SYNOPSIS

Final Clinical Study Report for Study CV181169

TITLE OF STUDY: A Multicenter, Randomized, Double-Blind, Active-Controlled, Parallel Group, Phase 3 Trial to Evaluate the Safety and Efficacy of Add-On Therapy with Saxagliptin and Dapagliflozin Added to Metformin Compared to Add-On Therapy with Saxagliptin in Combination with Metformin or Dapagliflozin in Combination with Metformin in Subjects with Type 2 Diabetes Who Have Inadequate Glycemic Control on Metformin Alone

INVESTIGATORS/STUDY CENTERS: 534 subjects treated at 145 sites in 8 countries

PUBLICATIONS: Not applicable.

STUDY PERIOD: Study Initiation Date: 05-Jun-2012 **CLINICAL PHASE:** 3
Study Completion Date: 17-Jan-2014

OBJECTIVES:

Primary Objective: To compare the mean change from baseline in glycated hemoglobin (HbA1c) achieved with concurrent addition of saxagliptin and dapagliflozin to metformin (referred to in this report as saxagliptin + dapagliflozin + metformin) versus (vs.) the addition of placebo and saxagliptin to metformin (referred to in this report as saxagliptin + metformin) and vs. the addition of placebo plus dapagliflozin to metformin (referred to in this report as dapagliflozin + metformin) after 24 weeks of double-blind treatment.

Secondary Objectives:

- To compare the mean change from baseline achieved with saxagliptin + dapagliflozin + metformin vs. saxagliptin + metformin and vs. dapagliflozin + metformin after 24 weeks of double-blind treatment in:
  1) 2-hour post prandial glucose from a liquid meal tolerance test (MTT)
  2) Fasting plasma glucose (FPG)
- To compare the proportion of subjects achieving therapeutic glycemic response, defined as HbA1c < 7.0%, after 24 weeks of double-blind treatment with saxagliptin + dapagliflozin + metformin vs. saxagliptin + metformin and vs. dapagliflozin + metformin.
- To compare the mean change in total body weight achieved with saxagliptin + dapagliflozin + metformin vs. saxagliptin + metformin.

Other Objectives:

- To assess the percent of subjects who required glycemic rescue or discontinuation of study treatment for lack of efficacy with saxagliptin + dapagliflozin + metformin vs. saxagliptin + metformin and vs. dapagliflozin + metformin after up to 24 weeks of double-blind treatment.
- To assess the time to glycemic rescue or discontinuation for lack of efficacy with saxagliptin + dapagliflozin + metformin vs. saxagliptin + metformin and vs. dapagliflozin + metformin after up to 24 weeks of double-blind treatment.

- To assess the mean change from baseline in area under the curve (AUC) of glucose, AUC insulin, AUC C-peptide, and AUC glucagon obtained during a MTT with saxagliptin + dapagliflozin + metformin vs. saxagliptin + metformin and vs. dapagliflozin + metformin after 24 weeks of double-blind treatment.
- To assess the mean percent change from baseline in fasting serum lipids (Total cholesterol (Total-C), Low density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG)) with saxagliptin + dapagliflozin + metformin vs. saxagliptin + metformin and vs. dapagliflozin + metformin during the double-blind treatment period.

Safety and tolerability:

