BRISTOL-MYERS SQUIBB COMPANY

SAXAGLIPTIN

Study Report Summary for Study CV181208

Bioequivalence Study of the Fixed Dosed Combination of 5 mg Saxagliptin and 1000 mg Metformin Extended Release Tablet Manufactured in Mt. Vernon, Indiana and Humacao, Puerto Rico Relative to the Fixed Dosed Combination Tablet Manufactured in Mt. Vernon, Indiana and Bioequivalence Study of the Fixed Dosed Combination of 5 mg Saxagliptin and 500 mg Metformin Extended Release Tablet Manufactured in Mt. Vernon, Indiana and Humacao, Puerto Rico Relative to the Fixed Dosed Combination Tablet Manufactured in Mt. Vernon, Indiana Administered to Healthy Subjects Under Fed Conditions

Indication:	Type 2 Diabetes Mellitus
Phase:	1
Study Initiation Date:	19-Jun-2013
Study Completion Date:	21-Jul-2013
Report Date:	25-Feb-2014
Document Control Number:	930076827

THIS STUDY WAS CONDUCTED IN ACCORDANCE WITH GOOD CLINICAL PRACTICE.

Name of Sponsor/Company: Bristol-Myers Squibb	Individual Study Table Referring to the Dossier	*(For National Authority Use Only)*
Name of Finished Product: Not applicable		
Name of Active Ingredient: saxagliptin (BMS-477118)		

SYNOPSIS

Study Report Summary for Study CV181208

TITLE OF STUDY: Bioequivalence Study of the Fixed Dosed Combination of 5 mg Saxagliptin and 1000 mg Metformin Extended Release Tablet Manufactured in Mt. Vernon, Indiana and Humacao, Puerto Rico Relative to the Fixed Dosed Combination Tablet Manufactured in Mt. Vernon, Indiana and Bioequivalence Study of the Fixed Dosed Combination of 5 mg Saxagliptin and 500 mg Metformin Extended Release Tablet Manufactured in Mt. Vernon, Indiana and Humacao, Puerto Rico Relative to the Fixed Dosed Combination Tablet Manufactured in Mt. Vernon, Indiana Administered to Healthy Subjects under Fed Conditions

PUBLICATIONS: Not applicable

STUDY PERIOD: Study Initiation Date: 19-Jun-2013 **CLINICAL PHASE:** 1

Study Completion Date: 21-Jul-2013

OBJECTIVES:

The primary objectives of the study were:

- To demonstrate bioequivalence of the 5 mg saxagliptin/1000 mg metformin extended release (XR) fixed dosed combination (FDC) manufactured in Mt. Vernon, Indiana and Humacao, Puerto Rico (5/1000 XR FDC [Mt. Vernon/Humacao]) to the 5 mg saxagliptin/1000 mg metformin XR FDC manufactured in Mt. Vernon, Indiana (5/1000 XR FDC [Mt. Vernon]) in healthy subjects under fed conditions.
- To demonstrate bioequivalence of the 5 mg saxagliptin/500 mg metformin XR FDC manufactured in Mt. Vernon, Indiana and Humacao, Puerto Rico (5/500 XR FDC [Mt. Vernon/Humacao]) to the 5 mg saxagliptin/500 mg metformin XR FDC manufactured in Mt. Vernon, Indiana (5/500 XR FDC [Mt. Vernon]) in healthy subjects under fed conditions.

The secondary objectives of the study were:

- To characterize the pharmacokinetics (PK) of the active metabolite of saxagliptin, 5-OH saxagliptin (BMS-510849) from the 5/1000 XR FDC (Mt. Vernon/Humacao) and the 5/1000 XR FDC (Mt. Vernon) in healthy subjects under fed conditions.
- To characterize the PK of 5-OH saxagliptin (BMS-510849) from the 5/500 XR FDC (Mt. Vernon/Humacao) and the 5/500 XR FDC (Mt. Vernon) in healthy subjects under fed conditions.
- To assess the safety and tolerability of the 5/1000 XR FDC (Mt. Vernon/Humacao) and the 5/1000 XR FDC (Mt. Vernon) in healthy subjects under fed conditions.
- To assess the safety and tolerability of the 5/500 XR FDC (Mt. Vernon/Humacao) and the 5/500 XR FDC (Mt. Vernon) in healthy subjects under fed conditions.

