.1 Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:12)

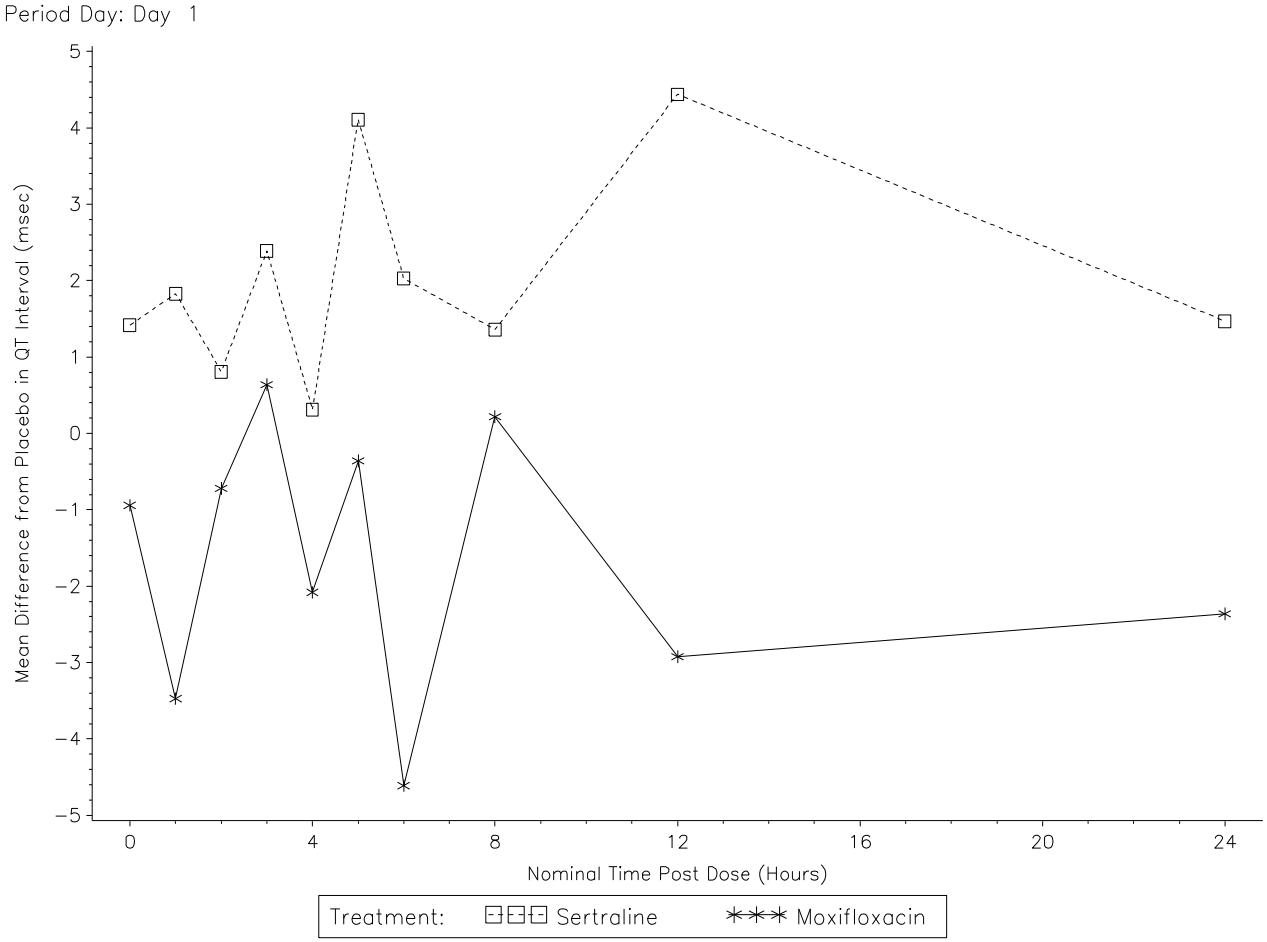
Figure 14.3.4.3.3.2.1
SERTRALINE Protocol A0501104
Mean Difference from Placebo of ECG Value in Heart Rate versus Time

Period Day: Day 14



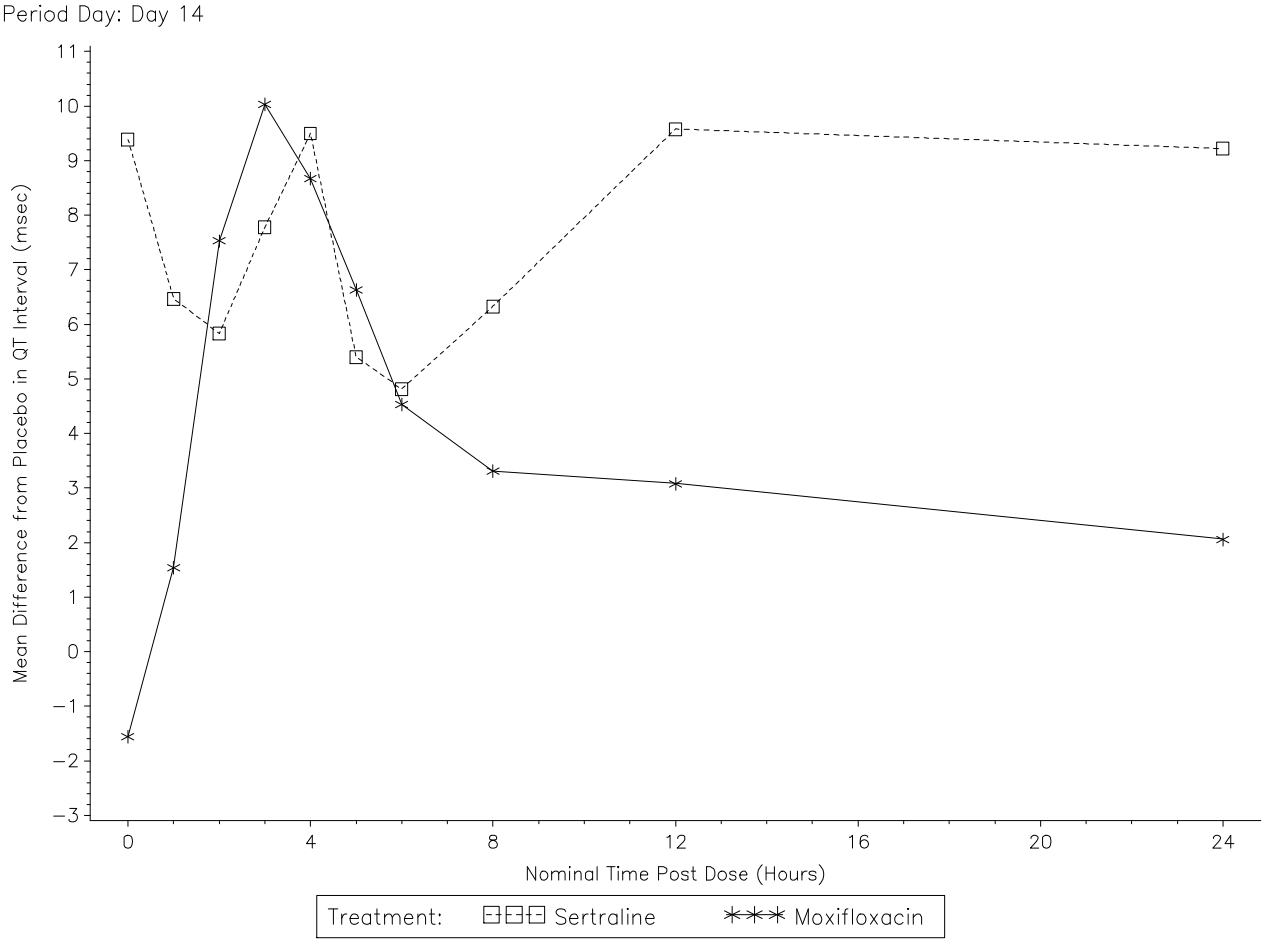
Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicate have been used in the calculations.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (−1 hours, −0.5 hours, 0 hours) before dosing within each period.
Unplanned readings have been excluded from the presentation.
[redacted] Source Data: Table 14.3.4.3.3.1 Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:12)

Figure 14.3.4.3.3.2.2
SERTRALINE Protocol A0501104
Mean Difference from Placebo of ECG Value in QT versus Time



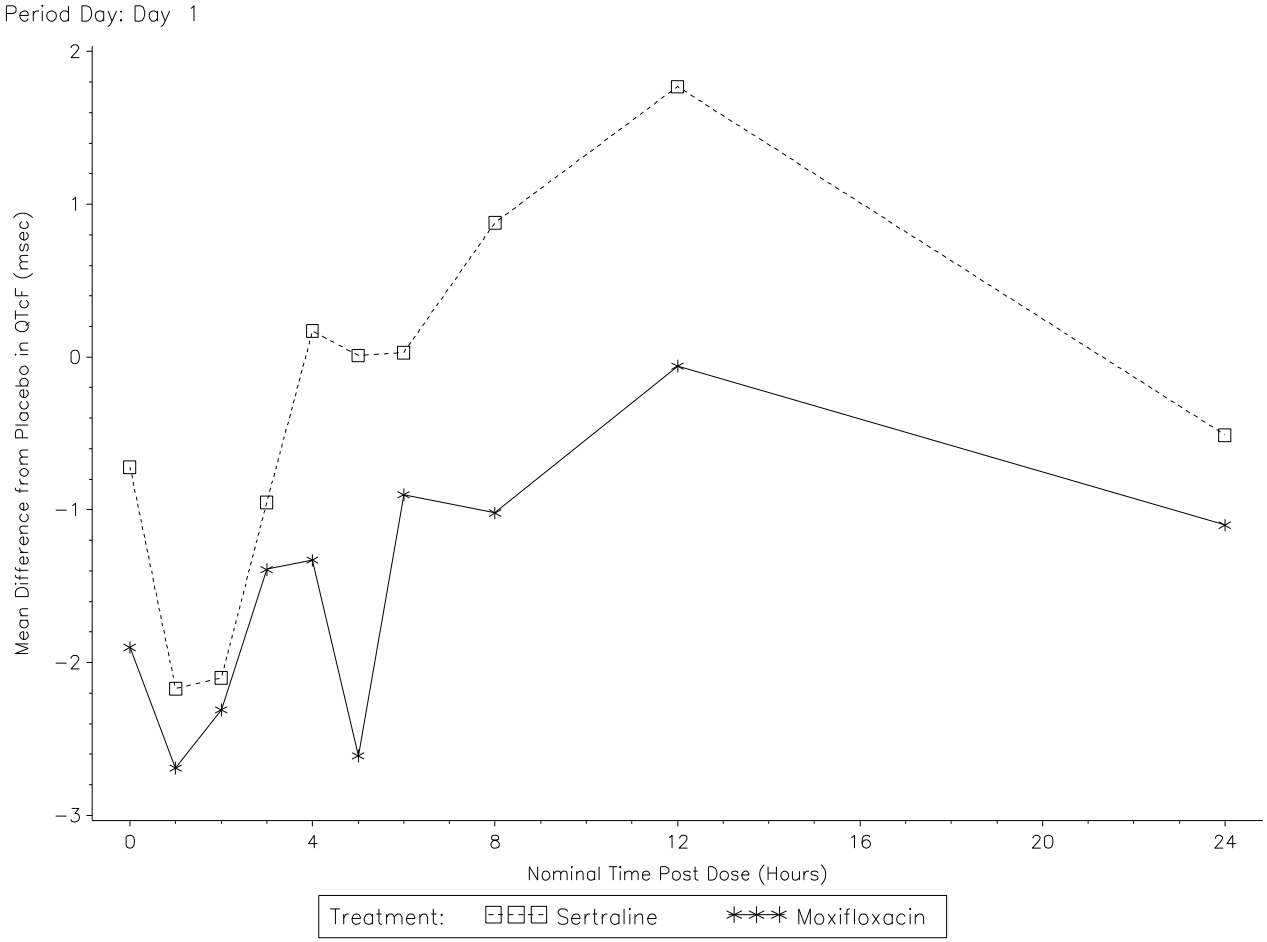
Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicate have been used in the calculations.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (−1 hours, −0.5 hours, 0 hours) before dosing within each period.
Unplanned readings have been excluded from the presentation.
[redacted] Source Data: Table 14.3.4.3.3.1 Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:13)

Figure 14.3.4.3.3.2.2
SERTRALINE Protocol A0501104
Mean Difference from Placebo of ECG Value in QT versus Time



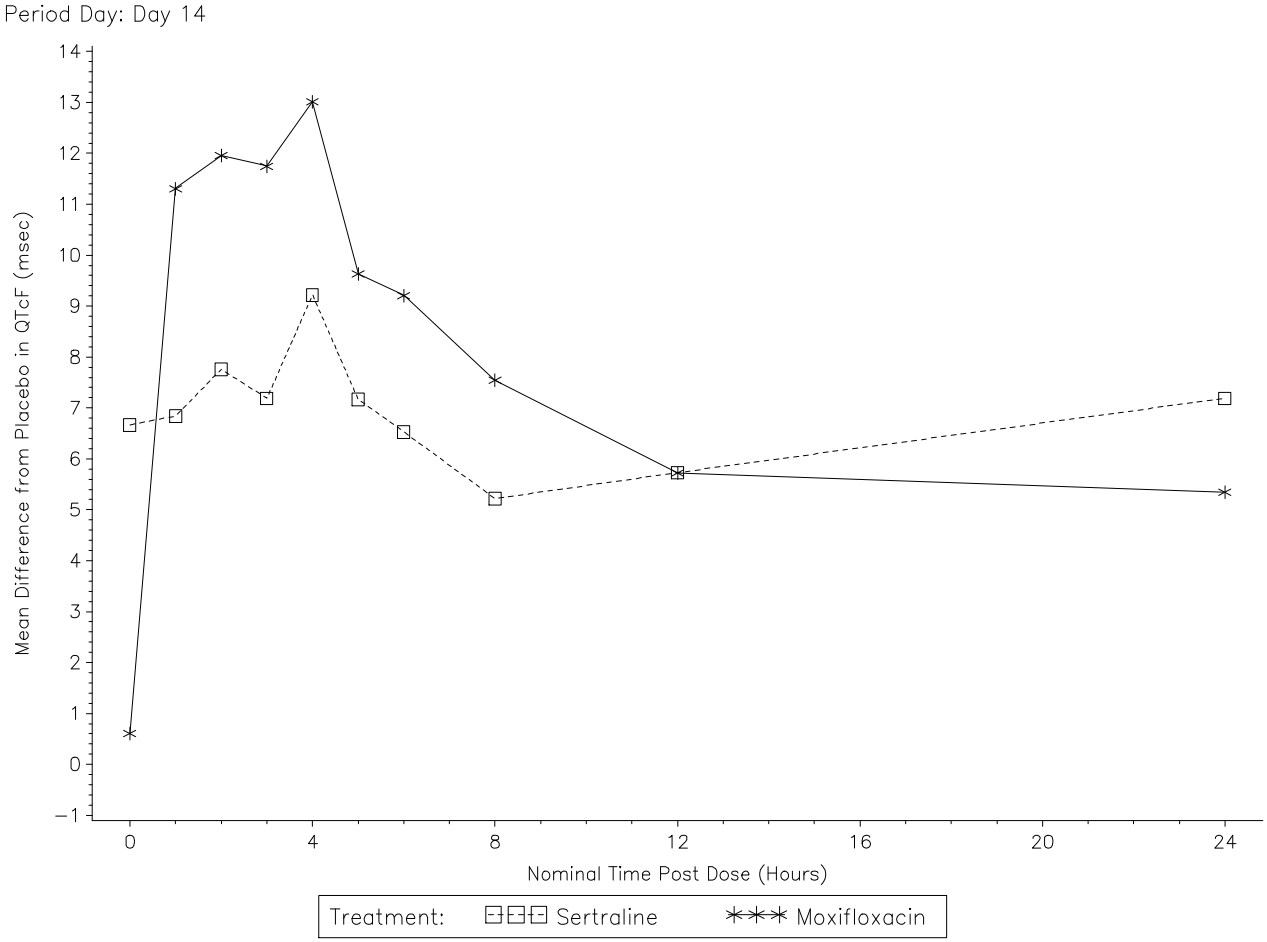
Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicate have been used in the calculations.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (−1 hours, −0.5 hours, 0 hours) before dosing within each period.
Unplanned readings have been excluded from the presentation.
[redacted] Source Data: Table 14.3.4.3.3.1 Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:13)

Figure 14.3.4.3.3.2.3
SERTRALINE Protocol A0501104
Mean Difference from Placebo of ECG Value in QTcF versus Time



Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicate have been used in the calculations.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (−1 hours, −0.5 hours, 0 hours) before dosing within each period.
Unplanned readings have been excluded from the presentation.
[redacted] Source Data: Table 14.3.4.3.3.1 Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:14)

Figure 14.3.4.3.3.2.3
SERTRALINE Protocol A0501104
Mean Difference from Placebo of ECG Value in QTcF versus Time



Means and Medians have been determined within a subject prior to summarizing across subjects.
Means of Replicate have been used in the calculations.
Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (−1 hours, −0.5 hours, 0 hours) before dosing within each period.
Unplanned readings have been excluded from the presentation.
[redacted] Source Data: Table 14.3.4.3.3.1 Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:14)

SERTRALINE Protocol A0501104
Maximum Absolute Values (Post-dose) for ECG Data (QTcF, QT, PR, RR, QRS and Heart Rate)

RR INTERVAL (msec)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	1129.4	1115.2	1123.0
Std.Dev.	114.12	126.68	121.29
Median	1141.7	1126.3	1129.0
Min	862	806	800
Max	1465	1478	1397

Means of replicate values have been used in the report.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:50)

SERTRALINE Protocol A0501104
Maximum Absolute Values (Post-dose) for ECG Data (QTcF, QT, PR, RR, QRS and Heart Rate)

HEART RATE (bpm)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	73.2	75.1	73.0
Std.Dev.	7.14	7.83	6.79
Median	71.7	74.5	72.7
Min	61	61	61
Max	99	100	95

Means of replicate values have been used in the report.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:50)

SERTRALINE Protocol A0501104
Maximum Absolute Values (Post-dose) for ECG Data (QTcF, QT, PR, RR, QRS and Heart Rate)

PR INTERVAL (msec)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	172.7	177.1	177.2
Std.Dev.	17.91	18.67	18.97
Median	170.7	174.7	175.3
Min	135	132	133
Max	220	219	217

Means of replicate values have been used in the report.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:50)

SERTRALINE Protocol A0501104
Maximum Absolute Values (Post-dose) for ECG Data (QTcF, QT, PR, RR, QRS and Heart Rate)

QRS COMPLEX (msec)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	95.9	95.9	95.9
Std.Dev.	8.27	7.95	7.84
Median	96.7	95.3	95.0
Min	79	81	79
Max	117	112	112

Means of replicate values have been used in the report.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:50)

SERTRALINE Protocol A0501104
Maximum Absolute Values (Post-dose) for ECG Data (QTcF, QT, PR, RR, QRS and Heart Rate)

QT INTERVAL (msec)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	433.3	433.1	427.8
Std.Dev.	21.54	22.91	22.67
Median	432.7	434.0	422.7
Min	387	389	384
Max	500	493	485

Means of replicate values have been used in the report.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:50)

SERTRALINE Protocol A0501104
Maximum Absolute Values (Post-dose) for ECG Data (QTcF, QT, PR, RR, QRS and Heart Rate)

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	424.9	426.6	420.6
Std.Dev.	15.84	16.66	16.96
Median	426.2	427.8	422.0
Min	392	396	386
Max	453	461	452

Means of replicate values have been used in the report.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:50)

SERTRALINE Protocol A0501104
Maximum Increase from Baseline for ECG Data (QTcF, QT, PR, RR, QRS and Heart Rate)

