Trial record **1 of 1** for: 28431754DIA3006
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The CANTATA-D Trial (CANagliflozin Treatment and Trial Analysis - DPP-4 Inhibitor Comparator Trial)

This study has been completed.

Sponsor:
Janssen Research & Development, LLC

Information provided by (Responsible Party):
Janssen Research & Development, LLC

ClinicalTrials.gov Identifier:
NCT01106677

First received: April 1, 2010
Last updated: July 25, 2013
Last verified: July 2013
History of Changes

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Results First Received: April 4, 2013

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator); Primary Purpose: Treatment
Condition:	Diabetes Mellitus, Type 2
Interventions:	Drug: Placebo Drug: Canagliflozin Drug: Sitagliptin Drug: Metformin immediate release

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
This study evaluated the efficacy and safety of canagliflozin compared with sitagliptin and placebo in patients with type 2 diabetes mellitus with inadequate control despite treatment with metformin. The study was conducted between 07 April 2010 and 17 August 2012 and recruited patients from 169 study centers in 22 countries worldwide.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
1,284 patients were randomly allocated to the 4 treatment arms. All patients received at least 1 dose of study drug and were included in the modified intent-to-treat (mITT) analysis set (used for the Week 26 and week 52 efficacy analyses). All 1,284 patients were included in the Week 26 and Week 52 safety analysis sets.

Reporting Groups

	Description
Placebo/Sitagliptin	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Participant Flow for 2 periods

Period 1: Core Period: Baseline to Week 26

	Placebo/Sitagliptin	Canagliflozin 100 mg	Canagliflozin 300 mg	Sitagliptin 100 mg
STARTED	183	368	367	366
COMPLETED	155	322	323	319
NOT COMPLETED	28	46	44	47
Adverse Event	7	18	6	8
Death	0	0	1	0
Lack of Efficacy	1	0	0	0
Lost to Follow-up	3	1	6	3
Physician Decision	2	1	3	1
Protocol Violation	0	1	0	3
Withdrawal by Subject	5	3	15	6
Creatinine or eGFR withdrawal criteria	1	2	2	3
Noncompliance with study drug	1	3	0	0
Study terminated by sponsor	0	1	2	0
Product quality complaint	0	1	1	0
Not specified	8	14	8	23
Pregnancy	0	1	0	0

Period 2: Extension Period: Week 26 to Week 52

	Placebo/Sitagliptin	Canagliflozin 100 mg	Canagliflozin 300 mg	Sitagliptin 100 mg
STARTED	153 [1]	316 [2]	321 [3]	313 [4]
COMPLETED	138	298	299	285
NOT COMPLETED	15	18	22	28
Adverse Event	1	1	5	9
Death	0	0	0	1
Lack of Efficacy	2	0	0	4
Lost to Follow-up	0	2	2	2
Physician Decision	2	3	2	3
Protocol Violation	1	0	0	0
Withdrawal by Subject	1	3	2	1
Creatinine or eGFR withdrawal criteria	2	4	3	2
Unable to take rescue therapy	0	0	0	1
Not specified	6	5	8	5

[1] 2 pts completed core but did not enter ext: protcol violation(1), lost to f/u(1).
[2] 6 pts completed core but did not enter ext: not specified(5), withdrawal by subject(1).
[3] 2 pts completed core but did not enter ext: not specified(1), withdrawal by subject(1).
[4] 6 pts completed core but did not enter ext: not specified(3), physician decision(2), lost to f/u(1).

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Placebo/Sitagliptin	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release.

Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Total	Total of all reporting groups

Baseline Measures

	Placebo/Sitagliptin	Canagliflozin 100 mg	Canagliflozin 300 mg	Sitagliptin 100 mg	Total
Number of Participants [units: participants]	**183**	**368**	**367**	**366**	**1284**
Age [units: participants]					
<=18 years	**0**	**0**	**0**	**0**	**0**
Between 18 and 65 years	**146**	**314**	**309**	**309**	**1078**
>=65 years	**37**	**54**	**58**	**57**	**206**
Age [units: years] Mean (Standard Deviation)	**55.3 (9.76)**	**55.5 (9.38)**	**55.3 (9.19)**	**55.5 (9.55)**	**55.4 (9.42)**
Gender [units: participants]					
Female	**89**	**194**	**202**	**194**	**679**
Male	**94**	**174**	**165**	**172**	**605**
Region Enroll [units: participants]					
ARGENTINA	**8**	**9**	**15**	**11**	**43**
BULGARIA	**4**	**2**	**1**	**3**	**10**
COLOMBIA	**4**	**15**	**8**	**15**	**42**
CZECH REPUBLIC	**7**	**8**	**8**	**7**	**30**
ESTONIA	**6**	**6**	**3**	**5**	**20**
GREECE	**1**	**1**	**3**	**4**	**9**
INDIA	**13**	**28**	**31**	**22**	**94**
ITALY	**2**	**3**	**3**	**1**	**9**
LATVIA	**3**	**7**	**6**	**10**	**26**
MALAYSIA	**9**	**7**	**11**	**7**	**34**
MEXICO	**12**	**20**	**26**	**18**	**76**
PERU	**16**	**36**	**30**	**37**	**119**
POLAND	**1**	**18**	**14**	**10**	**43**
PORTUGAL	**1**	**1**	**0**	**2**	**4**
RUSSIAN FEDERATION	**15**	**34**	**28**	**22**	**99**
SINGAPORE	**3**	**5**	**3**	**3**	**14**
SLOVAKIA	**12**	**16**	**21**	**17**	**66**
SWEDEN	**3**	**3**	**2**	**4**	**12**
THAILAND	**4**	**9**	**11**	**8**	**32**
TURKEY	**1**	**5**	**11**	**9**	**26**
UKRAINE	**8**	**24**	**29**	**30**	**91**
UNITED STATES	**50**	**111**	**103**	**121**	**385**

Outcome Measures

Hide All Outcome Measures

1. Primary: Change in HbA1c From Baseline to Week 26 [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Primary
Measure Title	Change in HbA1c From Baseline to Week 26
Measure Description	The table below shows the least-squares (LS) mean change in HbA1c from Baseline to Week 26 for each treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin or sitagliptin group minus placebo) in the LS mean change.
Time Frame	Day 1 (Baseline) and Week 26
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 26 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Placebo/Sitagliptin	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Measured Values

	Placebo/Sitagliptin	**Canagliflozin 100 mg**	**Canagliflozin 300 mg**	**Sitagliptin 100 mg**
Number of Participants Analyzed [units: participants]	**181**	**365**	**360**	**354**
Change in HbA1c From Baseline to Week 26 [units: Percent] Least Squares Mean (Standard Error)	**-0.17 (0.060)**	**-0.79 (0.044)**	**-0.94 (0.044)**	**-0.82 (0.044)**

Statistical Analysis 1 for Change in HbA1c From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 100 mg
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANCOVA
P Value [4]	<0.001
Least-Squares Mean Difference [5]	-0.62
Standard Error of the mean	(0.071)
95% Confidence Interval	-0.758 to -0.481

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Power calculation: assuming a difference between canagliflozin and placebo of 0.5% and a common standard deviation of 1.0%, and using a 2-sample, 1-sided t-test with a Type I error rate of 0.05, it was estimated that 86 subjects per group would provide 90% power to demonstrate superiority of canagliflozin over placebo.
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.

[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change in HbA1c From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 300 mg
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANCOVA
P Value [4]	<0.001
Least-Squares Mean Difference [5]	-0.77
Standard Error of the mean	(0.071)
95% Confidence Interval	-0.914 to -0.636

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Power calculation: assuming a difference between canagliflozin and placebo of 0.5% and a common standard deviation of 1.0%, and using a 2-sample, 1-sided t-test with a Type I error rate of 0.05, it was estimated that 86 subjects per group would provide 90% power to demonstrate superiority of canagliflozin over placebo.
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Change in HbA1c From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Sitagliptin 100 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	-0.66
Standard Error of the mean	(0.071)
95% Confidence Interval	-0.795 to -0.516

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	No text entered.