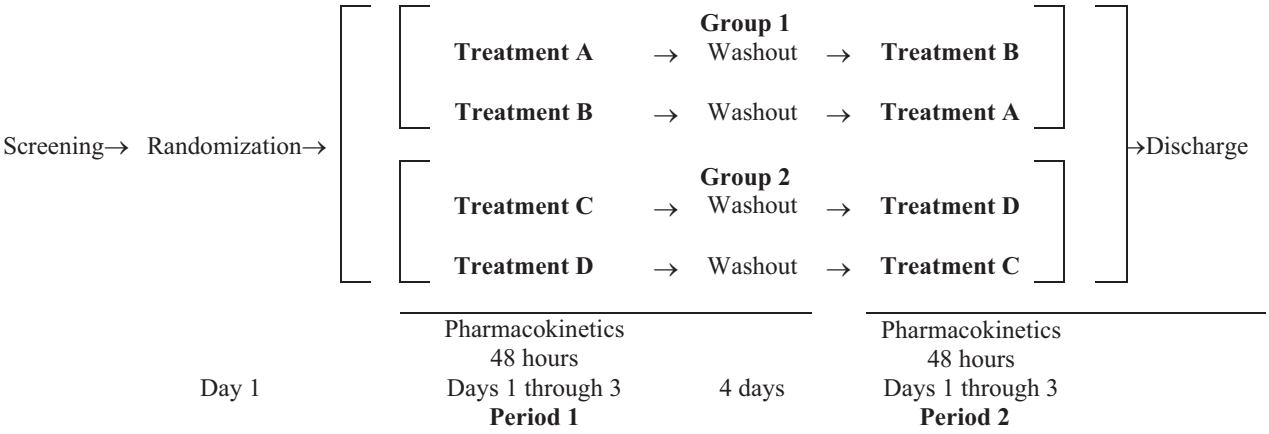
METHODOLOGY: This was a 2-group (Group 1 and Group 2), open-label, randomized, 2-treatment (per group), crossover study in healthy subjects. In each group, subjects were randomly assigned to 1 of 2 treatment sequences: AB or BA for Group 1 and CD or DC for Group 2.

Subjects underwent screening evaluations within 21 days of Day 1. Eligible subjects checked into the clinical pharmacology unit (CPU) on Day -1 and remained confined to the CPU until after the final safety blood draw on the discharge day. Subjects were randomly assigned to the sequence of treatments on Day 1. There was a 4-day washout between treatments; washout began immediately after the study drug was administered.

Subjects fasted for approximately 10 hours before the start of breakfast on dosing days (Day 1 of each period). Study drug was administered to subjects within 5 minutes of completing a standard meal (breakfast) in the morning. Subjects started the standard meal 30 minutes before study drug administration, were required to eat the meal within 25 minutes or less, and received a standard lunch 4 hours after study drug administration. The start and finish time of the meal was recorded in the electronic case report form. The standard meal (breakfast) consisted of 324 total kcal (11.1% protein, 10.5% fat, and 78.4% carbohydrate).

Safety assessments were performed throughout the study via adverse event (AE) monitoring, clinical laboratory testing, vital sign measurements, physical examination (PE) findings, 12-lead electrocardiogram (ECG) results, and physical measurements.

A summary of the study design is presented in the following figure.



Treatment A: Single oral dose of 5/1000 extended release (XR) fixed dosed combination (FDC) (Mt. Vernon/Humacao); fed (standard meal)

Treatment B: Single oral dose of 5/1000 XR FDC (Mt. Vernon); fed (standard meal)

Treatment C: Single oral dose of 5/500 XR FDC (Mt. Vernon/Humacao); fed (standard meal)

Treatment D: Single oral dose of 5/500 XR FDC (Mt. Vernon); fed (standard meal)

NUMBER OF SUBJECTS (Planned and Analyzed): Fifty-six subjects (28 per group; 14 per sequence) were planned for and received study drug. All 56 subjects completed the study per protocol and were included in the analysis.