RR INTERVAL (msec)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	104.6	103.1	113.3
Std.Dev.	85.12	54.26	72.12
Median	84.1	98.7	120.1
Min	-35	-65	-11
Max	364	226	310

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of replicate values have been used in the report.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:51)

SERTRALINE Protocol A0501104
Maximum Increase from Baseline for ECG Data (QTcF, QT, PR, RR, QRS and Heart Rate)

HEART RATE (bpm)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	13.7	15.0	12.7
Std.Dev.	6.98	5.19	4.55
Median	13.6	14.0	13.0
Min	-7	6	3
Max	34	31	21

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of replicate values have been used in the report.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:51)

SERTRALINE Protocol A0501104
Maximum Increase from Baseline for ECG Data (QTcF, QT, PR, RR, QRS and Heart Rate)

PR INTERVAL (msec)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	6.3	9.4	9.7
Std.Dev.	7.16	6.94	7.55
Median	4.0	8.0	10.0
Min	-6	1	-1
Max	29	38	41

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of replicate values have been used in the report.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:51)

SERTRALINE Protocol A0501104
Maximum Increase from Baseline for ECG Data (QTcF, QT, PR, RR, QRS and Heart Rate)

QRS COMPLEX (msec)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	3.8	4.0	3.6
Std.Dev.	2.66	3.70	2.73
Median	3.0	3.1	3.2
Min	-0	-1	-2
Max	10	19	14

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of replicate values have been used in the report.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:51)

SERTRALINE Protocol A0501104
Maximum Increase from Baseline for ECG Data (QTcF, QT, PR, RR, QRS and Heart Rate)

QT INTERVAL (msec)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	16.8	19.1	13.6
Std.Dev.	13.19	11.78	11.59
Median	16.4	21.1	13.6
Min	-4	-13	-6
Max	62	41	47

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of replicate values have been used in the report.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:51)

SERTRALINE Protocol A0501104
Maximum Increase from Baseline for ECG Data (QTcF, QT, PR, RR, QRS and Heart Rate)

QTCF INTERVAL (FRIDERICIA'S CORRECTION) (msec)

Summary Statistics	Sertraline	Moxifloxacin	Placebo
N	52	50	50
Mean	10.9	13.7	6.9
Std.Dev.	5.86	8.14	6.41
Median	9.6	15.2	6.7
Min	-2	-4	-7
Max	23	32	26

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Means of replicate values have been used in the report.
Unplanned readings have been excluded from the presentation.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:51)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcF for Sertraline vs. Placebo at Each Post-dose Time Point on Day 14 - Primary ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Sertraline - Placebo) LSMeans	Std.Error	90% CI
1	Sertraline	50	414.299	6.957	1.223	(4.942, 8.973)
	Placebo	50	407.341			
2	Sertraline	50	415.625	7.851	1.223	(5.835, 9.866)
	Placebo	50	407.775			
3	Sertraline	50	416.465	7.824	1.223	(5.808, 9.840)
	Placebo	50	408.641			
4	Sertraline	50	418.252	9.651	1.223	(7.635, 11.666)
	Placebo	50	408.601			
5	Sertraline	50	411.285	7.377	1.223	(5.362, 9.393)
	Placebo	50	403.908			
6	Sertraline	50	408.985	6.511	1.223	(4.495, 8.526)
	Placebo	50	402.475			
8	Sertraline	50	408.732	5.597	1.223	(3.582, 7.613)
	Placebo	50	403.135			
12	Sertraline	50	411.019	5.677	1.223	(3.662, 7.693)
	Placebo	50	405.341			
24	Sertraline	51	414.294	7.346	1.222	(5.331, 9.360)
	Placebo	50	406.948			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcF as a covariate were used.
Primary ECG analysis population is defined as all subjects randomized and treated who have at least 1 post-dose ECG measurement in at least 1 period.
Unplanned readings have been excluded from the presentation.
For primary analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:53)

SERTRALINE Protocol A0501104

Statistical Summary (1) of QTcF for Sertraline vs. Placebo at Each Post-dose Time Point on Day 14 - Completer ECG Analysis Population

Nominal Post Dose Time (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Sertraline - Placebo) LSMeans	Std.Error	90% CI
1	Sertraline	46	415.405	7.123	1.247	(5.067, 9.178)
	Placebo	46	408.282			
2	Sertraline	46	416.999	8.384	1.247	(6.328, 10.439)
	Placebo	46	408.615			
3	Sertraline	46	417.173	7.463	1.247	(5.408, 9.519)
	Placebo	46	409.709			
4	Sertraline	46	419.448	9.819	1.247	(7.763, 11.874)
	Placebo	46	409.630			
5	Sertraline	46	412.057	7.630	1.247	(5.575, 9.686)
	Placebo	46	404.427			
6	Sertraline	46	409.941	7.036	1.247	(4.980, 9.092)
	Placebo	46	402.905			
8	Sertraline	46	409.926	5.840	1.247	(3.785, 7.896)
	Placebo	46	404.086			
12	Sertraline	46	412.260	6.268	1.247	(4.212, 8.323)
	Placebo	46	405.992			
24	Sertraline	46	415.571	7.666	1.247	(5.611, 9.722)
	Placebo	46	407.905			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.

Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcF as a covariate were used.

Completer ECG Analysis Population is defined as all subjects randomized and treated and have completed all three treatment periods, at least up to Day 15 (24 hour Day 14) ECG measurements.

Unplanned readings have been excluded from the presentation.

For sensitivity analysis, ECG measurements on Day 14 up to 24 hours will be used.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:52)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcI for Sertraline vs. Placebo at Each Post-dose Time Point on Day 14 - Primary ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Sertraline - Placebo) LSMeans	Std.Error	90% CI
1	Sertraline	50	414.698	7.606	1.503	(5.127, 10.086)
	Placebo	50	407.092			
2	Sertraline	50	416.128	8.192	1.503	(5.713, 10.671)
	Placebo	50	407.936			
3	Sertraline	50	416.702	8.270	1.503	(5.791, 10.749)
	Placebo	50	408.431			
4	Sertraline	50	418.831	10.196	1.503	(7.717, 12.675)
	Placebo	50	408.635			
5	Sertraline	50	411.560	8.532	1.503	(6.053, 11.011)
	Placebo	50	403.029			
6	Sertraline	50	409.162	7.405	1.503	(4.926, 9.884)
	Placebo	50	401.757			
8	Sertraline	50	408.635	6.375	1.503	(3.896, 8.854)
	Placebo	50	402.259			
12	Sertraline	50	411.159	6.678	1.503	(4.198, 9.157)
	Placebo	50	404.481			
24	Sertraline	51	414.429	7.764	1.500	(5.289, 10.238)
	Placebo	50	406.665			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcI as a covariate were used.
Primary ECG analysis population is defined as all subjects randomized and treated who have at least 1 post-dose ECG measurement in at least 1 period.
Unplanned readings have been excluded from the presentation.
For primary analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (23:54)

SERTRALINE Protocol A0501104

Statistical Summary (1) of QTcI for Sertraline vs. Placebo at Each Post-dose Time Point on Day 14 - Completer ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Sertraline - Placebo) LSMeans	Std.Error	90% CI
1	Sertraline	46	415.370	7.737	1.534	(5.209, 10.266)
	Placebo	46	407.633			
2	Sertraline	46	417.121	8.721	1.534	(6.192, 11.249)
	Placebo	46	408.400			
3	Sertraline	46	417.066	7.932	1.534	(5.404, 10.460)
	Placebo	46	409.134			
4	Sertraline	46	419.762	10.445	1.534	(7.917, 12.974)
	Placebo	46	409.317			
5	Sertraline	46	412.340	8.856	1.534	(6.328, 11.385)
	Placebo	46	403.484			
6	Sertraline	46	410.042	7.997	1.534	(5.469, 10.526)
	Placebo	46	402.044			
8	Sertraline	46	409.712	6.841	1.534	(4.313, 9.370)
	Placebo	46	402.871			
12	Sertraline	46	412.249	7.264	1.534	(4.736, 9.793)
	Placebo	46	404.984			
24	Sertraline	46	415.480	8.240	1.534	(5.712, 10.769)
	Placebo	46	407.239			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcI as a covariate were used.
Completer ECG Analysis Population is defined as all subjects randomized and treated and have completed all three treatment periods, at least up to Day 15 (24 hour Day 14) ECG measurements.
Unplanned readings have been excluded from the presentation.
For sensitivity analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (00:58)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcN for Sertraline vs. Placebo at Each Post-dose Time Point on Day 14 - Primary ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Sertraline - Placebo) LSMeans	Std.Error	90% CI
1	Sertraline	50	414.216	7.102	1.221	(5.089, 9.114)
	Placebo	50	407.114			
2	Sertraline	50	415.475	7.985	1.221	(5.972, 9.997)
	Placebo	50	407.490			
3	Sertraline	50	416.378	7.953	1.221	(5.941, 9.966)
	Placebo	50	408.425			
4	Sertraline	50	418.126	9.737	1.221	(7.724, 11.749)
	Placebo	50	408.390			
5	Sertraline	50	411.592	7.552	1.221	(5.539, 9.564)
	Placebo	50	404.040			
6	Sertraline	50	409.238	6.613	1.221	(4.601, 8.626)
	Placebo	50	402.625			
8	Sertraline	50	408.815	5.661	1.221	(3.648, 7.673)
	Placebo	50	403.154			
12	Sertraline	50	411.200	5.674	1.221	(3.662, 7.687)
	Placebo	50	405.526			
24	Sertraline	51	414.320	7.367	1.220	(5.356, 9.378)
	Placebo	50	406.953			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcN as a covariate were used.
Primary ECG analysis population is defined as all subjects randomized and treated who have at least 1 post-dose ECG measurement in at least 1 period.
Unplanned readings have been excluded from the presentation.
For primary analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:00)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcN for Sertraline vs. Placebo at Each Post-dose Time Point on Day 14 - Completer ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Sertraline - Placebo) LSMeans	Std.Error	90% CI
1	Sertraline	46	415.342	7.286	1.244	(5.236, 9.335)
	Placebo	46	408.056			
2	Sertraline	46	416.848	8.512	1.244	(6.462, 10.562)
	Placebo	46	408.336			
3	Sertraline	46	417.084	7.596	1.244	(5.547, 9.646)
	Placebo	46	409.487			
4	Sertraline	46	419.319	9.911	1.244	(7.861, 11.961)
	Placebo	46	409.408			
5	Sertraline	46	412.359	7.793	1.244	(5.743, 9.842)
	Placebo	46	404.566			
6	Sertraline	46	410.199	7.151	1.244	(5.101, 9.200)
	Placebo	46	403.048			
8	Sertraline	46	410.022	5.922	1.244	(3.872, 7.972)
	Placebo	46	404.100			
12	Sertraline	46	412.430	6.264	1.244	(4.215, 8.314)
	Placebo	46	406.166			
24	Sertraline	46	415.585	7.674	1.244	(5.624, 9.724)
	Placebo	46	407.911			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcN as a covariate were used.
Completer ECG Analysis Population is defined as all subjects randomized and treated and have completed all three treatment periods, at least up to Day 15 (24 hour Day 14) ECG measurements.
Unplanned readings have been excluded from the presentation.
For sensitivity analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (00:59)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcF for Moxifloxacin vs. Placebo at 3 Hours Post-dose on Day 14 - Primary ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Moxifloxacin - Placebo) LSMeans	Std.Error	90% CI
3	Moxifloxacin	50	420.473	11.831	1.225	(9.813, 13.849)
	Placebo	50	408.641			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcF as a covariate were used.
Primary ECG analysis population is defined as all subjects randomized and treated who have at least 1 post-dose ECG measurement in at least 1 period.
Unplanned readings have been excluded from the presentation.
For primary analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:02)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcF for Moxifloxacin vs. Placebo at Each Post-dose Time Point on Day 14 - Primary ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Moxifloxacin - Placebo) LSMeans	Std.Error	90% CI
1	Moxifloxacin	50	418.886	11.544	1.225	(9.526, 13.563)
	Placebo	50	407.341			
2	Moxifloxacin	50	419.899	12.124	1.225	(10.106, 14.143)
	Placebo	50	407.775			
3	Moxifloxacin	50	420.473	11.831	1.225	(9.813, 13.849)
	Placebo	50	408.641			
4	Moxifloxacin	50	421.799	13.198	1.225	(11.179, 15.216)
	Placebo	50	408.601			
5	Moxifloxacin	50	413.413	9.504	1.225	(7.486, 11.523)
	Placebo	50	403.908			
6	Moxifloxacin	50	411.493	9.018	1.225	(6.999, 11.036)
	Placebo	50	402.475			
8	Moxifloxacin	50	410.639	7.504	1.225	(5.486, 9.523)
	Placebo	50	403.135			
12	Moxifloxacin	50	411.493	6.151	1.225	(4.133, 8.169)
	Placebo	50	405.341			
24	Moxifloxacin	50	412.599	5.651	1.225	(3.633, 7.669)
	Placebo	50	406.948			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcF as a covariate were used.
Primary ECG analysis population is defined as all subjects randomized and treated who have at least 1 post-dose ECG measurement in at least 1 period.
Unplanned readings have been excluded from the presentation.
For primary analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:03)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcF for Moxifloxacin vs. Placebo at 3 Hours Post-dose on Day 14 - Completer ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Moxifloxacin - Placebo) LSMeans	Std.Error	90% CI
3	Moxifloxacin	46	421.878	12.168	1.250	(10.109, 14.228)
	Placebo	46	409.709			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcF as a covariate were used.
Completer ECG Analysis Population is defined as all subjects randomized and treated and have completed all three treatment periods, at least up to Day 15 (24 hour Day 14) ECG measurements.
Unplanned readings have been excluded from the presentation.
For sensitivity analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:01)

SERTRALINE Protocol A0501104

Statistical Summary (1) of QTcF for Moxifloxacin vs. Placebo at Each Post-dose Time Point on Day 14 - Completer ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Moxifloxacin - Placebo) LSMeans	Std.Error	90% CI
1	Moxifloxacin	46	419.805	11.523	1.250	(9.464, 13.583)
	Placebo	46	408.282			
2	Moxifloxacin	46	421.182	12.567	1.250	(10.507, 14.627)
	Placebo	46	408.615			
3	Moxifloxacin	46	421.878	12.168	1.250	(10.109, 14.228)
	Placebo	46	409.709			
4	Moxifloxacin	46	423.095	13.466	1.250	(11.406, 15.525)
	Placebo	46	409.630			
5	Moxifloxacin	46	414.747	10.321	1.250	(8.261, 12.380)
	Placebo	46	404.427			
6	Moxifloxacin	46	412.813	9.908	1.250	(7.848, 11.967)
	Placebo	46	402.905			
8	Moxifloxacin	46	412.313	8.226	1.250	(6.167, 10.286)
	Placebo	46	404.086			
12	Moxifloxacin	46	412.124	6.132	1.250	(4.072, 8.192)
	Placebo	46	405.992			
24	Moxifloxacin	46	413.479	5.574	1.250	(3.515, 7.634)
	Placebo	46	407.905			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.

Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcF as a covariate were used.

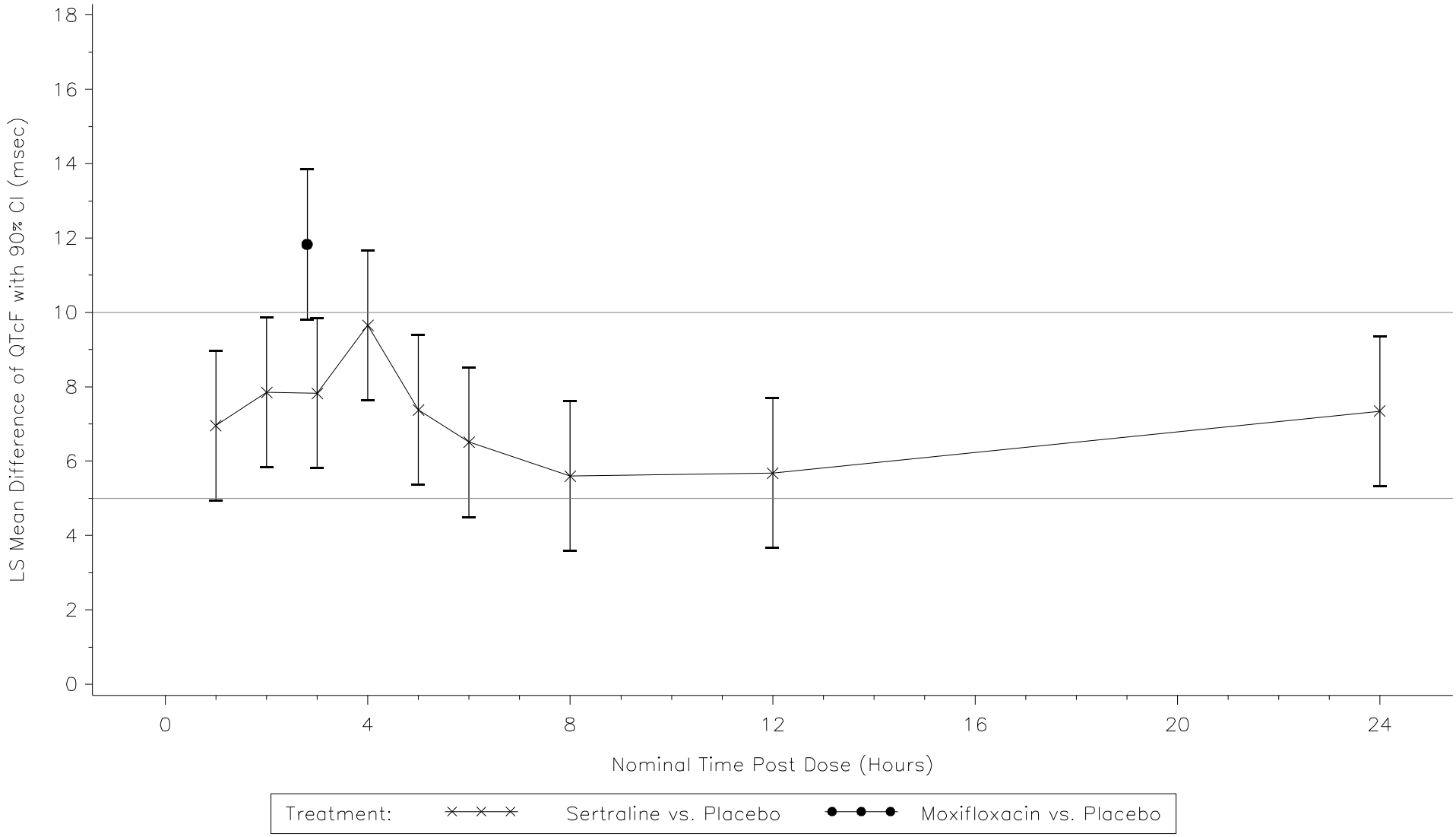
Completer ECG Analysis Population is defined as all subjects randomized and treated and have completed all three treatment periods, at least up to Day 15 (24 hour Day 14) ECG measurements.

Unplanned readings have been excluded from the presentation.

For sensitivity analysis, ECG measurements on Day 14 up to 24 hours will be used.