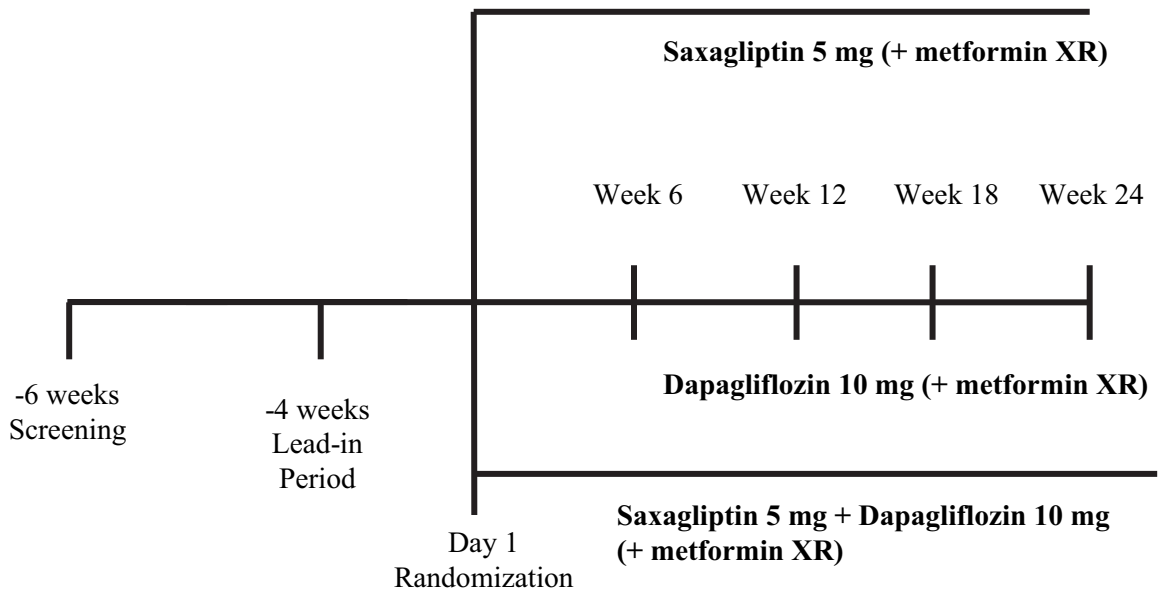
To evaluate the safety and tolerability of saxagliptin + dapagliflozin + metformin vs. saxagliptin + metformin and vs. dapagliflozin + metformin based on adverse events (AEs), clinical laboratory tests, electrocardiograms (ECGs), vital signs, and physical exam findings**.**

METHODOLOGY:

This was a Phase 3, double-blind, randomized, placebo-controlled study in 534 subjects with Type 2 diabetes mellitus (T2DM) and with a screening HbA1c > 8% and ≤ 12%, who were considered inadequately controlled on metformin monotherapy. This study compared the mean change from baseline in HbA1c achieved with saxagliptin + dapagliflozin + metformin vs. saxagliptin + metformin and vs. dapagliflozin + metformin after 24 weeks of double-blind treatment. A liquid meal tolerance test (MTT) was performed on Day 1 and at the study treatment termination visit/Week 24.

Figure 1 shows the study schematic for CV181169.

Figure -1: Study Design for CV181169



Subjects on metformin IR and XR were switched to the nearest multiple of metformin XR 500-mg tablets at Week -4. During the double-blind treatment period, eligible subjects entered the randomized, double-blind treatment period on Day 1. Subjects were followed for a total of 24 weeks on double-blind study medication. Scheduled visits occurred at Weeks 6, 12, 18 and 24.

Subjects with lack of glycemic control from Week 6 to 24 were eligible to receive open-label rescue medication, in addition to their current double blind treatment. All rescue decisions were based on central laboratory FPG and

repeat, confirmatory FPG. It was mandatory for subjects who met rescue criteria in the double-blind treatment period to first complete the rescue visit procedures before receiving open-label rescue medication in order to ensure important trial endpoint measurements were collected. Following completion of the rescue visit, subjects were given open-label antidiabetic rescue medication (insulin or other antidiabetic agents except glucagon-like peptide-1 (GLP-1) analogs, other DPP4/SGLT2 inhibitors or metformin) to be initiated at the lowest starting dose and titrated in accordance with the approved product label in the applicable country at the discretion of the Investigator, in addition to their double-blinded study medication. Rescued subjects then continued in the double-blind treatment period according to their original visit schedule.

NUMBER OF SUBJECTS (Planned and Analyzed):

Planned to Enroll: 1032 subjects; **Planned to Randomize:** 516 subjects. **Enrolled:** 1282 subjects; **Randomized and treated:** 534 subjects were randomized to three treatment arms: 179 in the saxagliptin + dapagliflozin + metformin treatment group, 176 saxagliptin + metformin treatment group, and 179 in the dapagliflozin + metformin treatment group. **Completed treatment:** 490 subjects. **Completed the 24-week treatment period:** 493 subjects.