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION: Healthy male and female subjects (as determined by medical history, PEs, vital sign measurements, 12-lead ECGs, and clinical laboratory evaluations), 18 to 45 years of age, inclusive, with body mass index (BMI) of 18.0 to 30.0 kg/m^2, inclusive, were eligible to participate in the study. Women of childbearing potential were not nursing or pregnant and were required to use an acceptable method of contraception for at least 4 weeks before dosing. All women had a negative pregnancy test within 24 hours before the start of study drug.

TEST PRODUCT, DOSE AND MODE OF ADMINISTRATION, DURATION OF TREATMENT, BATCH NUMBERS:

Saxagliptin/metformin XR FDC (Mt. Vernon/Humacao), 5 mg/1000 mg tablet, oral administration, single dose, Batch No. 1055

Saxagliptin/metformin XR FDC (Mt. Vernon/Humacao), 5 mg/500 mg tablet, oral administration, single dose, Batch No. 1004

REFERENCE THERAPY, DOSE AND MODE OF ADMINISTRATION, DURATION OF TREATMENT, BATCH NUMBERS:

Saxagliptin/metformin XR FDC (Mt. Vernon), 5 mg/1000 mg tablet, oral administration, single dose, Batch No. 1155

Saxagliptin/metformin XR FDC (Mt. Vernon), 5 mg/500 mg tablet, oral administration, single dose, Batch No. 1108

CRITERIA FOR EVALUATION:

Safety: Safety assessments, at selected timepoints, were based on medical review of AE reports and the results of clinical laboratory tests, vital sign measurements, PEs, and 12-lead ECGs. The incidence of observed AEs was tabulated and reviewed for potential significance and clinical importance.

Pharmacokinetics: The primary PK endpoints were the point estimates and 90% confidence intervals (CIs) for the ratio of geometric means for the following: maximum observed plasma concentration (Cmax), area under the plasma concentration-time curve (AUC) from time 0 to the time of the last quantifiable concentration (AUC(0-T)), and AUC from time 0 extrapolated to infinite time (AUC(INF)) for saxagliptin and metformin in the 5/1000 XR FDC (Mt. Vernon/Humacao) and 5/1000 XR FDC (Mt. Vernon) and the point estimates and 90% CIs for the ratio of geometric means for the following: Cmax, AUC(0-T), and AUC(INF) for saxagliptin and metformin in the 5/500 XR FDC (Mt. Vernon/Humacao) and 5/500 XR FDC (Mt. Vernon).

The secondary PK endpoints, for saxagliptin and metformin (Treatments A, B, C, and D), were time of maximum observed plasma concentration (Tmax) and terminal plasma half-life (T-HALF) and for 5-OH saxagliptin (Treatments A, B, C, and D) were Cmax, Tmax, T-HALF, AUC(0-T), and AUC(INF).

Serial blood samples for metformin, saxagliptin, and 5-OH saxagliptin were collected from predose through 48 hours after dosing (Treatments A, B, C, and D).

STATISTICAL CONSIDERATIONS:

Sample Size: Bioequivalence of the 5/1000 XR FDC (Mt. Vernon/Humacao) (test) relative to the 5/1000 XR FDC (Mt. Vernon) (reference) was concluded if the 90% CIs for the ratios of geometric means, test:reference, were contained within the bioequivalence interval from 80% to 125% for Cmax, AUC(0-T), and AUC(INF) of both saxagliptin and metformin. If the true ratio of geometric means was 100%, data from 24 subjects (12 per sequence) would provide at least 97% power for Cmax and at least 99% power for AUC of saxagliptin, and at least 98% power for both Cmax and AUC of metformin to conclude that the test 5/1000 XR FDC (Mt. Vernon/Humacao) was bioequivalent to the reference 5/1000 XR FDC (Mt. Vernon). In addition, the overall power of the study, adjusting for multiple comparisons and assuming complete independence of each statistical test, was at least 90%.