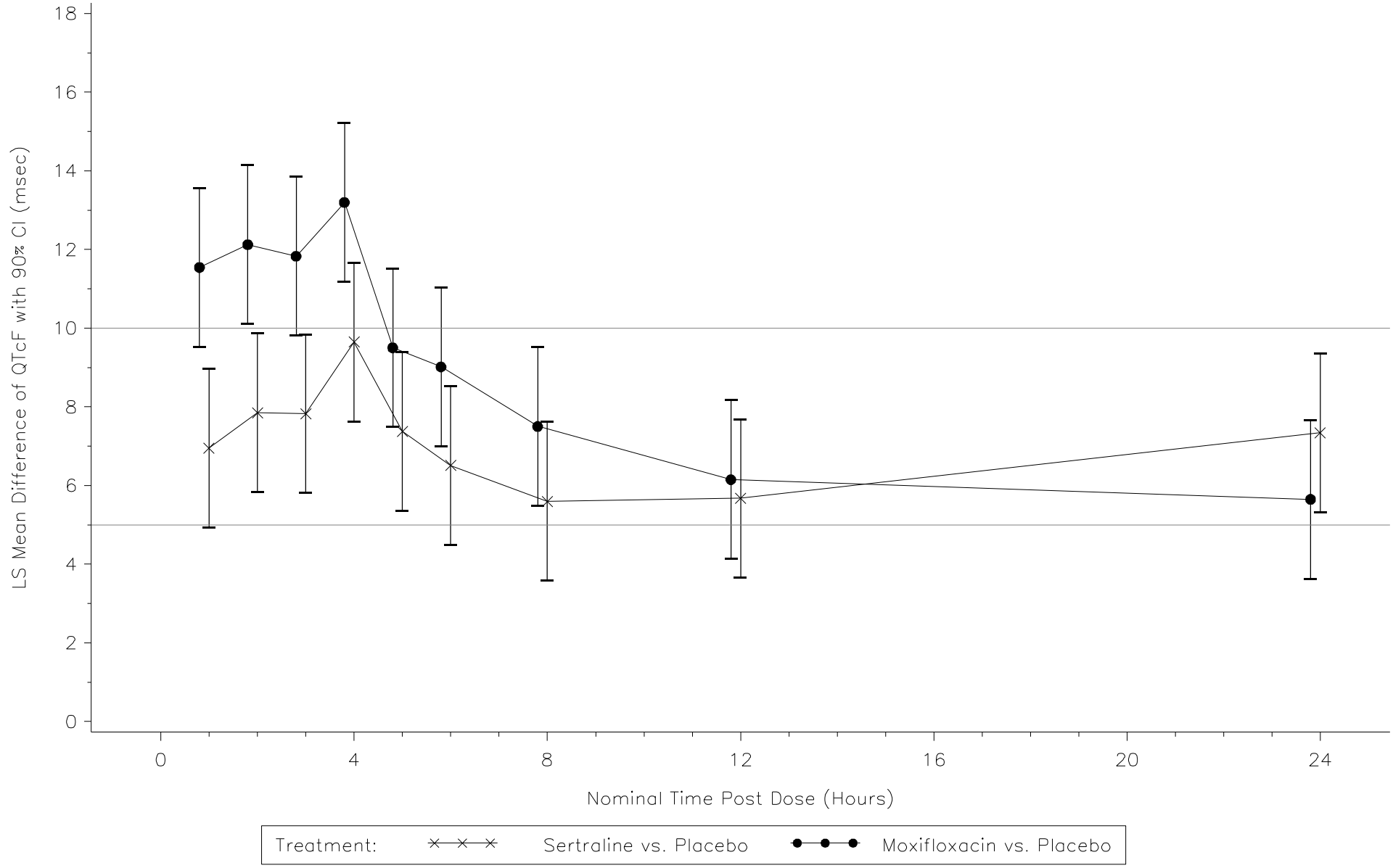
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:02)

SERTRALINE Protocol A0501104
Plot of LS Mean Difference of QTcF (1) between Sertraline vs. Placebo and Moxifloxacin vs. Placebo on Day 14 – Primary ECG Analysis Population



Change from placebo in QTcF of Sertraline was computed at each post–dose time point on Day 14.
Change from placebo in QTcF of Moxifloxacin was computed at 3 hours post–dose on Day 14.
Primary ECG analysis population is defined as all subjects randomized and treated who have at least 1 post–dose ECG measurement in at least 1 period.
Unplanned readings have been excluded from the presentation.
[redacted] Source Data: Table 14.3.4.3.5.1 and 14.3.4.3.6.1 Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:16)

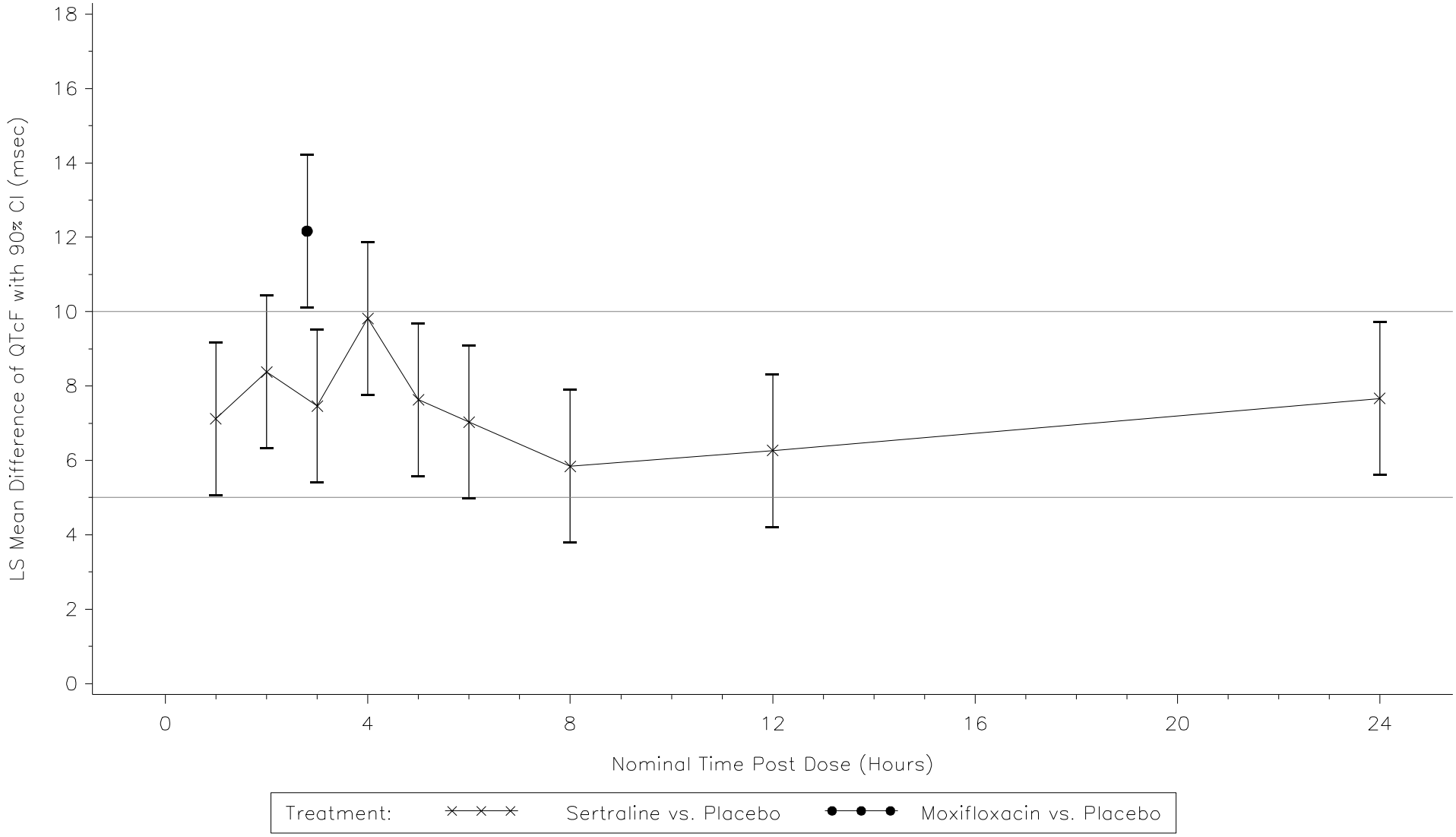
SERTRALINE Protocol A0501104
Plot of LS Mean Difference of QTcF (1) between Sertraline vs. Placebo and Moxifloxacin vs. Placebo at Each Post-dose Time Point on Day 14 – Primary ECG Analysis Population



Primary ECG analysis population is defined as all subjects randomized and treated who have at least 1 post-dose ECG measurement in at least 1 period. Unplanned readings have been excluded from the presentation.

[redacted] Source Data: Table 14.3.4.3.5.1 and 14.3.4.3.6.2 Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:17)

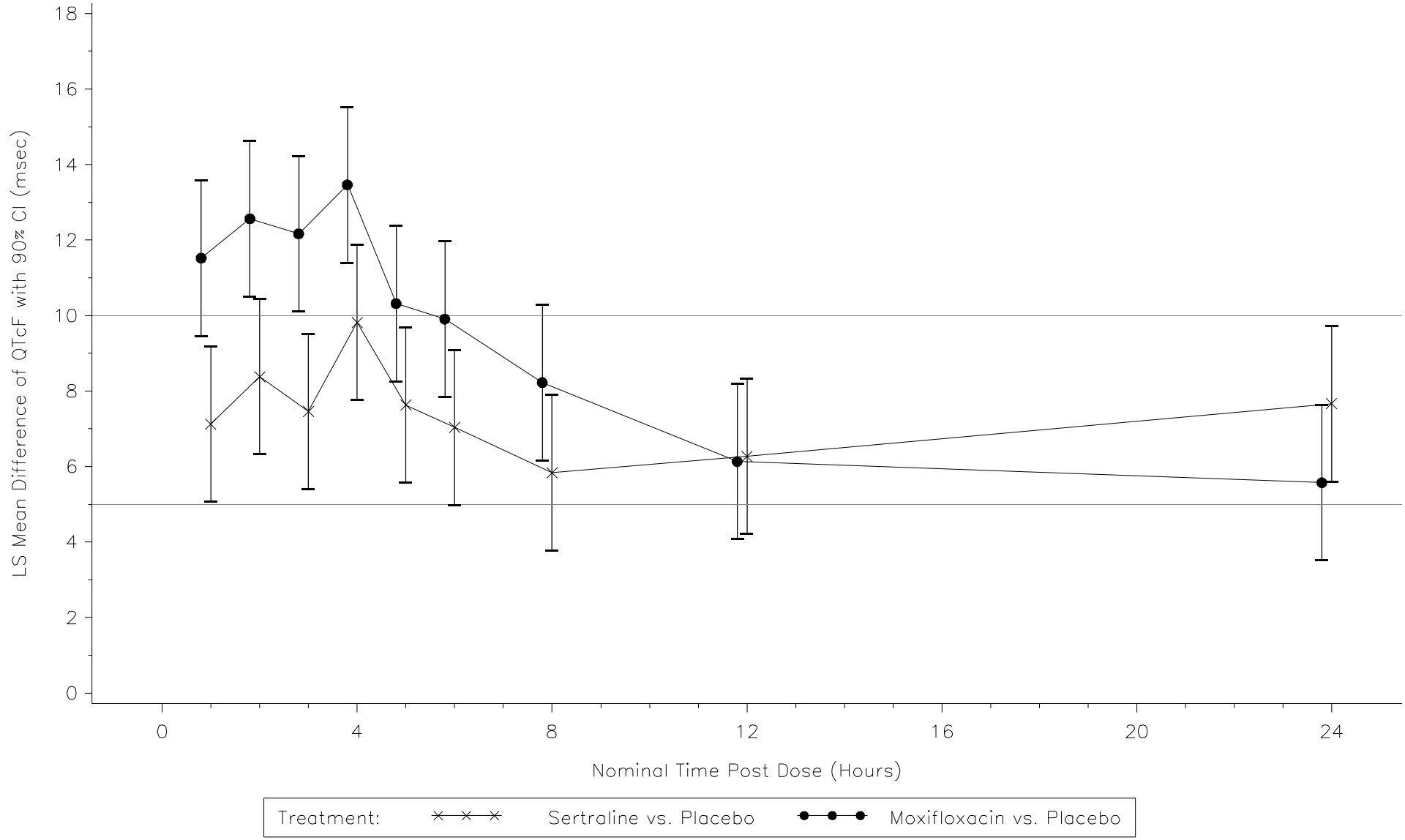
SERTRALINE Protocol A0501104
Plot of LS Mean Difference of QTcF (1) between Sertraline vs. Placebo and Moxifloxacin vs. Placebo on Day 14 – Completer ECG Analysis Population



Change from placebo in QTcF of Sertraline was computed at each post–dose time point on Day 14.
Change from placebo in QTcF of Moxifloxacin was computed at 3 hours post–dose on Day 14.
Completer ECG Analysis Population is defined as all subjects randomized and treated and have completed all three treatment periods, at least up to Day 15 (24 hour Day 14) ECG measurements.
Unplanned readings have been excluded from the presentation.
[redacted] Source Data: Table 14.3.4.3.5.2 and 14.3.4.3.6.3 Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:15)

SERTRALINE Protocol A0501104

Plot of LS Mean Difference of QTcF (1) between Sertraline vs. Placebo and Moxifloxacin vs. Placebo at Each Post-dose Time Point on Day 14 – Completer ECG Analysis Population



Completer ECG Analysis Population is defined as all subjects randomized and treated and have completed all three treatment periods, at least up to Day 15 (24 hour Day 14) ECG measurements.

Unplanned readings have been excluded from the presentation.

[redacted] Source Data: Table 14.3.4.3.5.2 and 14.3.4.3.6.4 Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:16)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcN for Moxifloxacin vs. Placebo at 3 Hours Post-dose on Day 14 - Primary ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Moxifloxacin - Placebo) LSMeans	Std.Error	90% CI
3	Moxifloxacin	50	420.315	11.891	1.222	(9.876, 13.905)
	Placebo	50	408.425			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcN as a covariate were used.
Primary ECG analysis population is defined as all subjects randomized and treated who have at least 1 post-dose ECG measurement in at least 1 period.
Unplanned readings have been excluded from the presentation.
For primary analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:07)

SERTRALINE Protocol A0501104

Statistical Summary (1) of QTcN for Moxifloxacin vs. Placebo at Each Post-dose Time Point on Day 14 - Primary ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Moxifloxacin - Placebo) LSMeans	Std.Error	90% CI
1	Moxifloxacin	50	418.848	11.734	1.222	(9.720, 13.749)
	Placebo	50	407.114			
2	Moxifloxacin	50	419.844	12.354	1.222	(10.339, 14.369)
	Placebo	50	407.490			
3	Moxifloxacin	50	420.315	11.891	1.222	(9.876, 13.905)
	Placebo	50	408.425			
4	Moxifloxacin	50	421.721	13.331	1.222	(11.316, 15.346)
	Placebo	50	408.390			
5	Moxifloxacin	50	413.610	9.569	1.222	(7.555, 11.584)
	Placebo	50	404.040			
6	Moxifloxacin	50	411.698	9.073	1.222	(7.058, 11.088)
	Placebo	50	402.625			
8	Moxifloxacin	50	410.767	7.613	1.222	(5.598, 9.628)
	Placebo	50	403.154			
12	Moxifloxacin	50	411.765	6.239	1.222	(4.224, 8.254)
	Placebo	50	405.526			
24	Moxifloxacin	50	412.616	5.663	1.222	(3.649, 7.678)
	Placebo	50	406.953			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.

Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcN as a covariate were used.

Primary ECG analysis population is defined as all subjects randomized and treated who have at least 1 post-dose ECG measurement in at least 1 period.

Unplanned readings have been excluded from the presentation.

For primary analysis, ECG measurements on Day 14 up to 24 hours will be used.

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:08)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcN for Moxifloxacin vs. Placebo at 3 Hours Post-dose on Day 14 - Completer ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Moxifloxacin - Placebo) LSMeans	Std.Error	90% CI
3	Moxifloxacin	46	421.716	12.229	1.246	(10.176, 14.282)
	Placebo	46	409.487			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcN as a covariate were used.
Completer ECG Analysis Population is defined as all subjects randomized and treated and have completed all three treatment periods, at least up to Day 15 (24 hour Day 14) ECG measurements.
Unplanned readings have been excluded from the presentation.
For sensitivity analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:06)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcN for Moxifloxacin vs. Placebo at Each Post-dose Time Point on Day 14 - Completer ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Moxifloxacin - Placebo) LSMeans	Std.Error	90% CI
1	Moxifloxacin	46	419.790	11.735	1.246	(9.681, 13.788)
	Placebo	46	408.056			
2	Moxifloxacin	46	421.127	12.791	1.246	(10.738, 14.844)
	Placebo	46	408.336			
3	Moxifloxacin	46	421.716	12.229	1.246	(10.176, 14.282)
	Placebo	46	409.487			
4	Moxifloxacin	46	423.047	13.639	1.246	(11.586, 15.692)
	Placebo	46	409.408			
5	Moxifloxacin	46	414.946	10.380	1.246	(8.327, 12.433)
	Placebo	46	404.566			
6	Moxifloxacin	46	413.030	9.982	1.246	(7.929, 12.035)
	Placebo	46	403.048			
8	Moxifloxacin	46	412.468	8.368	1.246	(6.315, 10.421)
	Placebo	46	404.100			
12	Moxifloxacin	46	412.416	6.250	1.246	(4.197, 8.304)
	Placebo	46	406.166			
24	Moxifloxacin	46	413.520	5.609	1.246	(3.556, 7.662)
	Placebo	46	407.911			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcN as a covariate were used.
Completer ECG Analysis Population is defined as all subjects randomized and treated and have completed all three treatment periods, at least up to Day 15 (24 hour Day 14) ECG measurements.
Unplanned readings have been excluded from the presentation.
For sensitivity analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:07)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcI for Moxifloxacin vs. Placebo at 3 Hours Post-dose on Day 14 - Primary ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Moxifloxacin - Placebo) LSMeans	Std.Error	90% CI
3	Moxifloxacin	50	421.000	12.569	1.506	(10.086, 15.052)
	Placebo	50	408.431			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcI as a covariate were used.
Primary ECG analysis population is defined as all subjects randomized and treated who have at least 1 post-dose ECG measurement in at least 1 period.
Unplanned readings have been excluded from the presentation.
For primary analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:05)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcI for Moxifloxacin vs. Placebo at Each Post-dose Time Point on Day 14 - Primary ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Moxifloxacin - Placebo) LSMeans	Std.Error	90% CI
1	Moxifloxacin	50	420.083	12.991	1.506	(10.508, 15.473)
	Placebo	50	407.092			
2	Moxifloxacin	50	420.584	12.648	1.506	(10.165, 15.131)
	Placebo	50	407.936			
3	Moxifloxacin	50	421.000	12.569	1.506	(10.086, 15.052)
	Placebo	50	408.431			
4	Moxifloxacin	50	422.336	13.702	1.506	(11.219, 16.184)
	Placebo	50	408.635			
5	Moxifloxacin	50	414.750	11.722	1.506	(9.239, 14.205)
	Placebo	50	403.029			
6	Moxifloxacin	50	412.251	10.493	1.506	(8.011, 12.976)
	Placebo	50	401.757			
8	Moxifloxacin	50	411.263	9.004	1.506	(6.521, 11.486)
	Placebo	50	402.259			
12	Moxifloxacin	50	411.916	7.435	1.506	(4.952, 9.918)
	Placebo	50	404.481			
24	Moxifloxacin	50	413.873	7.208	1.506	(4.725, 9.691)
	Placebo	50	406.665			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcI as a covariate were used.
Primary ECG analysis population is defined as all subjects randomized and treated who have at least 1 post-dose ECG measurement in at least 1 period.
Unplanned readings have been excluded from the presentation.
For primary analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:05)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcI for Moxifloxacin vs. Placebo at 3 Hours Post-dose on Day 14 - Completer ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Moxifloxacin - Placebo) LSMeans	Std.Error	90% CI
3	Moxifloxacin	46	422.423	13.288	1.538	(10.753, 15.823)
	Placebo	46	409.134			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcI as a covariate were used.
Completer ECG Analysis Population is defined as all subjects randomized and treated and have completed all three treatment periods, at least up to Day 15 (24 hour Day 14) ECG measurements.
Unplanned readings have been excluded from the presentation.
For sensitivity analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:03)