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION:

The main inclusion criteria to be eligible to participate in the study were based on the following:

1) Men and women, age ≥ 18 years at time of screening visit.
2) Subjects with T2DM with inadequate glycemic control defined as central laboratory HbA1c ≥ 8.0 and ≤ 12.0 % at the screening visit.
3) Stable metformin therapy for at least 8 weeks prior to screening at a dose ≥ 1500 mg per day.
4) C-peptide ≥ 1.0 ng/mL (0.34 nmol/L) at screening visit.
5) Body Mass Index (BMI) ≤ 45.0 kg/m^2 at the screening visit.
6) Women of childbearing potential (WOCBP) were required to use an acceptable method of contraception to avoid pregnancy throughout the study in such a manner that the risk of pregnancy was minimized. WOCBP needed to have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG) within 24 hours prior to the start of study treatment. Sexually active fertile men were required to use effective birth control if their partners were WOCBP.

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

- Saxagliptin 5-mg tablets (Batch numbers: 1C75251 and 1C75252) and dapagliflozin 10-mg tablets (Batch number: 2C77752), administered orally once daily for the 24-week double-blind treatment period.
- Open-label metformin 500-mg tablets, administered orally (Note: Subjects who entered the study on metformin XR had their dose modified if it was not based on 500-mg metformin XR tablets; Subjects on metformin IR were switched to open-label 500-mg metformin XR tablets).

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

- Placebo matching saxagliptin, administered orally (Batch numbers: 0B56792 and 1C75260).
- Placebo matching dapagliflozin, administered orally (Batch number:1K69723).

CRITERIA FOR EVALUATION:

Efficacy: To evaluate saxagliptin + dapagliflozin + metformin vs. saxagliptin + metformin and vs. dapagliflozin + metformin after 24 weeks of double-blind treatment for the following criteria:

1) The mean change from baseline in HbA1c at Week 24.

2) Mean change from baseline in 2-hour post-prandial glucose during a MTT at Week 24.
3) Mean change from baseline in FPG at Week 24.
4) Percent of subjects achieving a therapeutic glycemic response, defined as a HbA1c < 7.0% at Week 24.
5) Mean change in total body weight.
6) Glycemic rescue: The percent of subjects who required glycemic rescue or discontinuation of study treatment for lack of efficacy up to Week 24, and the time to glycemic rescue or discontinuation for lack of efficacy in the double-blind treatment period.
7) Mean change from baseline in AUC glucose, AUC insulin, AUC C-peptide and AUC glucagon obtained during the MTT at Week 24.
8) Mean percent change from baseline in fasting serum lipids (Total-C, LDL-C, HDL-C, TG) during the double-blind treatment period.
9) Hypoglycemic events, AEs, ECGs, serum creatinine.

Safety Criteria: Evaluate the safety and tolerability of the combination of saxagliptin and dapagliflozin during the 24-week double-blind treatment period based on AEs, and clinical laboratory tests, ECGs, vital signs, and physical examination findings.

STATISTICAL CONSIDERATIONS:

Sample Size and Power:

The mean change from baseline in HbA1c at Week 24 was assessed comparing the saxagliptin + dapagliflozin + metformin treatment group vs. the saxagliptin + metformin treatment group and vs. the dapagliflozin + metformin treatment group. The min test approach of Laska and Meisner was implemented to test saxagliptin + dapagliflozin + metformin vs. saxagliptin + metformin and vs. dapagliflozin + metformin. Statistical significance of the primary endpoint would be claimed if the p-values for both comparisons were significant at the 2-sided, 0.05 significance level.

Power calculations for longitudinal repeated measures analyses depend on many factors, including the pattern of drop out over time and correlations among the various time points included in the model. The choice of these parameters affect any estimates of power, and their true values may not be known. Based on comparisons of results of longitudinal repeated measures analyses and analysis of covariance using last observation carried forward (ANCOVA with LOCF) from previous diabetes trials, the estimated standard errors of the treatment differences were similar between analyses. Therefore, power calculations were based on ANCOVA with LOCF, with the expectation that this would provide a good estimate of the power for the primary analysis using a longitudinal repeated measures model.