If the true ratio of geometric means was between 95% and 105%, data from 24 subjects (12 per sequence) would provide at least 91% power for Cmax and at least 99% power for AUC of saxagliptin, and at least 94% power for both Cmax and AUC of metformin to conclude that the test 5/1000 XR FDC (Mt. Vernon/Humacao) was bioequivalent to the reference 5/1000 XR FDC (Mt. Vernon). In addition, the overall power of the study, adjusting for multiple comparisons and assuming complete independence of each statistical test, was at least 80%.

These calculations used the approach described by Diletti et al and assumed that both log(Cmax) and log(AUC) of saxagliptin and metformin were normally distributed with intrasubject coefficients of variation (%CV) no greater than 19.4% and 6.3% for saxagliptin (largest %CVs for Cmax and AUC(INF) for saxagliptin as an FDC observed in studies CV181111 and CV181112) and no greater than 17.7% and 18.1% for metformin (largest %CVs for Cmax and AUC(INF) for metformin as an FDC observed in studies CV181111 and CV181112), respectively.

The above also applied to the bioequivalence assessment of 5/500 XR FDC tablet (Mt. Vernon/Humacao) (test) relative to 5/500 XR FDC (Mt. Vernon) (reference).

To allow for possible dropouts, an additional 4 subjects (2 per sequence) were enrolled in each group for a total of 28 subjects per group.

Pharmacokinetics: To demonstrate bioequivalence, a linear mixed-effects model with treatment and period as fixed effects and measurement within each subject as repeated measures was performed on $\log_e$-transformed values of Cmax, AUC(0-T), and AUC(INF) of saxagliptin and metformin following administration of saxagliptin and metformin in the 5/1000 XR FDC (Mt. Vernon/Humacao) and 5/1000 XR FDC (Mt. Vernon) or saxagliptin and metformin in the 5/500 XR FDC (Mt. Vernon/Humacao) and 5/500 XR FDC (Mt. Vernon). Kenward-Rogers degrees of freedom were specified in the model. Estimation of the variance covariance was based on an unstructured R matrix assuming no common variances or covariances. Point estimates and 90% CIs for treatment differences on the $\log_e$ scale were exponentiated to obtain point estimates and 90% CIs for ratios of geometric means on the original scale. In the comparison, the XR FDC (Mt. Vernon) was used as the reference treatment. Group 1 and Group 2 were analyzed in separate models. No adjustments were made for multiplicity.

Safety: Adverse events were listed and tabulated by system organ class, preferred term (PT), and treatment. Clinical laboratory test results, vital sign measurements, and 12-lead ECG results and corresponding change from baseline values were listed and summarized by treatment. Any abnormal PE findings were also listed. Values for clinical laboratory tests and 12-lead ECG results outside the prespecified criteria were listed and summarized. Electrocardiogram recordings were evaluated by the investigator and abnormalities, if present, were listed.

SUMMARY OF RESULTS:

Disposition and Baseline/Demographic Characteristics:

Subject disposition is summarized in Table 1.

Table 1: Disposition of Subjects

	Total
Number of subjects enrolled	121
Number of subjects randomized (%)[a]	56 (46.3)
Number of subjects not randomized (%)[a]	65 (53.7)
Reason for not being randomized, number of subjects (%)[a]	
Subject withdrew consent	6 (5.0)
Subject no longer met study criteria	52 (43.0)
Other	7 (5.8)
Number of subjects completing the study (%)[b]	56 (100.0)
Number of subjects completing in Group 1 (%)[c]	28 (100.0)
Number of subjects completing in Group 2 (%)[d]	28 (100.0)

Abbreviations: % = percentage of subjects

[a] Percentage is based on the number of subjects enrolled.