2. Secondary: Percentage of Patients With HbA1c <7% at Week 26 [Time Frame: Week 26]

Measure Type	Secondary
Measure Title	Percentage of Patients With HbA1c <7% at Week 26
Measure Description	The table below shows the percentage of patients with HbA1c <7% at Week 26 in each treatment group. The statistical analyses show the treatment differences between each canagliflozin or sitagliptin group and placebo.
Time Frame	Week 26

Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 26 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Placebo/Sitagliptin	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Measured Values

	Placebo/Sitagliptin	**Canagliflozin 100 mg**	**Canagliflozin 300 mg**	**Sitagliptin 100 mg**
Number of Participants Analyzed [units: participants]	**181**	**365**	**360**	**354**
Percentage of Patients With HbA1c <7% at Week 26 [units: Percentage of patients]	**29.8**	**45.5**	**57.8**	**54.5**

Statistical Analysis 1 for Percentage of Patients With HbA1c <7% at Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 100 mg
Method [2]	Regression, Logistic
P Value [3]	<0.001
Odds Ratio (OR) [4]	2.29
95% Confidence Interval	1.50 to 3.50

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percentage of Patients With HbA1c <7% at Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 300 mg
Method [2]	Regression, Logistic
P Value [3]	<0.001
Odds Ratio (OR) [4]	4.39
95% Confidence Interval	2.85 to 6.77

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.

[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

3. Secondary: Change in Fasting Plasma Glucose (FPG) From Baseline to Week 26 [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Secondary
Measure Title	Change in Fasting Plasma Glucose (FPG) From Baseline to Week 26
Measure Description	The table below shows the least-squares (LS) mean change in FPG from Baseline to Week 26 for each treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin or sitagliptin group minus placebo) in the LS mean change.
Time Frame	Day 1 (Baseline) and Week 26
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 26 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Placebo/Sitagliptin	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Measured Values

	Placebo/Sitagliptin	**Canagliflozin 100 mg**	**Canagliflozin 300 mg**	**Sitagliptin 100 mg**
Number of Participants Analyzed [units: participants]	**181**	**365**	**360**	**354**
Change in Fasting Plasma Glucose (FPG) From Baseline to Week 26 [units: mg/dL] Least Squares Mean (Standard Error)	**2.47 (2.576)**	**-27.3 (1.873)**	**-37.8 (1.893)**	**-20.2 (1.908)**

Statistical Analysis 1 for Change in Fasting Plasma Glucose (FPG) From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-29.8
Standard Error of the mean	(3.044)
95% Confidence Interval	-35.76 to -23.81

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change in Fasting Plasma Glucose (FPG) From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 300 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-40.3
Standard Error of the mean	(3.055)
95% Confidence Interval	-46.25 to -34.26

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Change in Fasting Plasma Glucose (FPG) From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Sitagliptin 100 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	-22.7
Standard Error of the mean	(3.060)
95% Confidence Interval	-28.70 to -16.69

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	No text entered.

4. Secondary: Change in 2-hour Post-prandial Glucose From Baseline to Week 26 [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Secondary
Measure Title	Change in 2-hour Post-prandial Glucose From Baseline to Week 26
Measure Description	The table below shows the least-squares (LS) mean change in 2-hour post-prandial glucose from Baseline to Week 26 for each treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin or sitagliptin group minus placebo) in the LS mean change.
Time Frame	Day 1 (Baseline) and Week 26

Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 26 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Placebo/Sitagliptin	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Measured Values