SERTRALINE Protocol A0501104
Statistical Summary (1) of QTcI for Moxifloxacin vs. Placebo at Each Post-dose Time Point on Day 14 - Completer ECG Analysis Population

Nominal Time Post Dose (HOURS)	Treatment	n	LSMeans	Difference in LSMeans (Moxifloxacin - Placebo) LSMeans	Std.Error	90% CI
1	Moxifloxacin	46	420.898	13.266	1.538	(10.731, 15.801)
	Placebo	46	407.633			
2	Moxifloxacin	46	421.812	13.411	1.538	(10.876, 15.947)
	Placebo	46	408.400			
3	Moxifloxacin	46	422.423	13.288	1.538	(10.753, 15.823)
	Placebo	46	409.134			
4	Moxifloxacin	46	423.439	14.122	1.538	(11.587, 16.657)
	Placebo	46	409.317			
5	Moxifloxacin	46	415.889	12.406	1.538	(9.871, 14.941)
	Placebo	46	403.484			
6	Moxifloxacin	46	413.065	11.021	1.538	(8.486, 13.556)
	Placebo	46	402.044			
8	Moxifloxacin	46	412.505	9.634	1.538	(7.099, 12.170)
	Placebo	46	402.871			
12	Moxifloxacin	46	412.531	7.547	1.538	(5.012, 10.082)
	Placebo	46	404.984			
24	Moxifloxacin	46	414.361	7.122	1.538	(4.587, 9.657)
	Placebo	46	407.239			

Baseline is defined as the mean of the three average triplicate measurements taken at the following three time points (-1 hours, -0.5 hours, 0 hours) before dosing within each period.
Repeated measures model with sequence, period, treatment, time, treatment-by-time interaction as fixed effects, subjects within sequence as a random effect, and baseline QTcI as a covariate were used.
Completer ECG Analysis Population is defined as all subjects randomized and treated and have completed all three treatment periods, at least up to Day 15 (24 hour Day 14) ECG measurements.
Unplanned readings have been excluded from the presentation.
For sensitivity analysis, ECG measurements on Day 14 up to 24 hours will be used.
[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 18SEP2016 (01:04)

SERTRALINE Protocol A0501104
Administration Schedule

Subject ID	Treatment Received	First Dose Date	Last Dose Date	Duration (Days)
[redacted]	Placebo	08JAN2016	21JAN2016	14
	Sertraline	12FEB2016	25FEB2016	14
	Moxifloxacin	05APR2016	18APR2016	14
	Moxifloxacin	08JAN2016	21JAN2016	14
	Placebo	12FEB2016	25FEB2016	14
	Sertraline	05APR2016	18APR2016	14
	Sertraline	08JAN2016	21JAN2016	14
	Moxifloxacin	12FEB2016	25FEB2016	14
	Placebo	17MAR2016	30MAR2016	14
	Sertraline	08JAN2016	21JAN2016	14
	Placebo	12FEB2016	25FEB2016	14
	Moxifloxacin	05APR2016	18APR2016	14
	Moxifloxacin	08JAN2016	21JAN2016	14
	Sertraline	12FEB2016	25FEB2016	14
	Placebo	17MAR2016	30MAR2016	14
	Placebo	08JAN2016	21JAN2016	14
	Moxifloxacin	29FEB2016	13MAR2016	14
	Sertraline	22APR2016	05MAY2016	14
	Moxifloxacin	26JAN2016	08FEB2016	14
	Sertraline	29FEB2016	07MAR2016	8
	Placebo	26JAN2016	08FEB2016	14
	Moxifloxacin	29FEB2016	13MAR2016	14
	Sertraline	05APR2016	18APR2016	14
	Sertraline	26JAN2016	08FEB2016	14
	Placebo	29FEB2016	13MAR2016	14
	Moxifloxacin	05APR2016	18APR2016	14
	Sertraline	26JAN2016	08FEB2016	14
	Moxifloxacin	29FEB2016	13MAR2016	14
	Placebo	05APR2016	18APR2016	14
	Moxifloxacin	26JAN2016	08FEB2016	14
	Placebo	29FEB2016	13MAR2016	14
	Sertraline	05APR2016	18APR2016	14
	Placebo	26JAN2016	08FEB2016	14
	Sertraline	29FEB2016	13MAR2016	14
	Moxifloxacin	05APR2016	18APR2016	14
	Sertraline	29FEB2016	13MAR2016	14

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:51)

Subject ID	Treatment Received	First Dose Date	Last Dose Date	Duration (Days)
[redacted]	Moxifloxacin	05APR2016	18APR2016	14
	Placebo	09MAY2016	22MAY2016	14
	Sertraline	29FEB2016	13MAR2016	14
	Placebo	05APR2016	18APR2016	14
	Moxifloxacin	09MAY2016	22MAY2016	14
	Placebo	29FEB2016	13MAR2016	14
	Sertraline	05APR2016	18APR2016	14
	Moxifloxacin	20JUL2016	02AUG2016	14
	Moxifloxacin	29FEB2016	13MAR2016	14
	Placebo	05APR2016	18APR2016	14
	Sertraline	09MAY2016	22MAY2016	14
	Moxifloxacin	29FEB2016	13MAR2016	14
	Sertraline	05APR2016	18APR2016	14
	Placebo	09MAY2016	22MAY2016	14
	Placebo	29FEB2016	13MAR2016	14
	Moxifloxacin	05APR2016	18APR2016	14
	Sertraline	09MAY2016	22MAY2016	14
	Placebo	22APR2016	05MAY2016	14
	Moxifloxacin	26MAY2016	08JUN2016	14
	Sertraline	30JUN2016	13JUL2016	14
	Sertraline	22APR2016	05MAY2016	14
	Moxifloxacin	26MAY2016	08JUN2016	14
	Placebo	30JUN2016	13JUL2016	14
	Sertraline	09MAY2016	22MAY2016	14
	Placebo	13JUN2016	26JUN2016	14
	Moxifloxacin	18JUL2016	31JUL2016	14
	Placebo	09MAY2016	22MAY2016	14
	Sertraline	13JUN2016	26JUN2016	14
	Moxifloxacin	22APR2016	05MAY2016	14
	Sertraline	26MAY2016	08JUN2016	14
	Placebo	30JUN2016	13JUL2016	14
	Moxifloxacin	22APR2016	05MAY2016	14
	Placebo	26MAY2016	08JUN2016	14
	Sertraline	30JUN2016	13JUL2016	14
	Moxifloxacin	22APR2016	05MAY2016	14
	Placebo	26MAY2016	08JUN2016	14

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Administration Schedule

Subject ID	Treatment Received	First Dose Date	Last Dose Date	Duration (Days)
[redacted]	Sertraline	30JUN2016	13JUL2016	14
[redacted]	Sertraline	22APR2016	05MAY2016	14
	Moxifloxacin	26MAY2016	08JUN2016	14
	Placebo	30JUN2016	13JUL2016	14
[redacted]	Placebo	09MAY2016	22MAY2016	14
	Sertraline	13JUN2016	26JUN2016	14
	Moxifloxacin	18JUL2016	31JUL2016	14
[redacted]	Moxifloxacin	22APR2016	05MAY2016	14
	Sertraline	26MAY2016	08JUN2016	14
	Placebo	30JUN2016	13JUL2016	14
[redacted]	Placebo	09MAY2016	22MAY2016	14
	Moxifloxacin	13JUN2016	26JUN2016	14
	Sertraline	18JUL2016	31JUL2016	14
[redacted]	Sertraline	22APR2016	05MAY2016	14
[redacted]	Moxifloxacin	09MAY2016	22MAY2016	14
	Sertraline	13JUN2016	26JUN2016	14
	Placebo	18JUL2016	31JUL2016	14
[redacted]	Moxifloxacin	22APR2016	05MAY2016	14
	Placebo	26MAY2016	08JUN2016	14
	Sertraline	30JUN2016	13JUL2016	14
[redacted]	Placebo	09MAY2016	22MAY2016	14
	Sertraline	13JUN2016	26JUN2016	14
	Moxifloxacin	18JUL2016	31JUL2016	14
[redacted]	Sertraline	22APR2016	05MAY2016	14
	Placebo	26MAY2016	08JUN2016	14
	Moxifloxacin	30JUN2016	13JUL2016	14
[redacted]	Placebo	09MAY2016	22MAY2016	14
	Moxifloxacin	13JUN2016	26JUN2016	14
	Sertraline	18JUL2016	31JUL2016	14
[redacted]	Sertraline	09MAY2016	11MAY2016	3
[redacted]	Moxifloxacin	26MAY2016	08JUN2016	14
	Sertraline	04JUL2016	17JUL2016	14
	Placebo	03AUG2016	16AUG2016	14
[redacted]	Placebo	09MAY2016	22MAY2016	14
	Sertraline	13JUN2016	26JUN2016	14

Subject ID	Treatment Received	First Dose Date	Last Dose Date	Duration (Days)
[redacted]	Moxifloxacin	18JUL2016	31JUL2016	14
	Moxifloxacin	26MAY2016	08JUN2016	14
	Placebo	04JUL2016	17JUL2016	14
	Sertraline	03AUG2016	16AUG2016	14
	Placebo	09MAY2016	22MAY2016	14
	Moxifloxacin	13JUN2016	26JUN2016	14
	Sertraline	18JUL2016	31JUL2016	14
	Sertraline	26MAY2016	08JUN2016	14
	Moxifloxacin	04JUL2016	17JUL2016	14
	Placebo	03AUG2016	16AUG2016	14
	Sertraline	26MAY2016	08JUN2016	14
	Placebo	04JUL2016	17JUL2016	14
	Moxifloxacin	03AUG2016	16AUG2016	14
	Placebo	20JUN2016	03JUL2016	14
	Sertraline	20JUL2016	02AUG2016	14
	Moxifloxacin	16AUG2016	29AUG2016	14
	Moxifloxacin	20JUN2016	03JUL2016	14
	Sertraline	20JUL2016	02AUG2016	14
	Sertraline	20JUN2016	03JUL2016	14
	Placebo	20JUL2016	02AUG2016	14
	Moxifloxacin	20JUN2016	03JUL2016	14
	Placebo	20JUL2016	02AUG2016	14
	Sertraline	16AUG2016	29AUG2016	14
	Sertraline	20JUN2016	03JUL2016	14
	Moxifloxacin	20JUL2016	02AUG2016	14
	Placebo	16AUG2016	29AUG2016	14
	Placebo	20JUN2016	03JUL2016	14
	Moxifloxacin	20JUL2016	02AUG2016	14
	Sertraline	20JUN2016	03JUL2016	14
	Moxifloxacin	20JUL2016	02AUG2016	14
	Placebo	16AUG2016	29AUG2016	14
	Moxifloxacin	20JUN2016	03JUL2016	14
	Placebo	20JUL2016	02AUG2016	14
	Moxifloxacin	20JUN2016	03JUL2016	14
	Sertraline	20JUL2016	02AUG2016	14

Table 14.4.1
SERTRALINE Protocol A0501104
Administration Schedule

Subject ID	Treatment Received	First Dose Date	Last Dose Date	Duration (Days)
[redacted]	Placebo	16AUG2016	29AUG2016	14
	Placebo	20JUN2016	03JUL2016	14
	Sertraline	20JUL2016	02AUG2016	14
	Moxifloxacin	16AUG2016	29AUG2016	14
	Sertraline	20JUN2016	03JUL2016	14
	Placebo	20JUL2016	02AUG2016	14
	Moxifloxacin	16AUG2016	29AUG2016	14
	Placebo	20JUN2016	03JUL2016	14
	Moxifloxacin	20JUL2016	02AUG2016	14
	Sertraline	16AUG2016	29AUG2016	14

[redacted] Date of Reporting Dataset Creation: 12SEP2016 Date of Table Generation: 17SEP2016 (22:51)

SERTRALINE Protocol A0501104

Plasma Sertraline Concentration (NG/ML) versus Time Summary

Treatment Group=Sertraline

Dosing Day *	Planned Time Post Dose	N	NALQ	Mean	SD	CV (%)	Median	Min	Max
1	0 H	52	0						
	1 H	52	27	0.6333	0.78910	125	0.5380	0.000	3.34
	2 H	52	50	3.029	2.4932	82	2.250	0.000	10.2
	3 H	52	52	5.409	2.8555	53	4.605	1.31	11.6
	4 H	52	52	7.182	3.3261	46	6.560	2.18	14.6
	5 H	52	52	11.20	4.0884	37	11.05	4.26	27.5
	6 H	52	52	11.22	3.6973	33	11.65	4.05	20.1
	8 H	52	52	10.37	3.3944	33	10.15	3.22	20.7
	12 H	52	52	7.683	2.5656	33	7.725	3.04	14.6
	24 H	52	52	4.651	1.5693	34	4.570	1.71	8.88
14	0 H	50	50	193.1	63.857	33	180.5	60.9	369
	1 H	50	50	189.7	59.339	31	182.5	68.1	353
	2 H	50	50	198.9	66.797	34	195.0	65.9	378
	3 H	50	50	206.6	70.448	34	202.5	69.2	408
	4 H	50	50	213.1	72.835	34	198.5	73.9	400
	5 H	50	50	219.5	66.788	30	208.0	88.1	410
	6 H	50	50	234.2	74.075	32	221.5	94.1	447
	8 H	50	50	240.1	79.835	33	233.0	85.0	502
	12 H	50	50	205.3	72.140	35	201.5	61.8	419
	24 H	49	49	146.9	58.998	40	137.0	38.6	330
	48 H	49	49	90.20	44.022	49	83.80	21.4	218
	72 H	49	49	58.36	35.844	61	52.00	10.4	176

'N' = Number of observations (non-missing concentrations)

'NALQ' = Number of observations Above Lower limit of Quantification. Summary statistics are not presented if NALQ = 0.

Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero

* Dosing day refers to dosing day of treatment period for crossover studies and dosing study day for parallel group studies

The lower limit of quantification is 0.500 NG/ML.

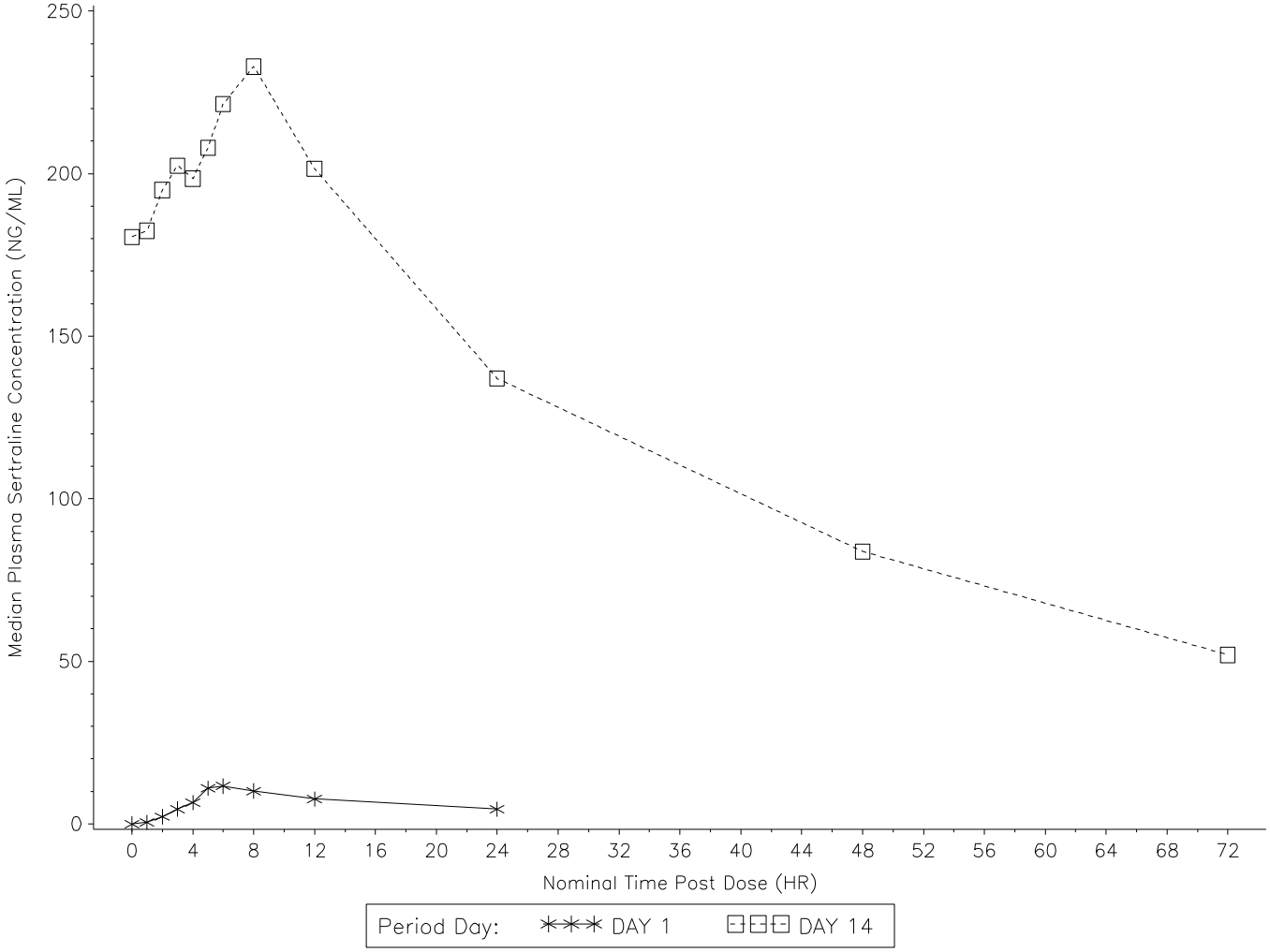
[redacted] Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:04)

SERTRALINE Protocol A0501104
Plasma N-Desmethylsertraline Concentration (NG/ML) versus Time Summary
Treatment Group=Sertraline

Dosing Day *	Planned Time Post Dose	N	NALQ	Mean	SD	CV (%)	Median	Min	Max
1	0 H	52	0						
	1 H	52	0						
	2 H	52	22	0.4139	0.54900	133	0.0000	0.000	1.80
	3 H	52	47	1.208	0.69825	58	1.185	0.000	2.97
	4 H	52	51	1.949	0.99622	51	1.730	0.000	5.35
	5 H	52	52	3.346	1.3815	41	3.095	1.54	9.99
	6 H	52	52	3.574	1.0545	30	3.570	1.80	6.36
	8 H	52	52	4.080	1.0732	26	3.985	2.24	7.39
	12 H	52	52	4.123	1.0461	25	4.090	2.57	6.91
	24 H	52	52	3.668	0.86164	23	3.585	2.30	5.66
14	0 H	50	50	205.6	42.194	21	204.0	99.8	289
	1 H	50	50	202.8	39.399	19	198.5	122	292
	2 H	50	50	214.7	45.259	21	207.5	109	331
	3 H	50	50	214.0	44.235	21	203.0	116	337
	4 H	50	50	223.5	49.525	22	214.5	124	386
	5 H	50	50	219.4	42.541	19	211.0	129	325
	6 H	50	50	232.5	46.722	20	227.5	128	344
	8 H	50	50	249.6	56.591	23	238.5	134	438
	12 H	50	50	235.6	51.406	22	224.5	116	372
	24 H	49	49	196.5	46.562	24	189.0	90.1	345
	48 H	49	49	169.5	45.393	27	172.0	71.7	310
	72 H	49	49	146.8	46.262	32	144.0	46.7	266