[b] Percentage is based on the number of subjects randomized.

[c] Percentage is based on the number of subjects randomized in Group 1.

[d] Percentage is based on the number of subjects randomized in Group 2.

Subject demographics and baseline characteristics are summarized in Table 2.

Table 2: Summary of Baseline Demographic Characteristics (All Treated Population)

Variable	Group 1 Total (N = 28)	Group 2 Total (N = 28)	Total (N = 56)
Age (years)			
Mean (SD)	30.5 (7.84)	30.8 (7.57)	30.6 (7.64)
Median (min, max)	29.5 (19, 45)	29.0 (20, 44)	29.0 (19, 45)
Age categorization, n (%)			
<65 years	28 (100.0)	28 (100.0)	56 (100.0)
≥65 years	0	0	0
Gender, n (%)			
Male	16 (57.1)	21 (75.0)	37 (66.1)
Female	12 (42.9)	7 (25.0)	19 (33.9)
Race, n (%)			
American Indian / Alaska Native	0	1 (3.6)	1 (1.8)
Asian	1 (3.6)	0	1 (1.8)
Black / African American	9 (32.1)	5 (17.9)	14 (25.0)
White	18 (64.3)	22 (78.6)	40 (71.4)
Ethnicity, n (%)			
Hispanic / Latino	14 (50.0)	19 (67.9)	33 (58.9)
Not Hispanic / Latino	14 (50.0)	9 (32.1)	23 (41.1)

Abbreviations: max = maximum; m = minimum; N = number of subjects; n = number of nonmissing observations; % = percentage of subjects; SD = standard deviation

Group 1 includes subjects randomized to treatment sequence AB or BA.

Group 2 includes subject randomized to treatment sequence CD or DC.

Baseline physical measurements are summarized in Table 3.

Table 3: Summary of Baseline Physical Measurements (All Treated Population)

Variable	Group 1 Total (N = 28)	Group 2 Total (N = 28)	Total (N=56)
Height (cm)			
Mean (SD)	168.79 (12.867)	171.83 (10.872)	170.31 (11.902)
Median	168.80	172.15	170.95
Q1, Q3	158.40, 178.75	165.80, 178.70	163.30, 178.75
Weight (kg)			
Mean (SD)	71.98 (14.374)	78.90 (11.634)	75.44 (13.419)
Median	69.55	81.05	74.90
Q1, Q3	62.75, 79.30	69.85, 83.95	65.10, 83.20
Body mass index (kg/m^2)			
Mean (SD)	25.11 (2.865)	26.64 (2.273)	25.88 (2.677)
Median	25.50	26.90	26.20
Q1, Q3	23.00, 27.80	24.95, 28.75	23.20, 28.50

Abbreviations: N = number of subjects; Q = quartile; SD = standard deviation

Baseline height was assessed at screening, and baseline weight and body mass index were assessed on Day -1.

Group 1 includes subjects randomized to treatment sequence AB or BA.

Group 2 includes subject randomized to treatment sequence CD or DC.

Safety Results:

A total of 121 subjects were enrolled, and 56 subjects received study drug. There were no deaths, serious AEs (SAEs), or AEs leading to discontinuation.

Overall, 9 of 56 (16.1%) subjects reported at least 1 AE. In Group 1, 5 of 28 (17.9%) subjects had at least 1 AE, and in Group 2, 4 of 28 (14.3%) subjects had at least 1 AE. No AEs were reported in ≥5% of subjects. Headache was reported in 2 of 56 (3.6%) subjects, and the remaining AEs were reported by only 1 (1.8%) subject each during the study.

Eight of 56 (14.3%) subjects had AEs of mild intensity, and 1 (1.8%) subject had an AE of moderate intensity (headache following Treatment D).

Three of 56 (5.4%) subjects had AEs that were considered by the investigator to be related to study drug. These AEs included lightheadedness (which was incorrectly reported as orthostatic hypotension as the subject's blood pressure was within normal limits and did not meet the criteria for orthostatic hypotension) during Treatment A, balance disorder during Treatment A, and fatigue during Treatment D.