With 163 subjects per treatment group, there was 90% power to detect a difference in mean HbA1c of 0.4% between the saxagliptin + dapagliflozin + metformin treatment group vs. the saxagliptin + metformin treatment group and vs. the dapagliflozin + metformin treatment group, assuming a standard deviation of 1.0%. Assuming that 5% of subjects would not have a post-baseline assessment, a total of approximately 516 subjects (172 subjects per treatment arm) needed to be randomized. Assuming that 50% of screened subjects would fail to meet screening criteria, a total of 1032 subjects needed to be screened.

SUMMARY OF RESULTS:

Table -1 shows the subject disposition for the study. The study had a high completion rate. Two subjects discontinued due to AEs.

Subject Disposition:

Table -1: CV181169 - Subject Disposition

	Saxa + Dapa +Met	Saxa + Met	Dapa + Met	Total
No. of Subjects Enrolled	-	-	-	1282
No. of Subjects Randomized and Treated	179	176	179	534

Table -1: CV181169 - Subject Disposition

	Saxa + Dapa +Met	Saxa + Met	Dapa + Met	Total
Completed, n (%)	169 (94.4)	161 (91.5)	160 (89.4)	490 (91.8)
Discontinued	10 (5.6)	15 (8.5)	19 (10.6)	44 (8.2)
Adverse event	1 (0.6)	0	1 (0.6)	2 (0.4)
Subject Request	1 (0.6)	0	2 (1.1)	3 (0.6)
Withdrew Consent	1 (0.6)	8 (4.5)	6 (3.4)	15 (2.8)
Poor/Non-compliance	0	1 (0.6)	0	1 (0.2)
Lost to Follow-up	5 (2.8)	6 (3.4)	8 (4.5)	19 (3.6)
Pregnancy	1 (0.6)	0	1 (0.6)	2 (0.4)
Other	1 (0.6)	0	1 (0.6)	2 (0.4)

Table -2 summarizes demographics and baseline characteristics for the randomized subjects. Study populations were similar across treatment groups.

Table -2: CV181169 - Demographics and Baseline Characteristics

	Saxa + Dapa +Met (N=179)	Saxa + Met (N=176)	Dapa + Met (N=179)	Total (N=534)
Age (mean (SD) years, %)	53.4 (9.8)	54.6 (9.6)	53.5 (9.7)	53.8 (9.7)
< 65 years old	160 (89.4)	148 (84.1)	158 (88.3)	466 (87.3)
≥ 65 years old	19 (10.6)	28 (15.9)	21 (11.7)	68 (12.7)
≥ 75 years old	2 (1.1)	0	1 (0.6)	3 (0.6)
Weight (mean (SD) kg)	87 (18)	88 (19)	86 (19)	87 (18)
Body Mass Index (mean (SD) kg/m^2)	31.76	31.80	31.46	31.67
Gender (n, M/F) (%)	85 (47.5) / 94 (52.5)	94 (53.4) / 82 (46.6)	89 (49.7) / 90 (50.3)	268 (50.2) / 266 (49.8)
Race, n (%)				
White	120 (67)	121 (68.8)	131 (73.2)	372 (69.7)
Black / African American	22 (12.3)	22 (12.5)	16 (8.9)	60 (11.2)
Asian	12 (6.7)	11 (6.3)	10 (5.6)	33 (6.2)
Other	25 (14.0)	22 (12.5)	22 (12.3)	69 (12.9)
T2DM duration (mean (SD) years)	7.1 (5.03)[a]	8.2 (5.52)	7.4 (5.39)	7.6 (5.33)
Lipids, n (%)				
Hyperlipidemia	63 (35.2)	65 (36.9)	61 (34.1)	189 (35.4)
Dyslipidemia	46 (25.7)	52 (29.5)	44 (24.6)	142 (26.6)