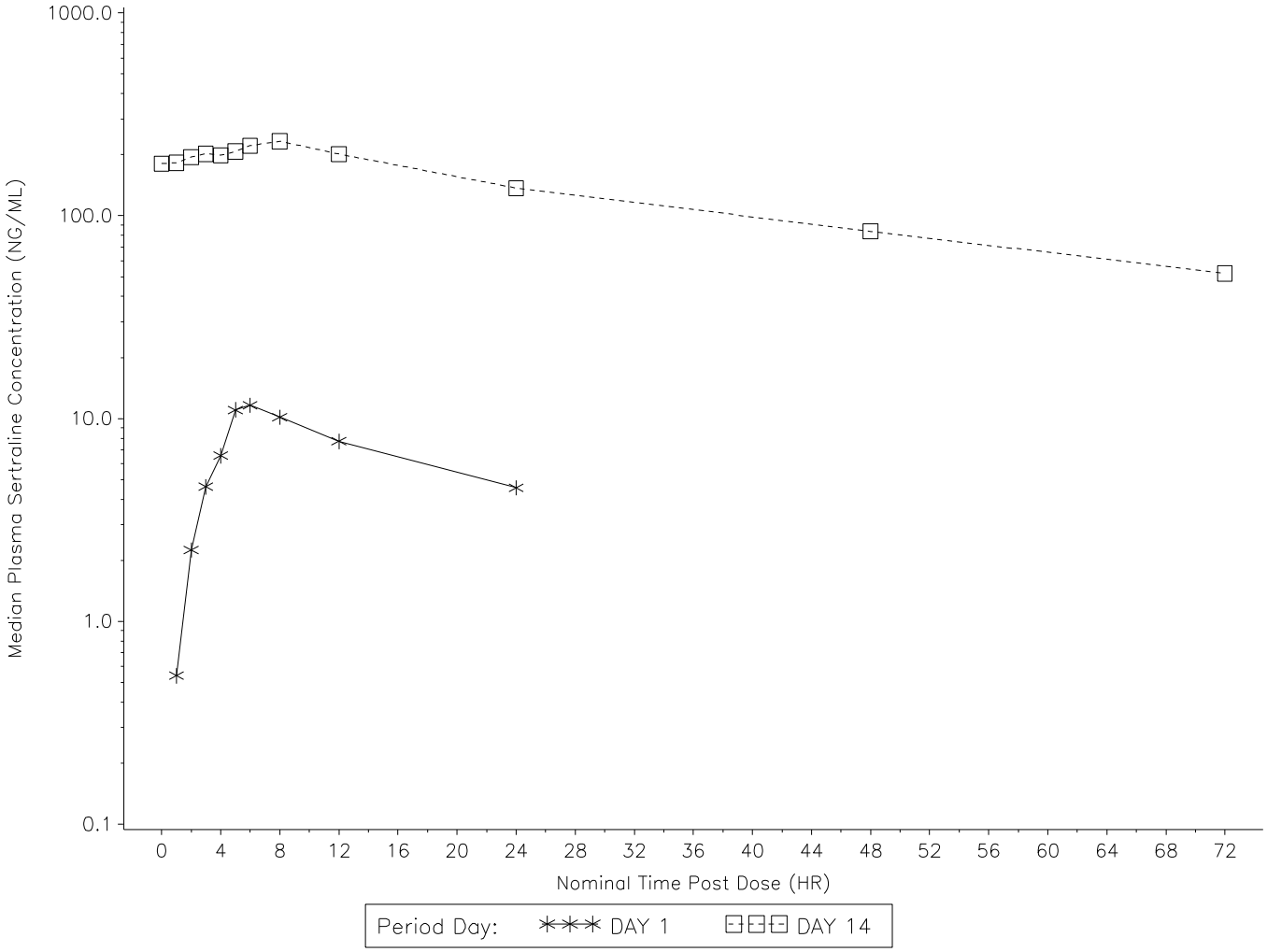
'N' = Number of observations (non-missing concentrations)
'NALQ' = Number of observations Above Lower limit of Quantification. Summary statistics are not presented if NALQ = 0.
Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero
* Dosing day refers to dosing day of treatment period for crossover studies and dosing study day for parallel group studies
The lower limit of quantification is 0.500 NG/ML.
[redacted] Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:04)

Figure 14.4.2.2.1
SERTRALINE Protocol A0501104
Median Plasma Sertraline Concentration – Time Plot (Linear Scale)



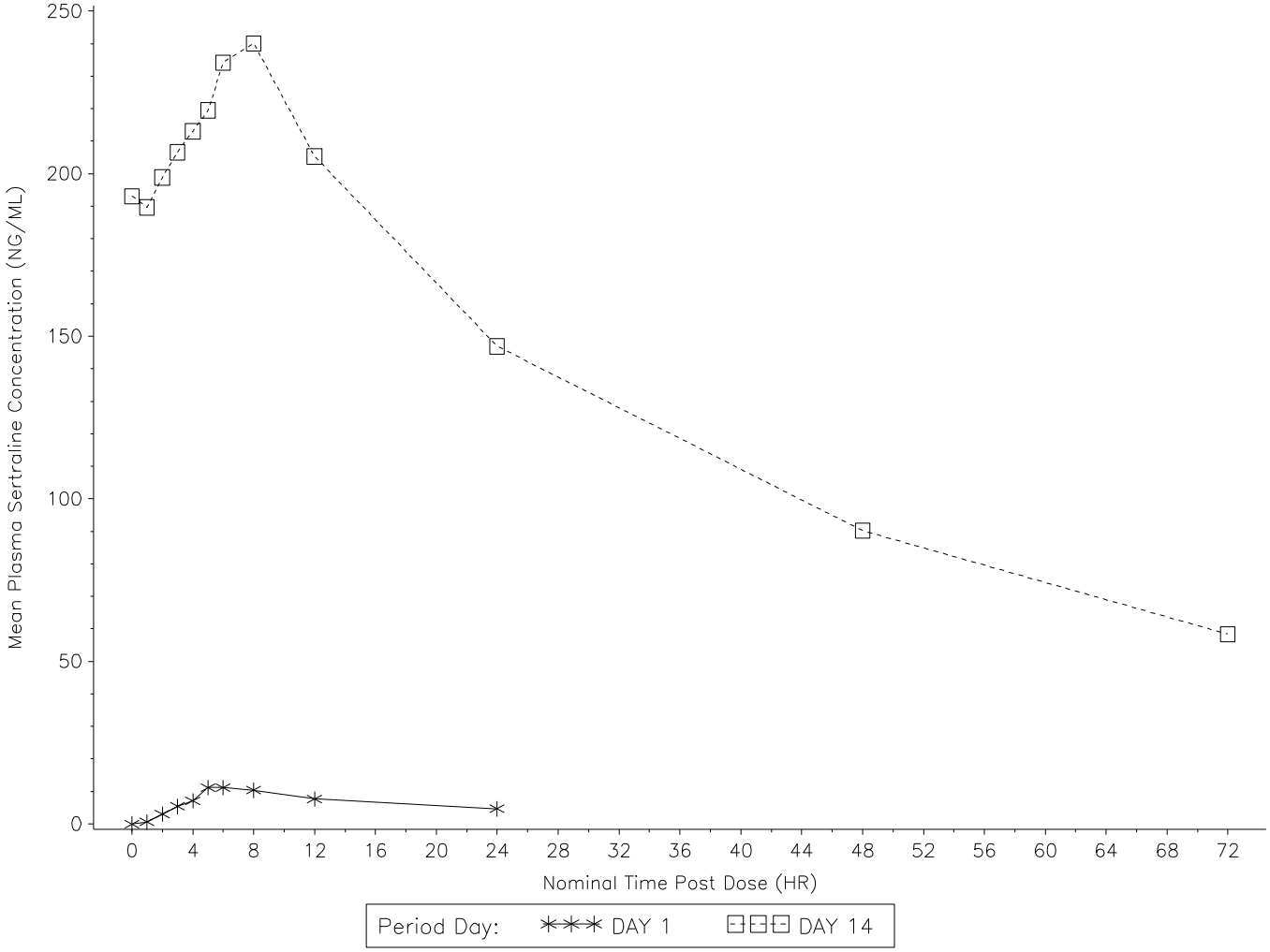
Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.
[redacted] Source Data: Table 14.4.2.1.1 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:05)

Figure 14.4.2.2.2
SERTRALINE Protocol A0501104
Median Plasma Sertraline Concentration – Time Plot (Semi–log Scale)



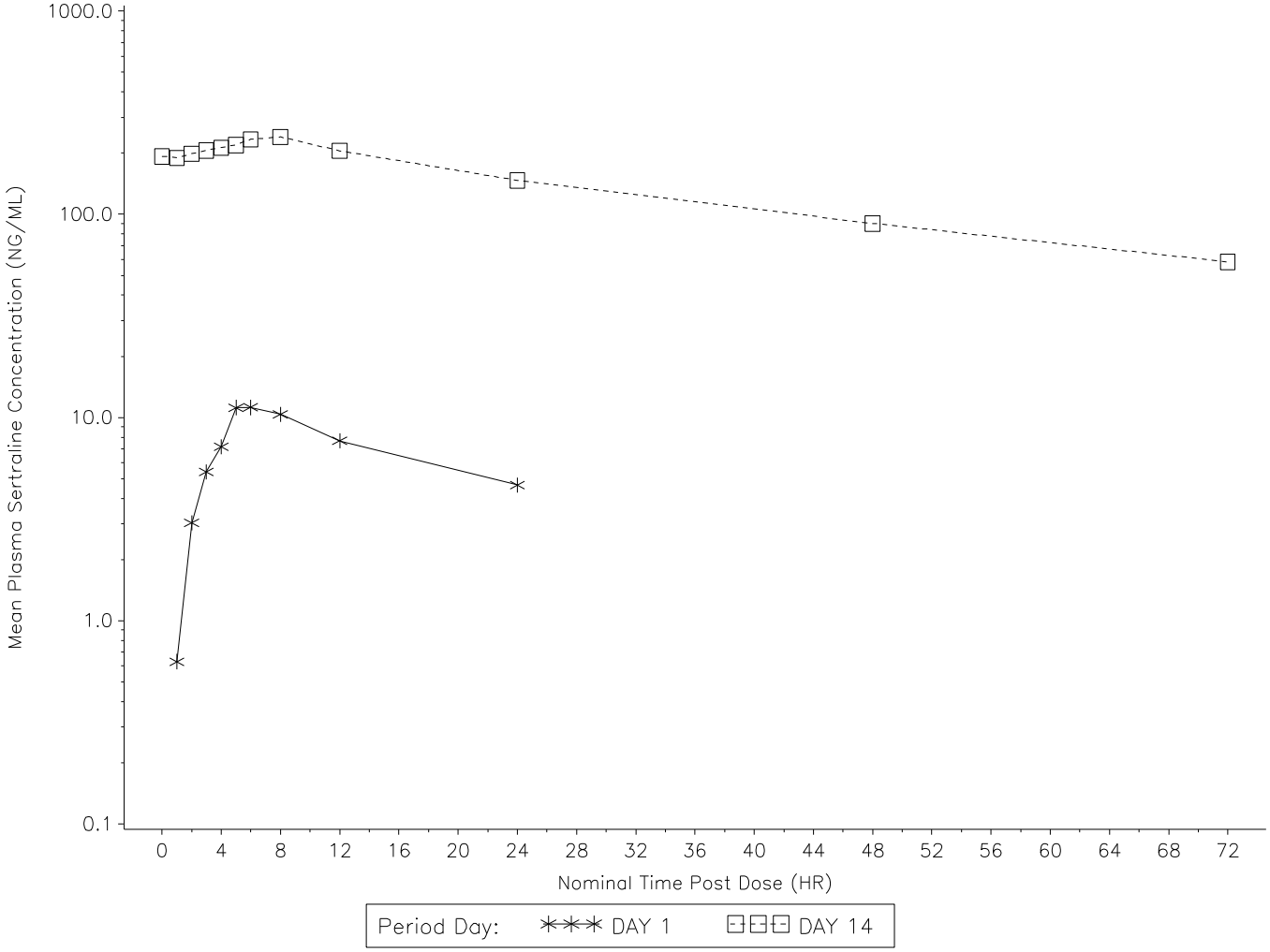
Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.
[redacted] Source Data: Table 14.4.2.1.1 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:06)

Figure 14.4.2.2.3
SERTRALINE Protocol A0501104
Mean Plasma Sertraline Concentration – Time Plot (Linear Scale)



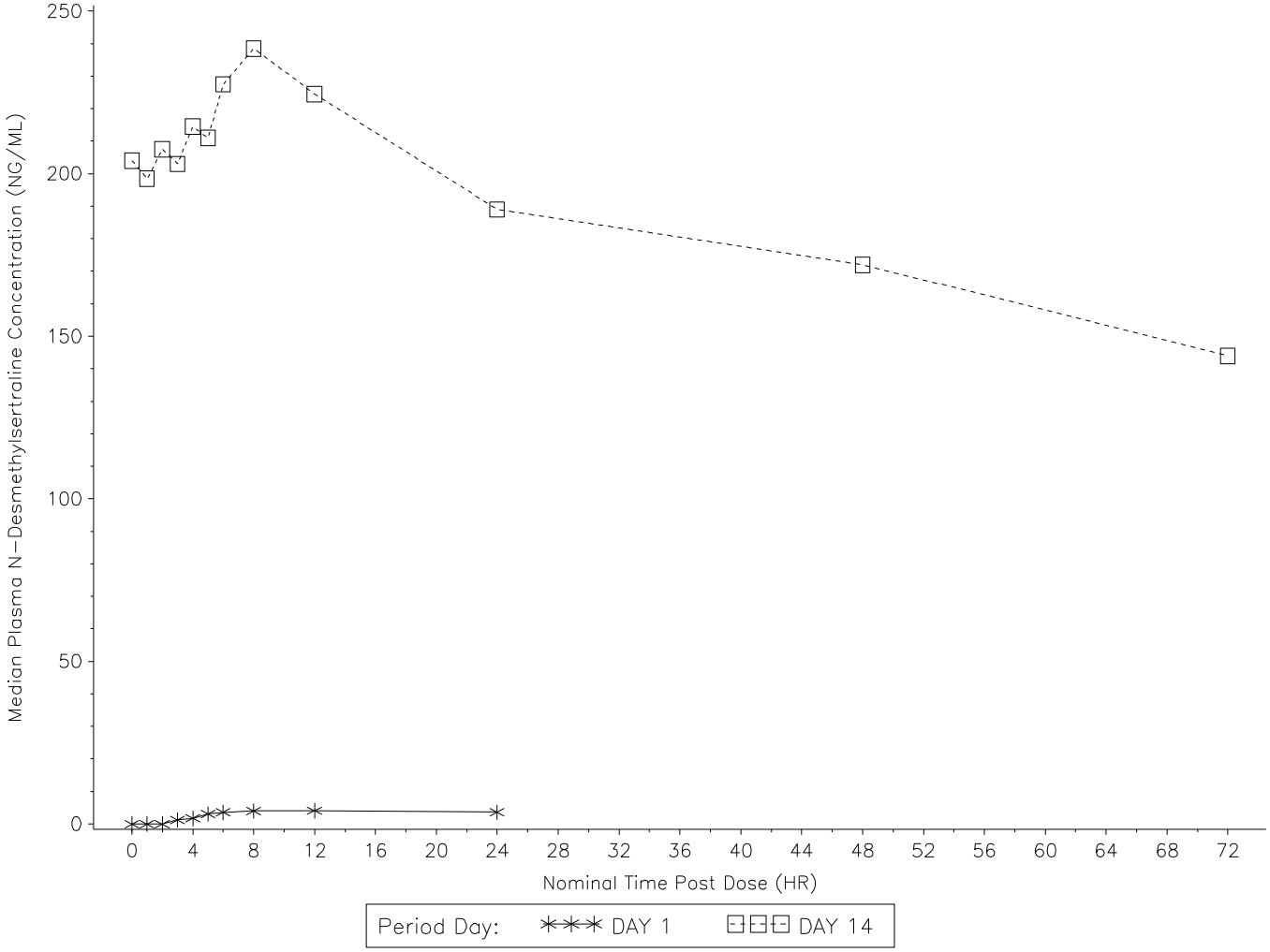
Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.
[redacted] Source Data: Table 14.4.2.1.1 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:07)

Figure 14.4.2.2.4
SERTRALINE Protocol A0501104
Mean Plasma Sertraline Concentration – Time Plot (Semi–log Scale)



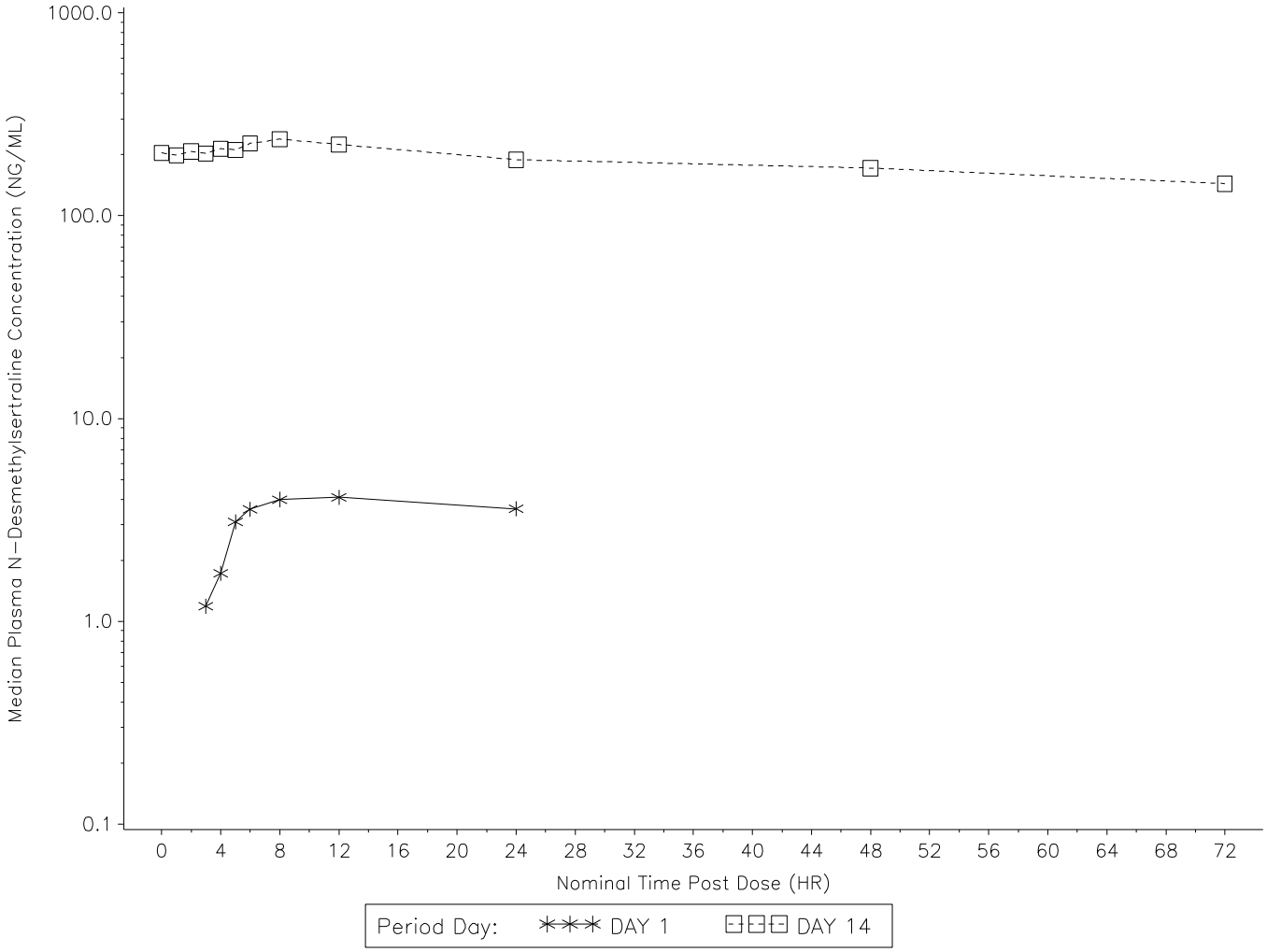
Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.
[redacted] Source Data: Table 14.4.2.1.1 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:08)