All AEs resolved by the end of the study with no sequelae.

There were no clinically significant findings in vital signs, ECGs, or PEs during the study.

An overall AE summary is presented in Table 4.

Table 4: Overall Adverse Event Summary (All Treated Population)

	Treatment A N=28 (n [%])	Treatment B N=28 (n [%])	Treatment C N=28 (n [%])	Treatment D N=28 (n [%])	Group 1 Total N=28 (n [%])	Group 2 Total N=28 (n [%])
Total subjects with an AE	4 (14.3)	1 (3.6)	1 (3.6)	3 (10.7)	5 (17.9)	4 (14.3)
Total subjects with an AE with an incidence of ≥5%	0	0	0	0	0	0
Total subjects with an AE leading to discontinuation	0	0	0	0	0	0
Total subjects with an SAE	0	0	0	0	0	0
Total subjects with an AE by intensity						
Mild	4 (13.4)	1 (3.6)	1 (3.6)	2 (7.1)	5 (17.9)	3 (10.7)
Moderate	0	0	0	1 (3.6)	0	1 (3.6)
Severe	0	0	0	0	0	0
Very severe	0	0	0	0	0	0

Abbreviations: AE = adverse event; N = number of subjects; n = number of nonmissing observations; % = percentage of subjects; SAE = serious adverse event

Treatment: A = 5/1000 XR FDC (Mt. Vernon/Humacao); B = 5/1000 XR FDC (Mt. Vernon); C = 5/500 XR FDC (Mt. Vernon/Humacao); D = 5/500 XR FDC (Mt. Vernon)

Group 1 includes subjects randomized to sequence AB or BA.

Group 2 includes subjects randomized to sequence CD or DC.

Adverse events are summarized by PT and treatment in Table 5.

Table 5: Adverse Event Summary by Preferred Term and Treatment (All Treated Population)

Preferred term	Treatment A N=28 (n [%])	Treatment B N=28 (n [%])	Treatment C N=28 (n [%])	Treatment D N=28 (n [%])	Group 1 Total N=28 (n [%])	Group 2 Total N=28 (n [%])
Total subjects with an AE	4 (14.3)	1 (3.6)	1 (3.6)	3 (10.7)	5 (17.9)	4 (14.3)
Abdominal pain lower	1 (3.6)	0	0	0	1 (3.6)	0
Balance disorder	1 (3.6)	0	0	0	1 (3.6)	0
Fatigue	0	0	0	1 (3.6)	0	1 (3.6)
Headache	0	1 (3.6)	0	1 (3.6)	1 (3.6)	1 (3.6)
Muscle spasms	1 (3.6)	0	0	0	1 (3.6)	0
Orthostatic hypotension[a]	1 (3.6)	0	0	0	1 (3.6)	0
Vessel puncture site haematoma	0	0	1 (3.6)	0	0	1 (3.6)
Vessel puncture site pain	0	0	0	1 (3.6)	0	1 (3.6)

Abbreviations: AE = adverse event; N = number of subjects; n = number of nonmissing observations; % = percentage of subjects

Treatment: A = 5/1000 XR FDC (Mt. Vernon/Humacao); B = 5/1000 XR FDC (Mt. Vernon); C = 5/500 XR FDC (Mt. Vernon/Humacao); D = 5/500 XR FDC (Mt. Vernon)

Group 1 includes subjects randomized to sequence AB or BA.

Group 2 includes subjects randomized to sequence CD or DC.

[a] This was lightheadedness in a subject whose blood pressure was within normal limits and did not meet the criteria for orthostatic hypotension. This was incorrectly reported as orthostatic hypotension.

Pharmacokinetic Results:

The statistical analyses demonstrating bioequivalence based on the PK of saxagliptin are presented for Group 1 and Group 2 in Tables 6 and 7, respectively.