Table -2: CV181169 - Demographics and Baseline Characteristics

	Saxa + Dapa +Met (N=179)	Saxa + Met (N=176)	Dapa + Met (N=179)	Total (N=534)
HbA1c (mean (SD) %)	8.92 (1.18)	9.03 (1.05)	8.87 (1.16)	8.94 (1.13)
Fasting Plasma Glucose (mean (SD) mg/dL)	180.4 (45.5)	191.8 (45.3)	185.0 (48.4)	185.7 (46.6)
Post-Prandial Glucose (mean (SD) mg/dL)	215.3 (58.2)[b]	232.5 (65.7)	223.1 (58.0)	223.6 (61.0)
C-peptide (mean (SD) ng/mL)	2.17 (0.996)	2.12 (0.899)	2.22 (1.027)	2.17 (0.975)
eGFR (mean (SD) ml/min/1.73m^2)	96.6 (19.60)	92.5 (19.47)	93.9 (19.91)	94.4 (19.70)

[a] n=177
[b] n=178

Efficacy Results: The primary endpoint was met for the trial: the adjusted mean reduction from baseline in HbA1c over the 24-week period in the saxagliptin + dapagliflozin + metformin treatment group showed simultaneous superiority against the other treatment groups, saxagliptin + metformin and dapagliflozin + metformin, respectively.

The secondary endpoint of 120-minute PPG was not met, and the adjusted mean change from baseline in PPG or FPG was significantly greater only against the saxagliptin + metformin group. The secondary endpoint of number of subjects achieving glycemic target of < 7% HbA1C nearly doubled after the combination of saxagliptin + dapagliflozin + metformin. There was approximately a 2-kg weight loss after treatment with the saxagliptin + dapagliflozin + metformin and dapagliflozin + metformin treatment groups. Dapagliflozin-containing treatments had approximately half the number of subjects who discontinued for lack of glycemic control or who required rescued than the saxagliptin + metformin treatment group. (Table -3 summarizes the primary and secondary objectives for the study.)

At 180 minutes into the MTT, post-prandial glucose fell more after treatment with saxagliptin + dapagliflozin + metformin than with saxagliptin + metformin and to a similar degree compared to dapagliflozin + metformin. The differences in adjusted mean change from baseline were similar between the saxagliptin + dapagliflozin + metformin and dapagliflozin + metformin groups and different for the saxagliptin + dapagliflozin + metformin group compared to the saxagliptin + metformin group. The AUC for the analytes encompasses all timepoints. In alignment with the significant improvements observed in HbA1c, all 3 treatment groups had reductions in post-MTT glucose excursions (glucose area-under-the-curve: ($AUC_{glucose}$) after 24 weeks of treatment.

Table -3: Primary and Secondary Efficacy Endpoints at Week 24 - Randomized Subjects

Endpoint	Comparison	Saxagliptin + Dapagliflozin + Metformin XR	Saxagliptin + Metformin XR	Dapagliflozin + Metformin XR
A1c (%) Adjusted Mean Change from Baseline[a] (95% CI)	Mean Change from Baseline	-1.47% (-1.62, -1.31)	-0.88% (-1.03, -0.72)	-1.20% (-1.35, -1.04)
	Saxa/Dapa + Met XR *vs.* Saxa + Met XR	-0.59% (-0.81, -0.37) p<0.0001		
	Saxa/Dapa + Met XR *vs.* Dapa + Met XR	-0.27% (-0.48, -0.05) p = 0.0166		

Table -3: Primary and Secondary Efficacy Endpoints at Week 24 - Randomized Subjects