Figure 14.4.2.2.5
SERTRALINE Protocol A0501104
Median Plasma N-Desmethylsertraline Concentration – Time Plot (Linear Scale)



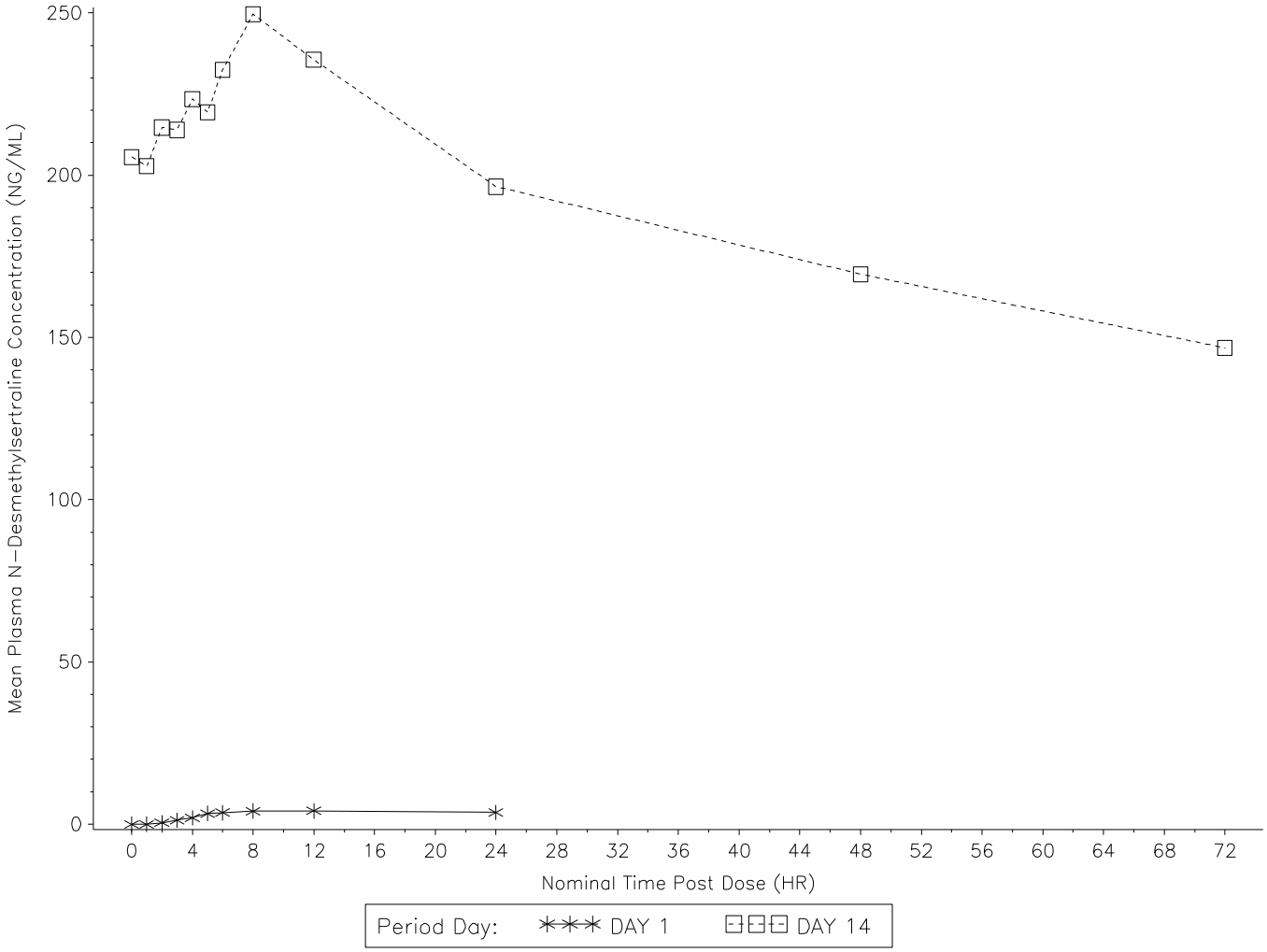
Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.
[redacted] Source Data: Table 14.4.2.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:09)

Figure 14.4.2.2.6
SERTRALINE Protocol A0501104
Median Plasma N-Desmethylsertraline Concentration – Time Plot (Semi-log Scale)



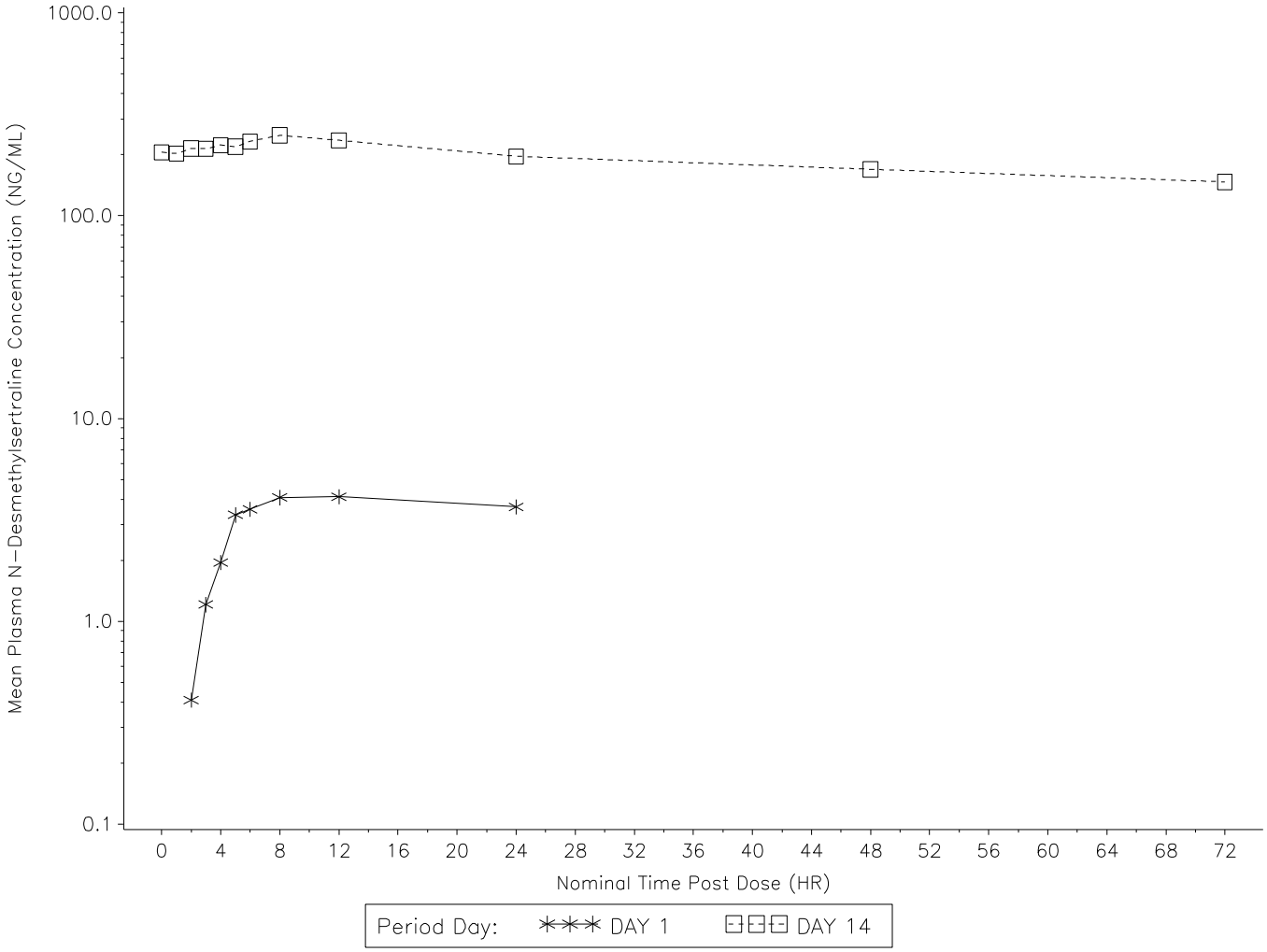
Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.
[redacted] Source Data: Table 14.4.2.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:10)

Figure 14.4.2.2.7
SERTRALINE Protocol A0501104
Mean Plasma N-Desmethylsertraline Concentration – Time Plot (Linear Scale)



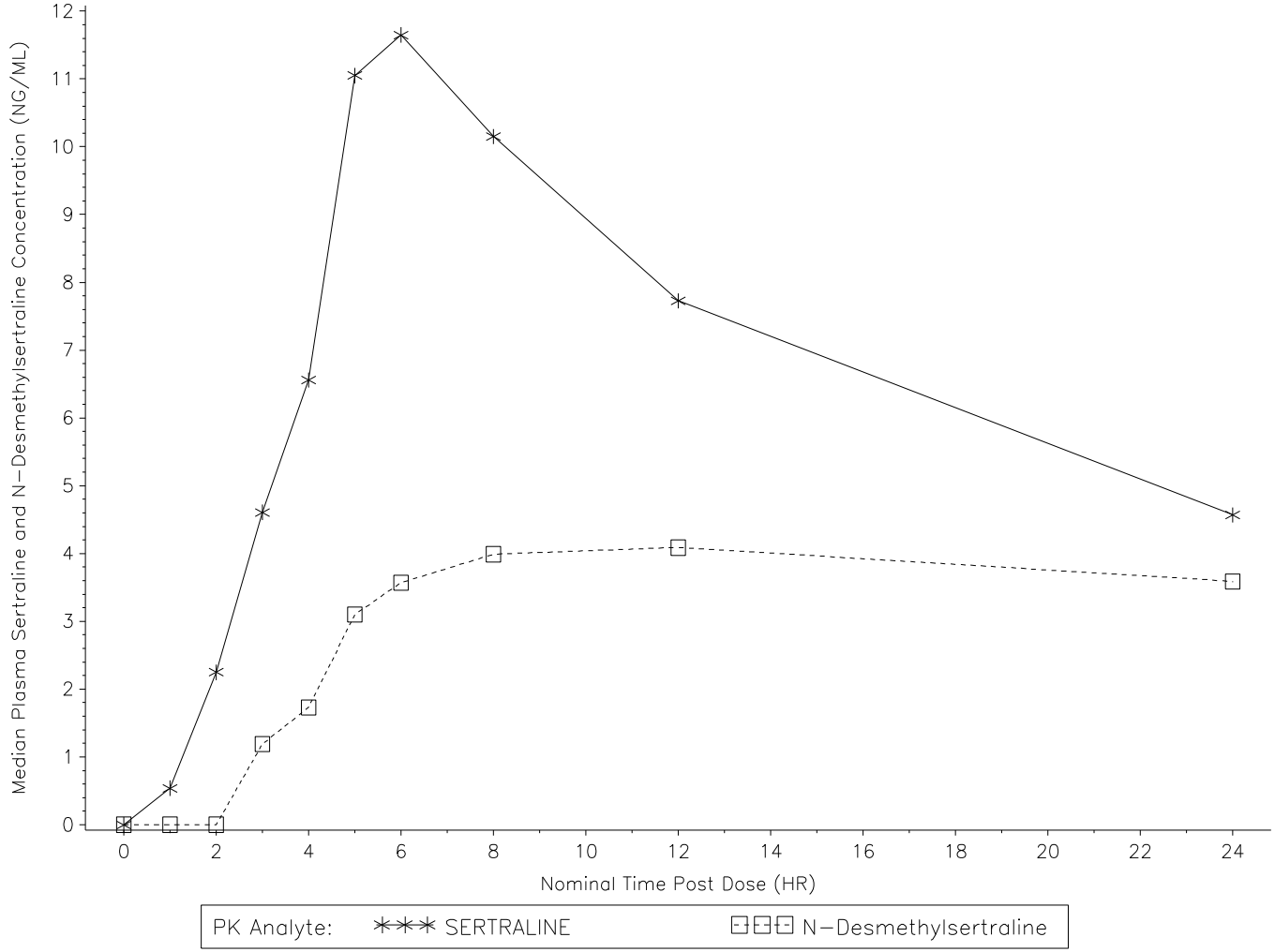
Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.
[redacted] Source Data: Table 14.4.2.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:11)

Figure 14.4.2.2.8
SERTRALINE Protocol A0501104
Mean Plasma N-Desmethylsertraline Concentration – Time Plot (Semi-log Scale)



Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.
[redacted] Source Data: Table 14.4.2.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:12)

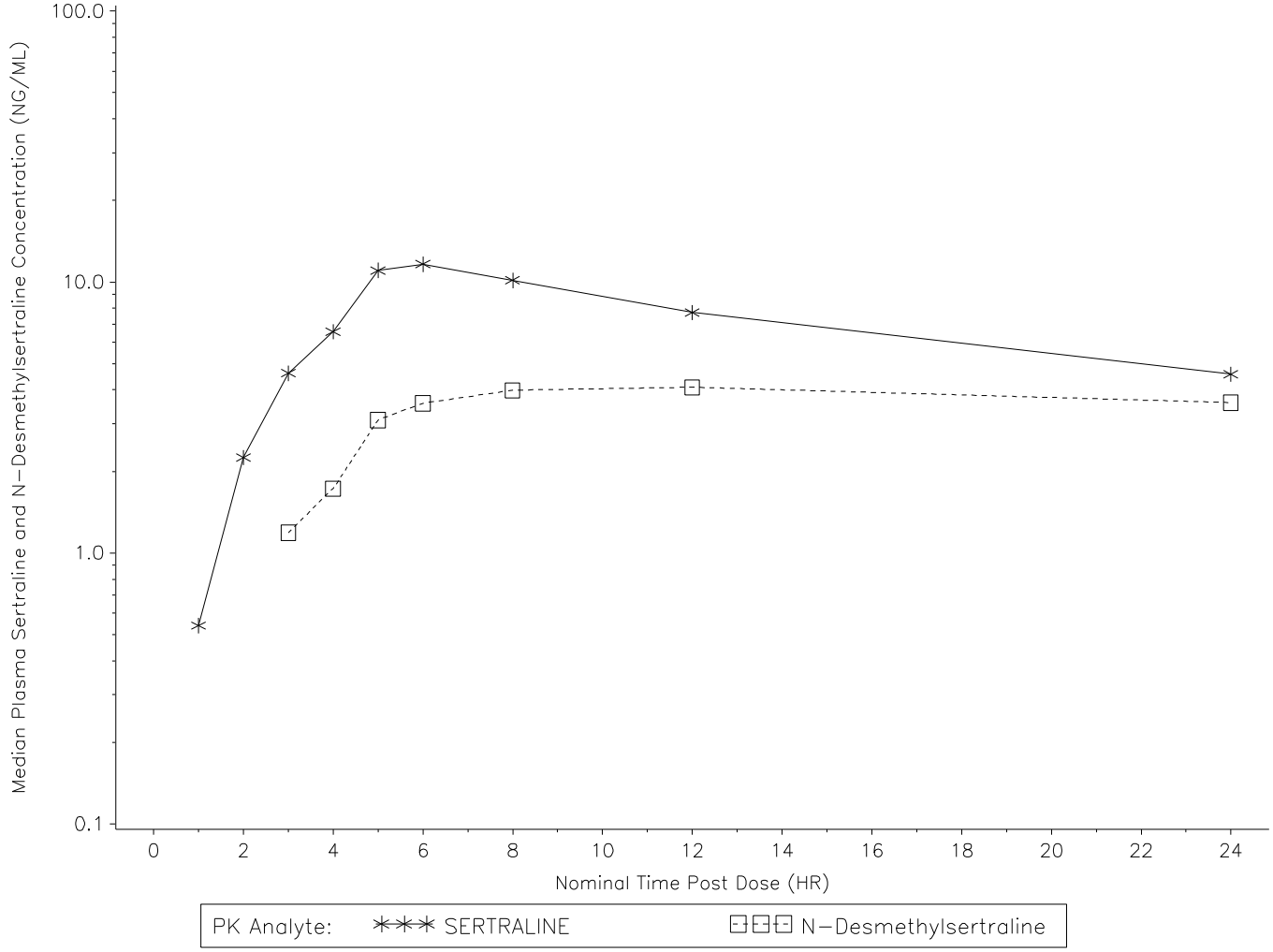
Figure 14.4.2.2.9
SERTRALINE Protocol A0501104
Median Plasma Sertraline and N-Desmethylsertraline Concentration vs Time on Day 1 (Linear Scale)



Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.

[redacted] Source Data: Table 14.4.2.1.1 & Table 14.4.2.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:13)

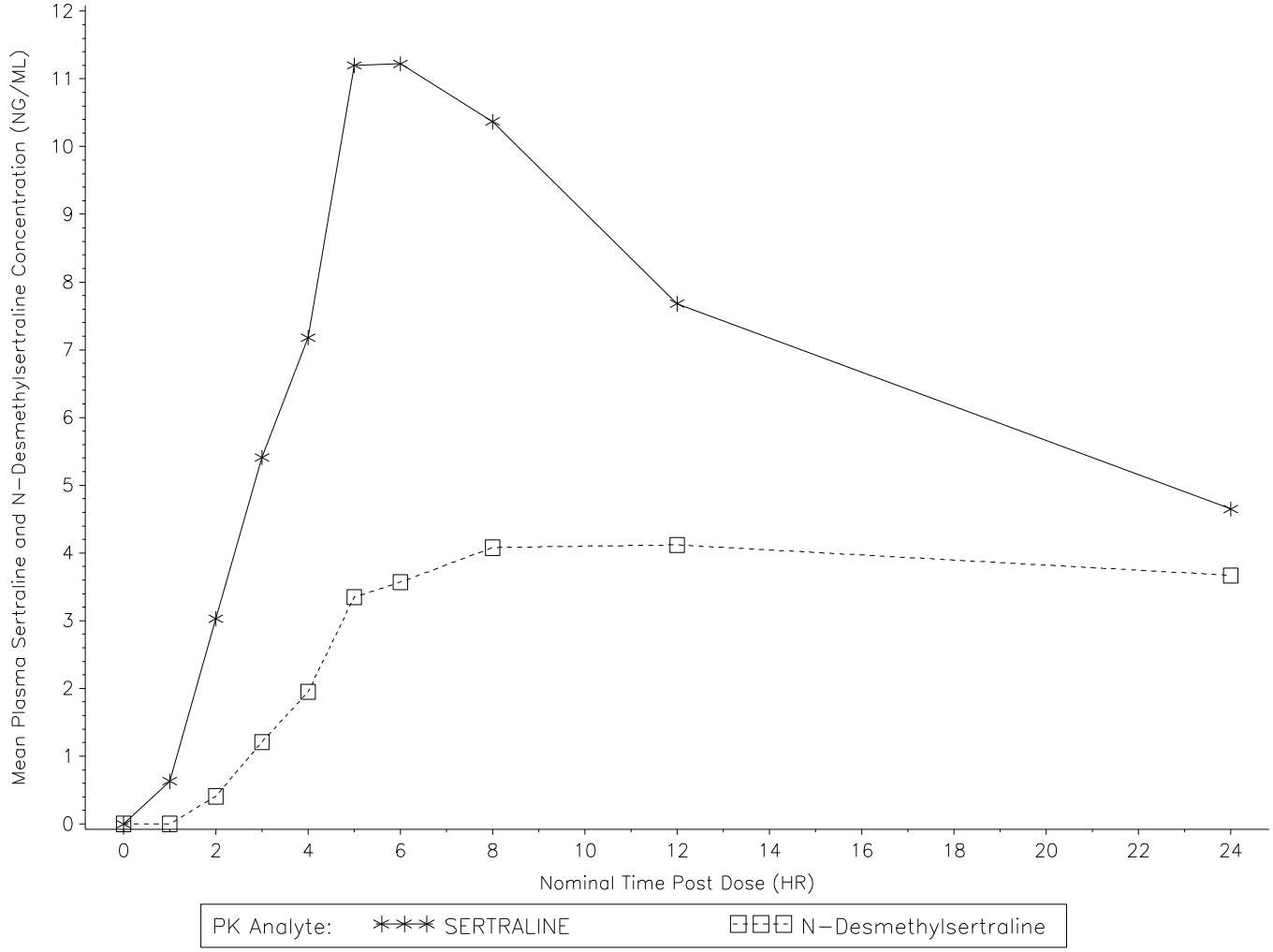
Figure 14.4.2.2.10
SERTRALINE Protocol A0501104
Median Plasma Sertraline and N-Desmethylsertraline Concentration vs Time on Day 1 (Semi-log Scale)



Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.