Table 6: Statistical Analysis of Saxagliptin Pharmacokinetic Parameters for Group 1 (PK Evaluable Population)

PK Parameter	Treatment and Comparison	Adjusted Geometric Mean	90% Confidence Interval
Cmax (ng/mL)	A	26.3	(23.3, 29.5)
	B	25.4	(22.7, 28.5)
	A versus B[a]	1.033	(0.954, 1.120)
AUC(0-T) (ng*h/mL)	A	96.5	(90.8, 102)
	B	92.6	(86.7, 99.0)
	A versus B[a]	1.041	(1.007, 1.076)
AUC(INF) (ng*h/mL)	A	98.7	(93.2, 105)
	B	94.2	(88.2, 101)
	A versus B[a]	1.048	(1.010, 1.087)

Treatment: A = 5/1000 XR FDC (Mt. Vernon/Humacao); B = 5/1000 XR FDC (Mt. Vernon)

[a] Adjusted geometric mean ratio for Treatment A versus Treatment B comparison

Table 7: Statistical Analysis of Saxagliptin Pharmacokinetic Parameters for Group 2 (PK Evaluable Population)

PK Parameter	Treatment and Comparison	Adjusted Geometric Mean	90% Confidence Interval
Cmax (ng/mL)	C	25.9	(23.1 , 29.0)
	D	24.6	(21.8, 27.7)
	C versus D[a]	1.055	(0.969, 1.148)
AUC(0-T) (ng*h/mL)	C	106	(98.6, 114)
	D	104	(96.2, 112)
	C versus D[a]	1.023	(0.997, 1.051)
AUC(INF) (ng*h/mL)	C	108	(100, 116)
	D	106	(98.1, 114)
	C versus D[a]	1.021	(0.995, 1.049)

Treatment: C = 5/500 XR FDC (Mt. Vernon/Humacao); D = 5/500 XR FDC (Mt. Vernon)

[a] Adjusted geometric mean ratio for Treatment C versus Treatment D comparison

The statistical analyses demonstrating bioequivalence based on the PK of metformin are presented for Group 1 and Group 2 in Tables 8 and 9, respectively.

Table 8: Statistical Analysis of Metformin Pharmacokinetic Parameters for Group 1 (PK Evaluable Population)

PK Parameter	Treatment and Comparison	Adjusted Geometric Mean	90% Confidence Interval
Cmax (ng/mL)	A	1043	(966, 1125)
	B	1080	(995, 1173)
	A versus B[a]	0.965	(0.906, 1.028)
AUC(0-T) (ng*h/mL)	A	9610	(8788, 10508)
	B	9016	(8220, 9888)
	A versus B[a]	1.066	(0.984, 1.154)
AUC(INF) (ng*h/mL)	A	9832	(9026, 10708)
	B	9213	(8407, 10096)
	A versus B[a]	1.067	(0.989, 1.151)

Treatment: A = 5/1000 XR FDC (Mt. Vernon/Humacao); B = 5/1000 XR FDC (Mt. Vernon)

[a] Adjusted geometric mean ratio for Treatment A versus Treatment B comparison

Table 9: Statistical Analysis of Metformin Pharmacokinetic Parameters for Group 2 (PK Evaluable Population)

PK Parameter	Treatment and Comparison	Adjusted Geometric Mean	90% Confidence Interval
Cmax (ng/mL)	C	620	(572, 671)
	D	595	(549, 645)
	C versus D[a]	1.041	(0.982, 1.104)
AUC(0-T) (ng*h/mL)	C	5869	(5310, 6487)
	D	5331	(4785, 5939)
	C versus D[a]	1.101	(1.032, 1.175)
AUC(INF) (ng*h/mL)	C	5947	(5383, 6569)
	D	5399	(4849, 6010)
	C versus D[a]	1.102	(1.033, 1.174)

Treatment: C = 5/500 XR FDC (Mt. Vernon/Humacao); D = 5/500 XR FDC (Mt. Vernon)

[a] Adjusted geometric mean ratio for Treatment C versus Treatment D comparison

DATE OF STUDTY REPORT SUMMARY: 25-Feb-2014