Endpoint	Comparison	Saxagliptin + Dapagliflozin + Metformin XR	Saxagliptin + Metformin XR	Dapagliflozin + Metformin XR
120-minute PPG (mg/dL) Adjusted Mean Change from Baseline[b] (95% CI)	Mean Change from Baseline	-79.6 (-86.3, -72.8)	-35.6 (-42.5, -28.7)	-70.4 (-77.4, -63.5)
	Saxa/Dapa + Met XR *vs.* Saxa + Met XR	-44.0 (-53.7, -34.3) p<0.0001		
	Saxa/Dapa + Met XR *vs.* Dapa + Met XR	-9.1 (-18.8, 0.5) p = 0.0639		
FPG (mg/dL) Adjusted Mean Change from Baseline[b] (95% CI)	Mean Change from Baseline	-37.8 (-43.2, -32.3)	-14.0 (-19.6, -8.4)	-31.7 (-37.3, -26.2)
	Saxa/Dapa + Met XR *vs.* Saxa + Met XR	-23.8 (-31.6, -15.9)		
	Saxa/Dapa + Met XR *vs.* Dapa + Met XR	-6.1 (-13.8, 1.7)		
% Subjects with A1c < 7.0% @ Week 24[b] (95% CI)	Mean Change from Baseline	41.4% (34.5, 48.2)	18.3% (13.0, 23.5)	22.2% (16.1, 28.3)
	Saxa/Dapa + Met XR *vs.* Saxa + Met	23.1% (14.7, 31.5)		
	Saxa/Dapa + Met XR *vs.* Dapa + Met XR	19.1% (10.1, 28.1)		
Subjects Discontinued for Lack of Glycemic Control or Who Were Rescued (Adjusted %)[c]		5.5%	9.4%	3.4%
Body Weight (kg) Adjusted Mean Change from Baseline[b] (95% CI)	Mean Change from Baseline	-2.05 (-2.52, -1.58)	0.00 (-0.48, 0.49)	-2.39 (-2.87, -1.91)
	Saxa/Dapa + Met XR *vs.* Saxa + Met XR	-2.05 (-2.73, -1.37		

[a] Primary objective endpoint

[b] Secondary objective endpoint

[c] Other objective endpoint

Safety Results: Generally, the combination of saxagliptin + dapagliflozin + metformin was well tolerated in this population. There were no deaths or malignancies reported during the study for any treatment group. The frequency of serious adverse events (SAEs) was low, 2 subjects (1.1%), 6 subjects (3.4%), and 2 subjects (1.1%) in the saxagliptin + dapagliflozin + metformin, saxagliptin + metformin, and dapagliflozin + metformin treatment groups, respectively. Two subjects discontinued due to AEs, one subject prior to receiving the double-blind study medication, and assigned to the dapagliflozin + metformin treatment group (metformin intolerance on Day 1, pre-dose), and one in the saxagliptin + dapagliflozin + metformin group due to decrease in estimated glomerular filtration rate (eGRF).

Overall, the incidence of AEs was similar across the 3 treatment groups (see Table -4): 87 (49%) subjects in the saxagliptin + dapagliflozin + metformin treatment group experienced at least one AE, 93 (53%) subjects in the saxagliptin + metformin group, and 87 (49%) subjects in the dapagliflozin + metformin group.

The most common AE reported in the saxagliptin + dapagliflozin + metformin treatment group was arthralgia (4%), which occurred at a higher proportion compared to the other two treatment groups (1%). Nasopharyngitis was also reported frequently and was consistent across treatment groups.

For AEs of special interest:

- There was similar and low risk of hypoglycemia across treatment groups (≤ 1.1% of subjects), with no episodes of confirmed hypoglycemia with a glucose value ≤ 50 mg/dL.
- There were no cases of matching the predefined list of preferred terms (PTs) for worsening renal function. In the saxagliptin + metformin group, there was one AE of renal impairment and one AE of renal failure. There were 4 AEs of decrease in eGRF: 3 in the saxagliptin + dapagliflozin + metformin group, and 1 in the saxagliptin + metformin group.
- No events of opportunistic infections or kidney infections were reported during the study.
- The number of subjects with infections was slightly lower in the saxagliptin + dapagliflozin + metformin group, 34 subjects (19%), vs. in the saxagliptin + metformin, and dapagliflozin + metformin treatment groups: 45 subjects (26%), and 44 subjects (25%), respectively.
- No subject in the saxagliptin + dapagliflozin + metformin treatment group had an event of genital infection. Genital infections occurred more frequently in the dapagliflozin + metformin treatment group, (10 subjects, 5.6%), compared to the saxagliptin + metformin group (1 subject (0.6%)).
- Events of urinary tract infections were less common in the saxagliptin + dapagliflozin + metformin group (1 subject, 0.6%) vs. the saxagliptin + metformin and dapagliflozin + metformin groups (9 subjects, 5.1%, 7 subjects, 3.9%, respectively).
- No fractures were reported in the saxagliptin + dapagliflozin + metformin treatment group. 2 subjects in the saxagliptin + metformin treatment group reported a fracture, and 1 subject in the dapagliflozin + metformin treatment group. No subjects with event of fractures had reports of hypoglycemia, nocturia or volume depletion during the study.
- Four subjects had Investigator-reported adjudicated cardiovascular (CV) AEs during double-blind treatment: 1 (0.6%) in the saxagliptin + dapagliflozin + metformin treatment group, 2 (1.1%) in the saxagliptin + metformin treatment group and 1 (0.6%) in the dapagliflozin + metformin treatment group. None of the CV AEs led to study discontinuation.
- There were no reports of decreased lymphocyte or thrombocyte counts during the study.
- In the saxagliptin + metformin treatment group, there was one report of skin exfoliation, which was described as fine scaling over the left plantar foot with no ulceration. No other subjects reported a similar event in the two other treatment groups.
- There were no reports of hypersensitivity during the study.
- A low number of subjects had hepatic disorder AEs (3 subjects (2%) in the saxagliptin + dapagliflozin + metformin group, and saxagliptin + metformin group reported AEs of hepatic disorder).
- No subject in any of the 3 treatment groups had both aspartate aminotransferase (AST) > 5x the upper limit of normal (ULN). One subject had an AE of elevated ALT (ALT > 5) in the saxagliptin + dapagliflozin + metformin group, considered not related to study treatment. Additionally, no subjects had alanine aminotransferase (ALT) elevation > 10x ULN. Two subjects had bilirubin elevation of > 1.5x ULN in the saxagliptin + metformin treatment group, but no subjects had > 2x ULN total bilirubin elevation.
- There were no events of hypotension, dehydration or hypovolemia.

Clinical laboratory evaluations were generally stable over time, including hepatic and renal analytes. There were also similar and low frequency of marked laboratory abnormalities across treatments.

No treatment-related, clinically meaningful adverse safety findings related to ECGs or vital signs were reported. There was a small decrease in blood pressure in dapagliflozin-containing treatment groups that was not present in saxagliptin + metformin treatment group.

Table -4: Overall Adverse Event Summary - 24-Week Double-blind Treatment Period - Treated Subjects

	Number of Subjects (Percent)		
	SAXA+DAPA+MET N = 179	SAXA+MET N = 176	DAPA+MET N = 179
AT LEAST ONE ADVERSE EVENT	87 (48.6)	93 (52.8)	87 (48.6)
AT LEAST ONE HYPOGLYCEMIA	2 (1.1)	2 (1.1)	2 (1.1)
AT LEAST ONE AE OR HYPOGLYCEMIA	87 (48.6)	94 (53.4)	87 (48.6)
AT LEAST ONE RELATED ADVERSE EVENT	12 (6.7)	8 (4.5)	13 (7.3)
DEATHS	0	0	0
AT LEAST ONE SAE	2 (1.1)	6 (3.4)	2 (1.1)
AT LEAST ONE RELATED SAE	0	1 (0.6)	0
SAE LEADING TO DISC. OF STUDY MED.	0	0	0
AE LEADING TO DISC. OF STUDY MED.	1 (0.6)	0	1 (0.6)
HYPOGLYCEMIA LEADING TO DISC. OF STUDY MED.	0	0	0

Treated subjects are those who received at least one dose of double-blind medication during the short-term double-blind treatment.
Percentages are based on the total number of subjects in the respective treatment group.
All listed events are treatment emergent, which is defined as non-serious AEs and serious AEs with an onset from Day 1 of the short-term double-blind treatment up to and including 4 days and 30 days respectively, after the last dose date in the short-term double-blind treatment period.
MedDRA Version: 16.1.
Only hypoglycemia reported as a SAE is included in the AE categories.
All reported hypoglycemia events starting day 1 of the short-term double-blind treatment and up to 4 days after the last day of short-term double-blind treatment are included in the hypoglycemia line.
Program Source: /projects/bms208546/stats/primary/prog/tables/rt-ae-st-overall.sas 29MAR2014:16:35:21