[redacted] Source Data: Table 14.4.2.1.1 & Table 14.4.2.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:21)

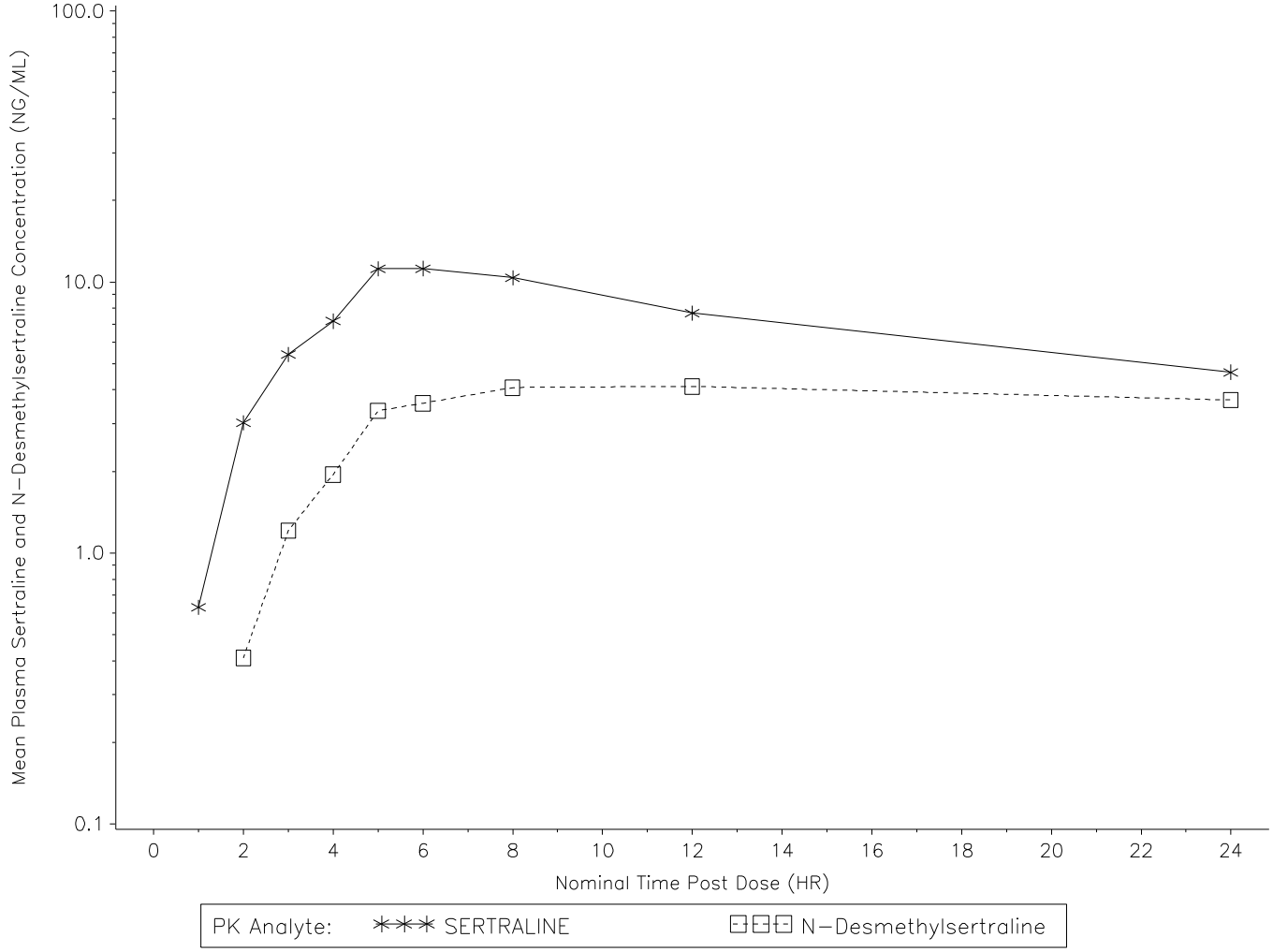
Figure 14.4.2.2.11
SERTRALINE Protocol A0501104
Mean Plasma Sertraline and N–Desmethylsertraline Concentration vs Time on Day 1 (Linear Scale)



Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.

[redacted] Source Data: Table 14.4.2.1.1 & Table 14.4.2.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:22)

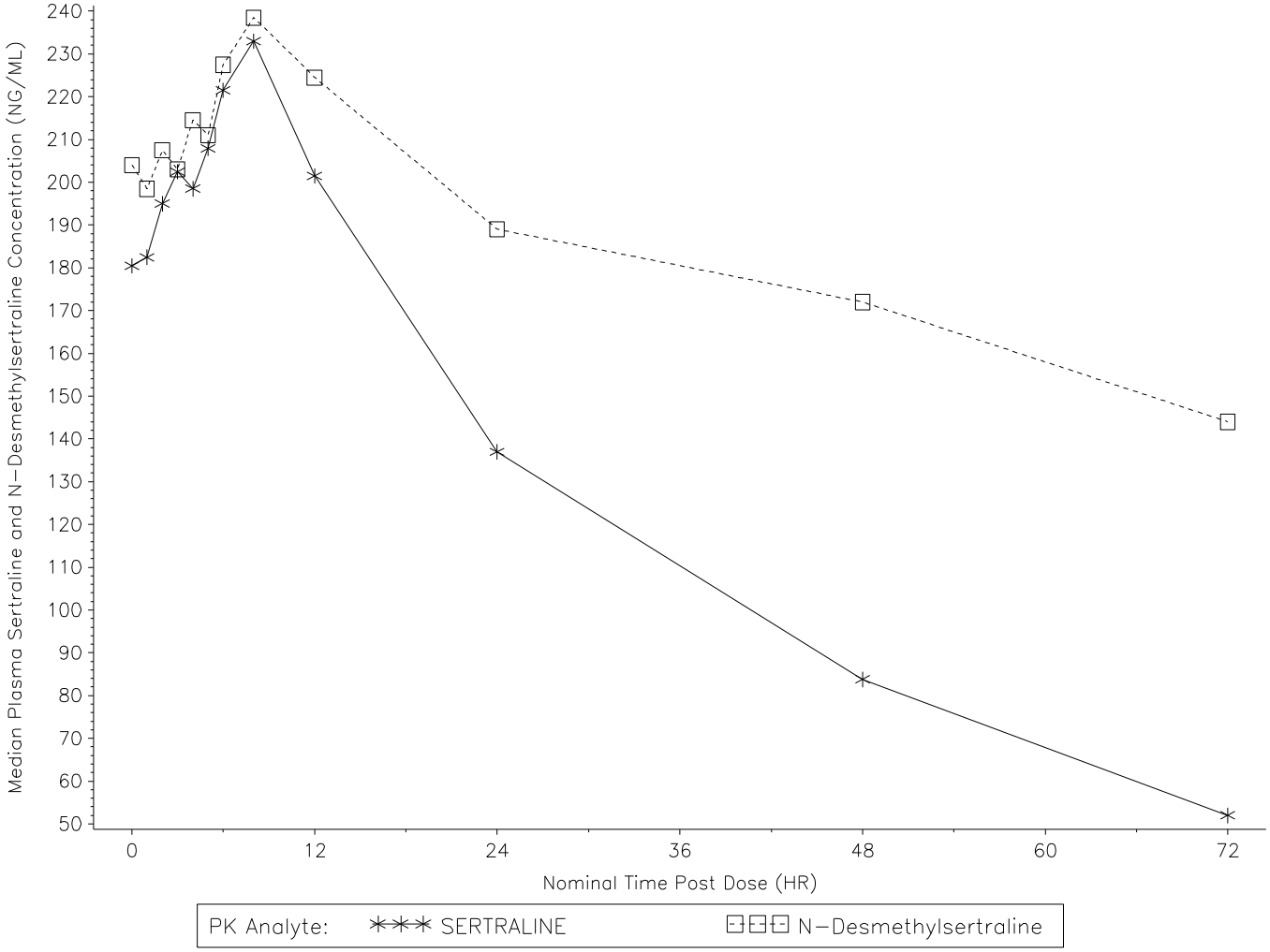
Figure 14.4.2.2.12
SERTRALINE Protocol A0501104
Mean Plasma Sertraline and N–Desmethylsertraline Concentration vs Time on Day 1 (Semi–log Scale)



Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.

[redacted] Source Data: Table 14.4.2.1.1 & Table 14.4.2.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 02NOV2016 (01:59)

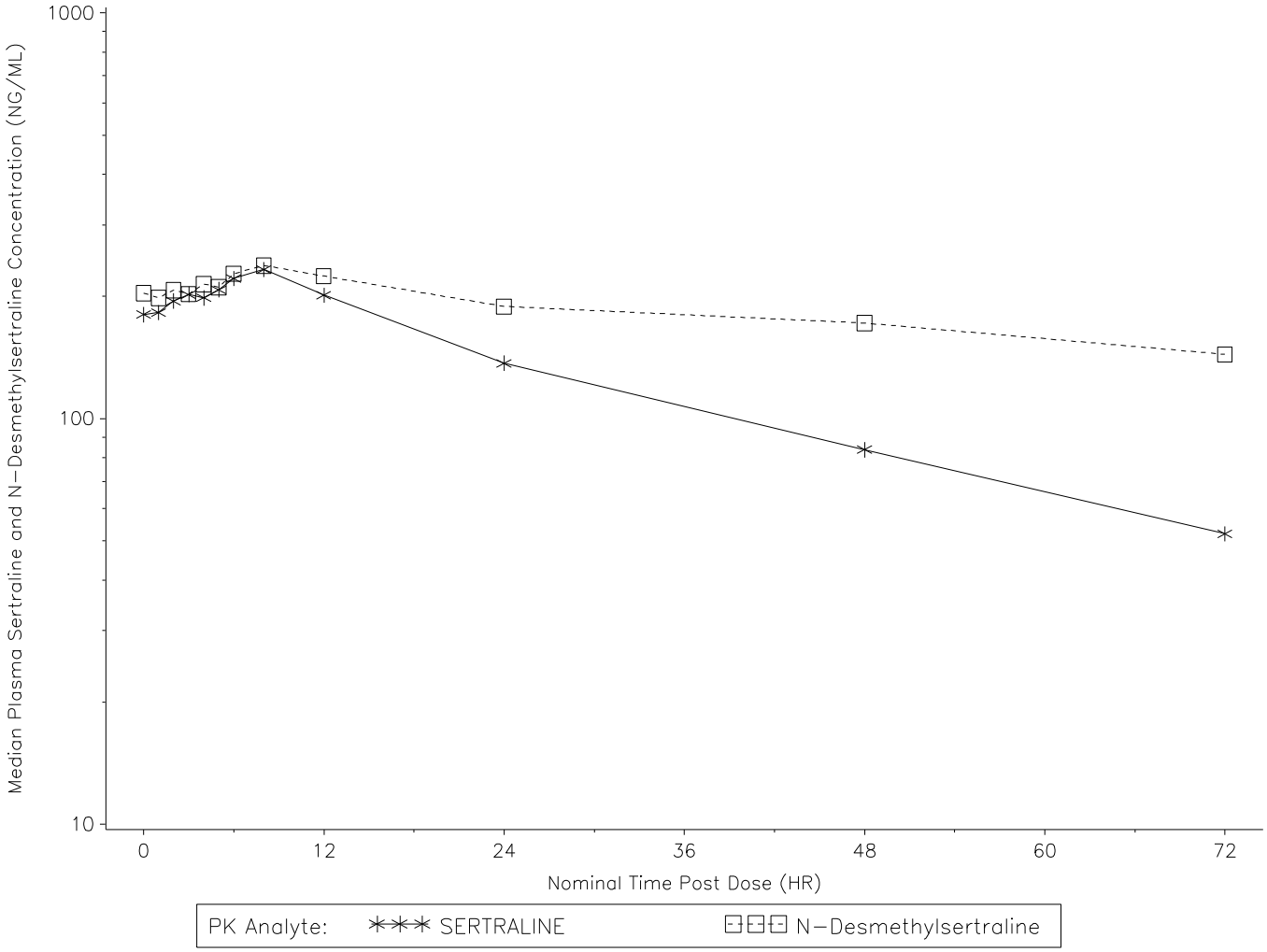
Figure 14.4.2.2.13
SERTRALINE Protocol A0501104
Median Plasma Sertraline and N-Desmethylsertraline Concentration vs Time on Day 14 (Linear Scale)



Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.

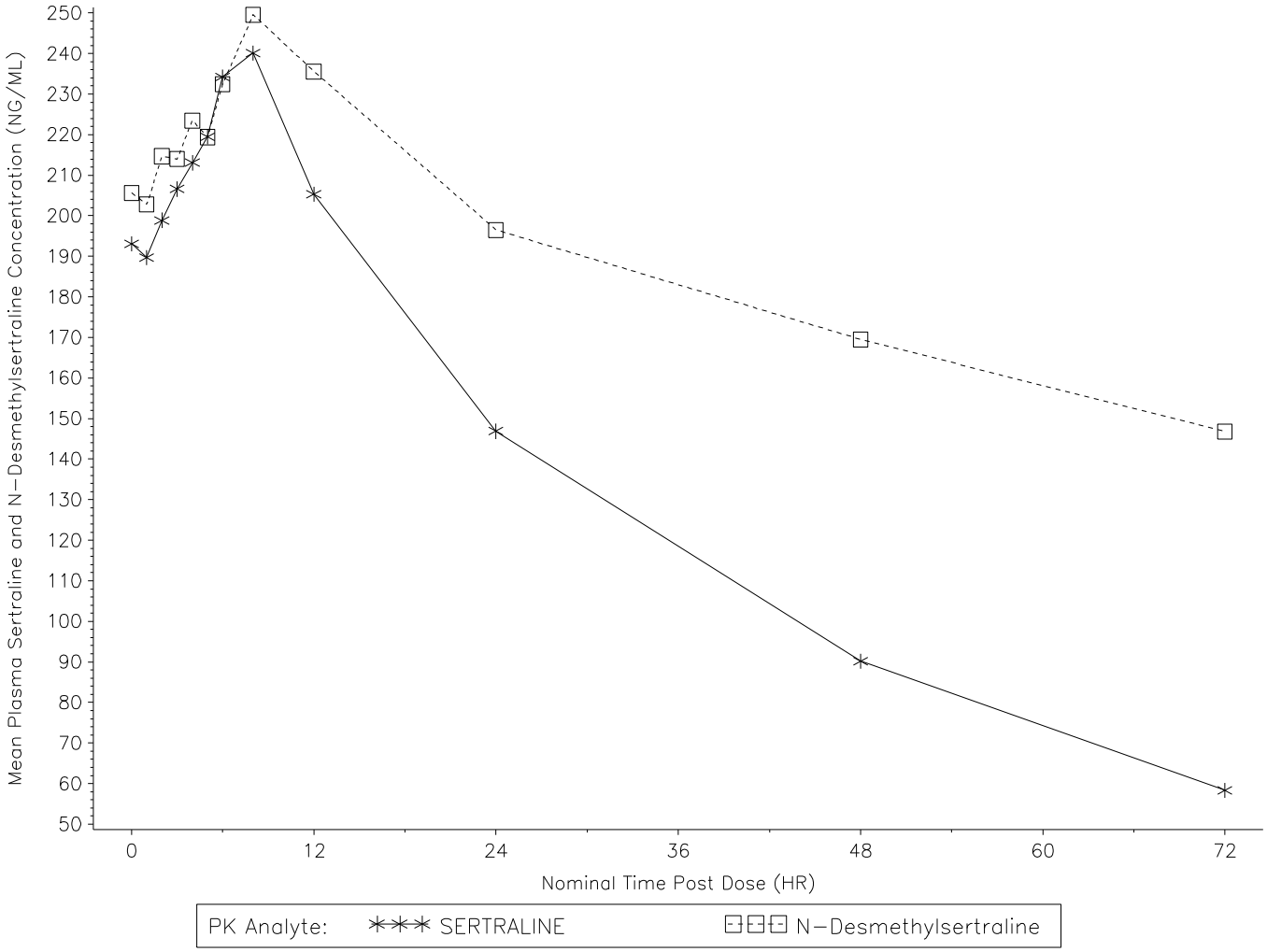
[redacted] Source Data: Table 14.4.2.1.1 & Table 14.4.2.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:23)

Figure 14.4.2.2.14
SERTRALINE Protocol A0501104
Median Plasma Sertraline and N-Desmethylsertraline Concentration vs Time on Day 14 (Semi-log Scale)



Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.
[redacted] Source Data: Table 14.4.2.1.1 & Table 14.4.2.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 02NOV2016 (01:32)

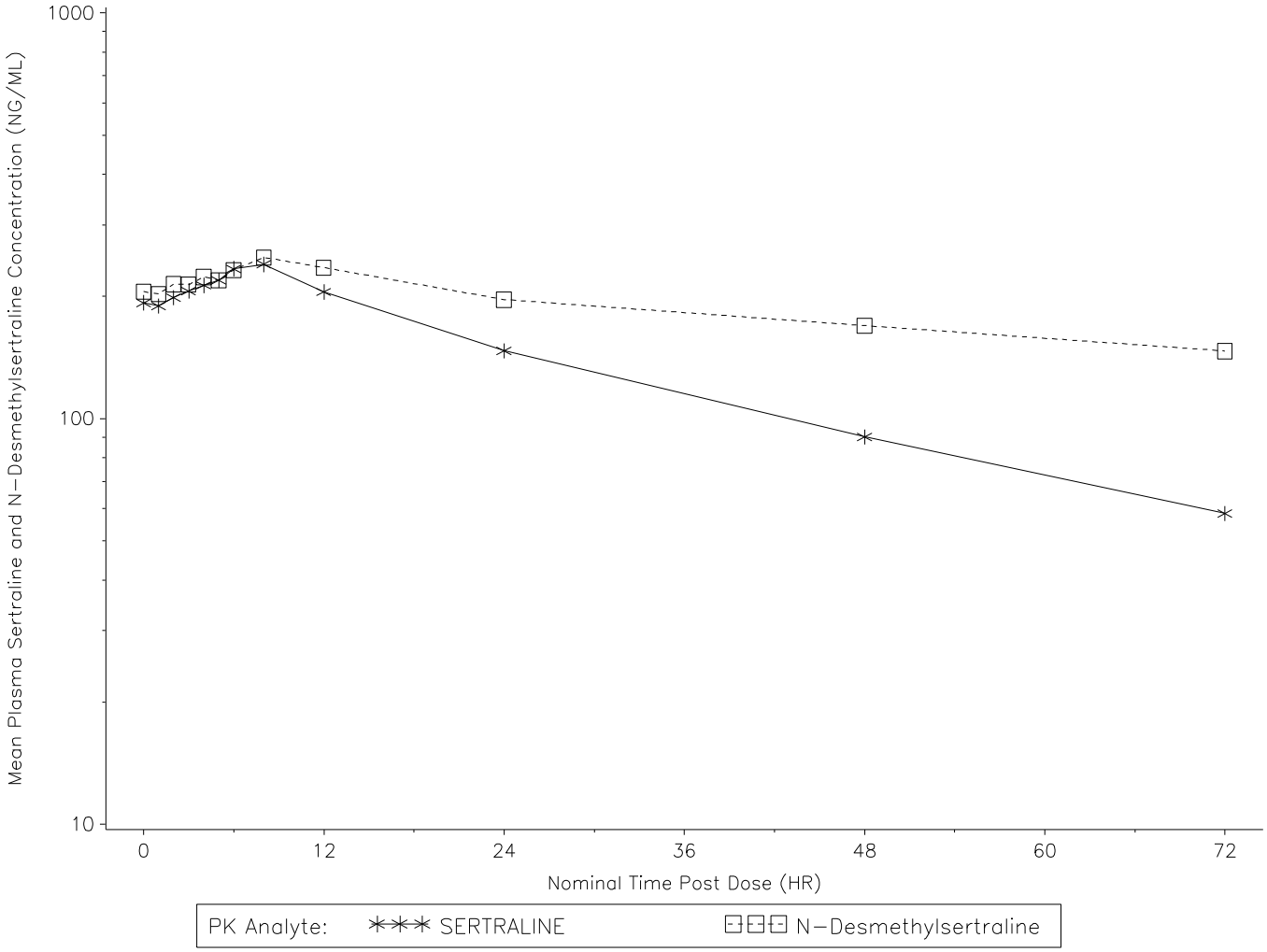
Figure 14.4.2.2.15
SERTRALINE Protocol A0501104
Mean Plasma Sertraline and N–Desmethylsertraline Concentration vs Time on Day 14 (Linear Scale)



Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.

[redacted] Source Data: Table 14.4.2.1.1 & Table 14.4.2.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:25)

Figure 14.4.2.2.16
SERTRALINE Protocol A0501104
Mean Plasma Sertraline and N–Desmethylsertraline Concentration vs Time on Day 14 (Semi–log Scale)



Summary statistics have been calculated by setting concentration values below the lower limit of quantification to zero.
The lower limit of quantification is 0.500 NG/ML.

[redacted] Source Data: Table 14.4.2.1.1 & Table 14.4.2.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 02NOV2016 (01:35)

SERTRALINE Protocol A0501104
Descriptive Summary of Plasma Sertraline PK Parameters on Day 1

Parameter (units)	Sertraline (N = 52)[1]
AUC24 (ng.hr/mL)	
N[2]	52
Geometric Mean	154.3
Geometric CV (%)	34
Arithmetic Mean	162.3
Standard Deviation	50.257
Coefficient of Variation (%)	31
Median	158.5
Minimum	59.9
Maximum	279
AUC24(dn) (ng.hr/mL/mg)	
N[2]	52
Geometric Mean	3.086
Geometric CV (%)	34
Arithmetic Mean	3.245
Standard Deviation	1.0052
Coefficient of Variation (%)	31
Median	3.165
Minimum	1.20
Maximum	5.59
Cmax (ng/mL)	
N[2]	52
Geometric Mean	11.39
Geometric CV (%)	37
Arithmetic Mean	12.11
Standard Deviation	4.3387
Coefficient of Variation (%)	36
Median	12.05
Minimum	4.26
Maximum	27.5
Cmax(dn) (ng/mL/mg)	
N[2]	52
Geometric Mean	0.2277
Geometric CV (%)	37
Arithmetic Mean	0.2423
Standard Deviation	0.086770
Coefficient of Variation (%)	36
Median	0.2410
Minimum	0.0852
Maximum	0.550

[1]Total number of subjects in the treatment group in the indicated population.
[2]Number of subjects contributing to the summary statistics.

[redacted] Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (12:05)

Descriptive Summary of Plasma Sertraline PK Parameters on Day 1

Parameter (units)	Sertraline (N = 52)[1]
Tmax (hr)	
N[2]	52
Median	5.06
Minimum	4.02
Maximum	8.05

[1]Total number of subjects in the treatment group in the indicated population.
[2]Number of subjects contributing to the summary statistics.

[redacted] Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (12:05)

SERTRALINE Protocol A0501104
Descriptive Summary of Plasma Sertraline PK Parameters on Day 14

Parameter (units)	Sertraline (N = 50)[1]
AUC24 (ng.hr/mL)	
N[2]	49
Geometric Mean	4388
Geometric CV (%)	36
Arithmetic Mean	4648
Standard Deviation	1575.7
Coefficient of Variation (%)	34
Median	4540
Minimum	1500
Maximum	9200
AUC24(dn) (ng.hr/mL/mg)	
N[2]	49
Geometric Mean	21.94
Geometric CV (%)	36
Arithmetic Mean	23.24
Standard Deviation	7.8804
Coefficient of Variation (%)	34
Median	22.70
Minimum	7.52
Maximum	46.0
AUClast (ng.hr/mL)	
N[2]	49
Geometric Mean	8489
Geometric CV (%)	43
Arithmetic Mean	9194
Standard Deviation	3724.1
Coefficient of Variation (%)	41
Median	8620
Minimum	2570
Maximum	20200
Cmax (ng/mL)	
N[2]	50
Geometric Mean	234.2
Geometric CV (%)	34
Arithmetic Mean	246.5
Standard Deviation	80.561
Coefficient of Variation (%)	33
Median	234.0
Minimum	94.1
Maximum	502

[1]Total number of subjects in the treatment group in the indicated population.
[2]Number of subjects contributing to the summary statistics.

[redacted] Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (12:06)

SERTRALINE Protocol A0501104
Descriptive Summary of Plasma Sertraline PK Parameters on Day 14

Parameter (units)	Sertraline (N = 50)[1]
Cmax(dn) (ng/mL/mg)	
N[2]	50
Geometric Mean	1.173
Geometric CV (%)	34
Arithmetic Mean	1.235
Standard Deviation	0.40342
Coefficient of Variation (%)	33
Median	1.175
Minimum	0.471
Maximum	2.51
Cmin (ng/mL)	
N[2]	49
Geometric Mean	135.3
Geometric CV (%)	43
Arithmetic Mean	146.1
Standard Deviation	57.093
Coefficient of Variation (%)	39
Median	137.0
Minimum	38.6
Maximum	330
Rac	
N[2]	49
Geometric Mean	7.238
Geometric CV (%)	23
Arithmetic Mean	7.417
Standard Deviation	1.6465
Coefficient of Variation (%)	22
Median	7.380
Minimum	4.70
Maximum	10.8
Rac,Cmax	
N[2]	50
Geometric Mean	5.206
Geometric CV (%)	32
Arithmetic Mean	5.451
Standard Deviation	1.6345
Coefficient of Variation (%)	30
Median	5.330
Minimum	2.14
Maximum	10.4

[1]Total number of subjects in the treatment group in the indicated population.
[2]Number of subjects contributing to the summary statistics.

[redacted] Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (12:06)

SERTRALINE Protocol A0501104
Descriptive Summary of Plasma Sertraline PK Parameters on Day 14

Parameter (units)	Sertraline (N = 50)[1]
Tmax (hr)	
N[2]	50
Median	7.15
Minimum	3.00
Maximum	8.08
thalf (hr)	
N[2]	23
Arithmetic Mean	26.93
Standard Deviation	2.7109
Coefficient of Variation (%)	10
Median	27.10
Minimum	22.1
Maximum	31.2

[1]Total number of subjects in the treatment group in the indicated population.
[2]Number of subjects contributing to the summary statistics.

[redacted] Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (12:06)

SERTRALINE Protocol A0501104
Descriptive Summary of Plasma N-Desmethylsertraline PK Parameters on Day 1

Parameter (units)	Sertraline (N = 52)[1]
AUC24 (ng.hr/mL)	
N[2]	52
Geometric Mean	76.87
Geometric CV (%)	24
Arithmetic Mean	79.03
Standard Deviation	19.199
Coefficient of Variation (%)	24
Median	77.05
Minimum	51.5
Maximum	131
Cmax (ng/mL)	
N[2]	52
Geometric Mean	4.269
Geometric CV (%)	27
Arithmetic Mean	4.428
Standard Deviation	1.3189
Coefficient of Variation (%)	30
Median	4.265
Minimum	2.75
Maximum	9.99
MRAUC24	
N[2]	52
Geometric Mean	0.5222
Geometric CV (%)	34
Arithmetic Mean	0.5493
Standard Deviation	0.17427
Coefficient of Variation (%)	32
Median	0.5370
Minimum	0.246
Maximum	1.04
Tmax (hr)	
N[2]	52
Median	12.0
Minimum	5.00
Maximum	23.9

[1]Total number of subjects in the treatment group in the indicated population.
[2]Number of subjects contributing to the summary statistics.

[redacted] Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (12:06)

SERTRALINE Protocol A0501104
Descriptive Summary of Plasma N-Desmethylsertraline PK Parameters on Day 14

Parameter (units)	Sertraline (N = 50)[1]
AUC24 (ng.hr/mL)	
N[2]	49
Geometric Mean	5227
Geometric CV (%)	22
Arithmetic Mean	5342
Standard Deviation	1109.5
Coefficient of Variation (%)	21
Median	5110
Minimum	2710
Maximum	8400
AUClast (ng.hr/mL)	
N[2]	49
Geometric Mean	13110
Geometric CV (%)	25
Arithmetic Mean	13500
Standard Deviation	3225.2
Coefficient of Variation (%)	24
Median	13000
Minimum	6040
Maximum	23200
Cmax (ng/mL)	
N[2]	50
Geometric Mean	249.6
Geometric CV (%)	23
Arithmetic Mean	255.8
Standard Deviation	58.383
Coefficient of Variation (%)	23
Median	242.0
Minimum	134
Maximum	438
Cmin (ng/mL)	
N[2]	49
Geometric Mean	184.1
Geometric CV (%)	23
Arithmetic Mean	188.4
Standard Deviation	39.567
Coefficient of Variation (%)	21
Median	187.0
Minimum	90.1
Maximum	286

[1]Total number of subjects in the treatment group in the indicated population.
[2]Number of subjects contributing to the summary statistics.

[redacted] Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (12:07)

SERTRALINE Protocol A0501104
Descriptive Summary of Plasma N-Desmethylsertraline PK Parameters on Day 14

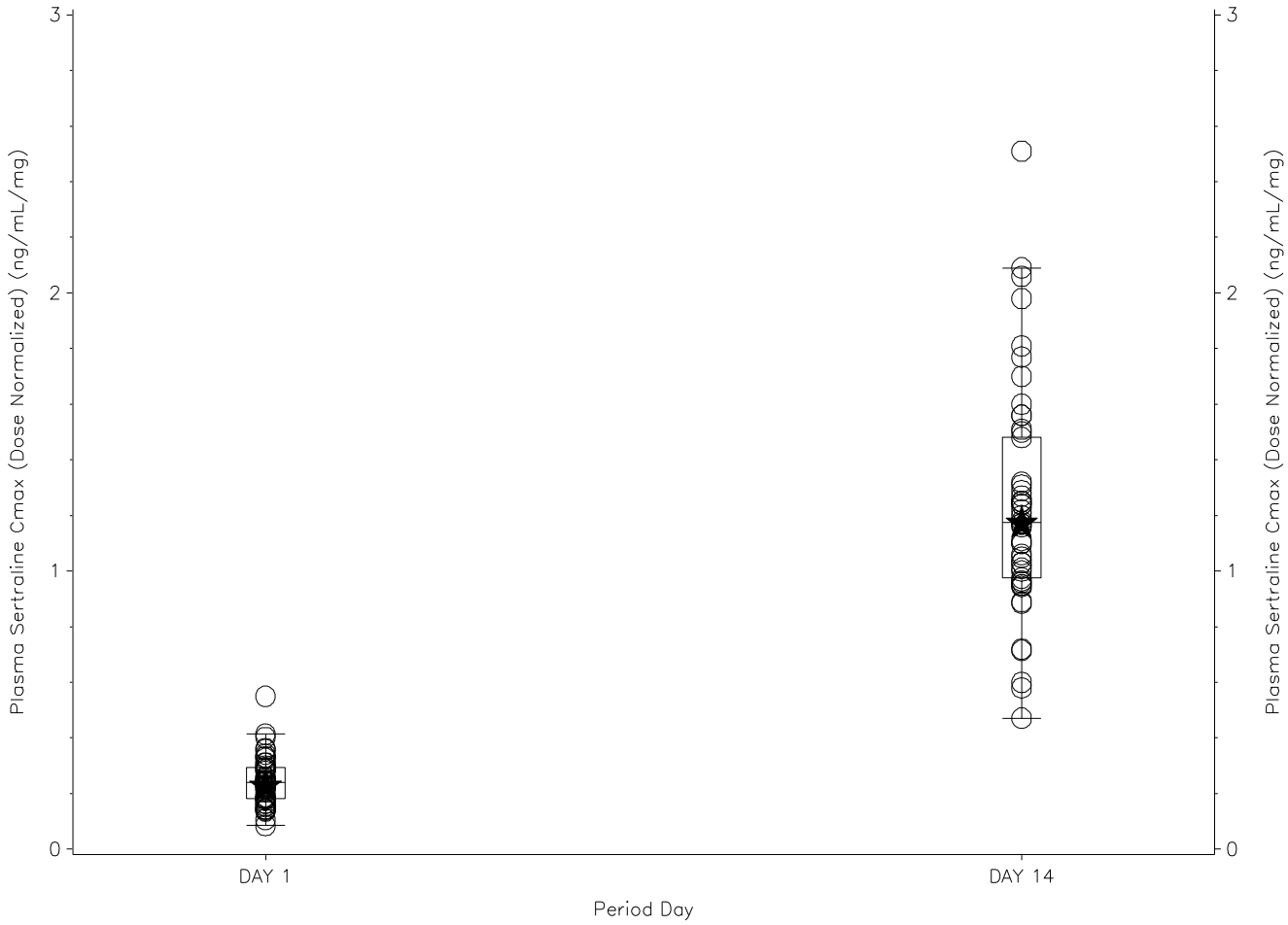
Parameter (units)	Sertraline (N = 50)[1]
MRAUC24	
N[2]	49
Geometric Mean	1.248
Geometric CV (%)	24
Arithmetic Mean	1.283
Standard Deviation	0.30751
Coefficient of Variation (%)	24
Median	1.220
Minimum	0.726
Maximum	2.12
Tmax (hr)	
N[2]	50
Median	8.00
Minimum	1.07
Maximum	12.1

[1]Total number of subjects in the treatment group in the indicated population.
[2]Number of subjects contributing to the summary statistics.

[redacted] Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (12:07)

Figure 14.4.3.2.1
SERTRALINE Protocol A0501104
Plot of Individual and Geometric Mean Plasma Sertraline Cmax (Dose Normalized)

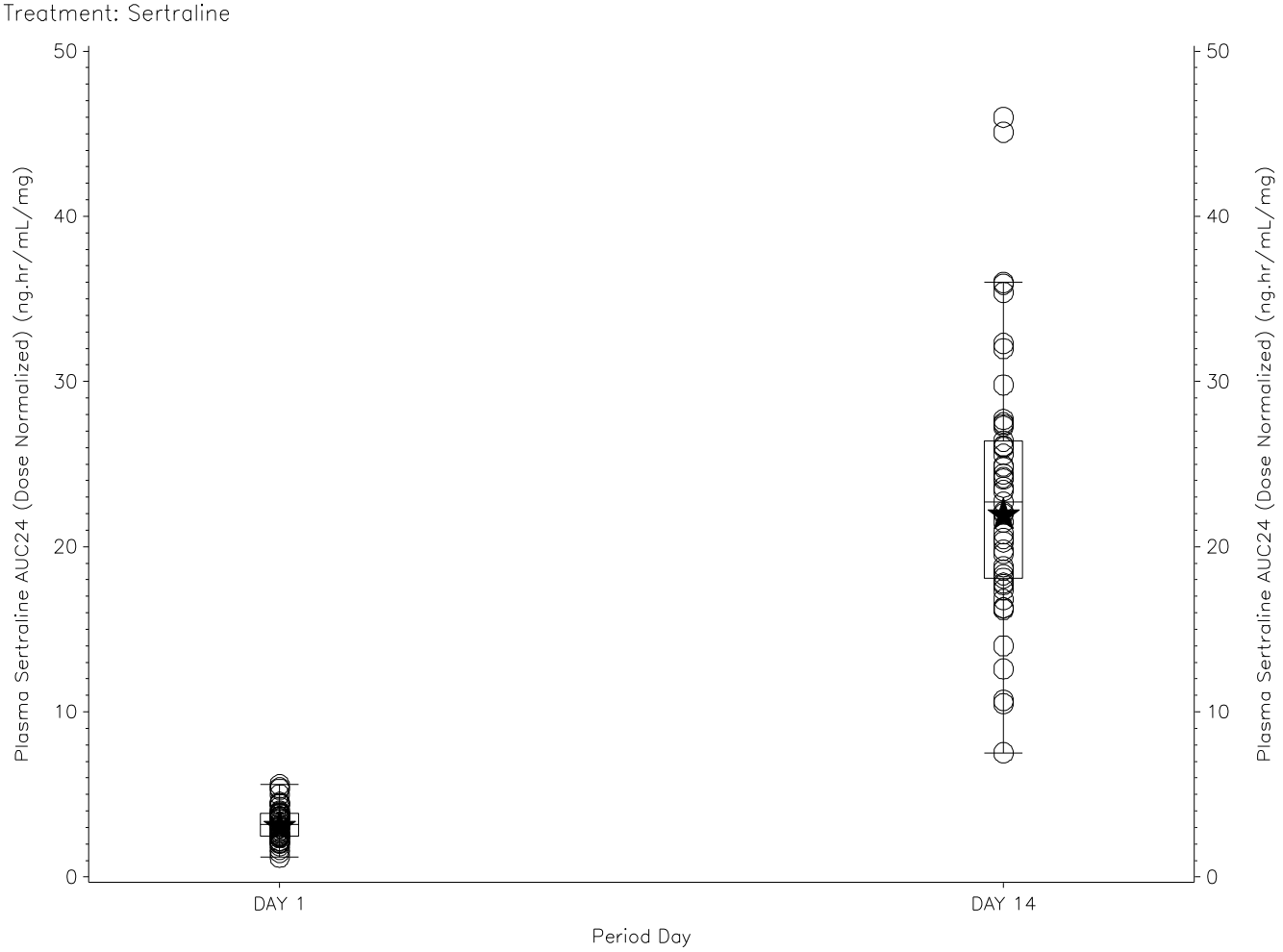
Treatment: Sertraline



Geometric mean is calculated for each period day.
Circles represent the individual values and star represents geometric mean.
Box plot provides Median and 25%/75% quartiles with whiskers to the last point within 1.5 times interquartile range.

[redacted] Source Data: Table 14.4.3.1.1 & Table 14.4.3.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:58)

Figure 14.4.3.2.2
SERTRALINE Protocol A0501104
Plot of Individual and Geometric Mean Plasma Sertraline AUC24 (Dose Normalized)



Geometric mean is calculated for each period day.
Circles represent the individual values and star represents geometric mean.
Box plot provides Median and 25%/75% quartiles with whiskers to the last point within 1.5 times interquartile range.

[redacted] Source Data: Table 14.4.3.1.1 & Table 14.4.3.1.2 Date of Reporting Dataset Creation: 01NOV2016 Date of Table Generation: 01NOV2016 (11:59)

15. REFERENCES

[redacted]