	Placebo/Sitagliptin	**Canagliflozin 100 mg**	**Canagliflozin 300 mg**	**Sitagliptin 100 mg**
Number of Participants Analyzed [units: participants]	**129**	**298**	**288**	**295**
Change in 2-hour Post-prandial Glucose From Baseline to Week 26 [units: mg/dL] Least Squares Mean (Standard Error)	**-9.79 (4.860)**	**-47.9 (3.305)**	**-57.1 (3.356)**	**-49.3 (3.340)**

Statistical Analysis 1 for Change in 2-hour Post-prandial Glucose From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-38.1
Standard Error of the mean	(5.601)
95% Confidence Interval	-49.14 to -27.16

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change in 2-hour Post-prandial Glucose From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 300 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-47.3

Standard Error of the mean	(5.635)
95% Confidence Interval	-58.40 to -36.29

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Change in 2-hour Post-prandial Glucose From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Sitagliptin 100 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	-39.6
Standard Error of the mean	(5.608)
95% Confidence Interval	-50.56 to -28.55

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	No text entered.

5. Secondary: Percent Change in Body Weight From Baseline to Week 26 [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Secondary
Measure Title	Percent Change in Body Weight From Baseline to Week 26
Measure Description	The table below shows the least-squares (LS) mean percent change in body weight from Baseline to Week 26 for each treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin or sitagliptin group minus placebo) in the LS mean percent change.
Time Frame	Day 1 (Baseline) and Week 26
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 26 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Placebo/Sitagliptin	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate

	release.

Measured Values

	Placebo/Sitagliptin	Canagliflozin 100 mg	Canagliflozin 300 mg	Sitagliptin 100 mg
Number of Participants Analyzed [units: participants]	**181**	**365**	**360**	**355**
Percent Change in Body Weight From Baseline to Week 26 [units: Percent change] Least Squares Mean (Standard Error)	**-1.2 (0.3)**	**-3.7 (0.2)**	**-4.2 (0.2)**	**-1.2 (0.2)**

Statistical Analysis 1 for Percent Change in Body Weight From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-2.5
Standard Error of the mean	(0.3)
95% Confidence Interval	-3.1 to -1.9

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change in Body Weight From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 300 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-2.9
Standard Error of the mean	(0.3)
95% Confidence Interval	-3.5 to -2.3

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Percent Change in Body Weight From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Sitagliptin 100 mg
Method [2]	ANCOVA

Least-Squares Mean Difference [3]	0
Standard Error of the mean	(0.3)
95% Confidence Interval	-0.6 to 0.6

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	No text entered.

6. Secondary: Change in Systolic Blood Pressure (SBP) From Baseline to Week 26 [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Secondary
Measure Title	Change in Systolic Blood Pressure (SBP) From Baseline to Week 26
Measure Description	The table below shows the least-squares (LS) mean change in SBP from Baseline to Week 26 for each treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin or sitagliptin group minus placebo) in the LS mean change.
Time Frame	Day 1 (Baseline) and Week 26
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 26 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Placebo/Sitagliptin	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Measured Values

	Placebo/Sitagliptin	**Canagliflozin 100 mg**	**Canagliflozin 300 mg**	**Sitagliptin 100 mg**
Number of Participants Analyzed [units: participants]	**181**	**365**	**360**	**355**
Change in Systolic Blood Pressure (SBP) From Baseline to Week 26 [units: mmHg] Least Squares Mean (Standard Error)	**1.52 (0.829)**	**-3.84 (0.602)**	**-5.06 (0.605)**	**-1.83 (0.611)**

Statistical Analysis 1 for Change in Systolic Blood Pressure (SBP) From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001

Least-Squares Mean Difference [4]	-5.36
Standard Error of the mean	(0.979)
95% Confidence Interval	-7.280 to -3.439

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change in Systolic Blood Pressure (SBP) From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 300 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-6.58
Standard Error of the mean	(0.981)
95% Confidence Interval	-8.504 to -4.653

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Change in Systolic Blood Pressure (SBP) From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Sitagliptin 100 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	-3.34
Standard Error of the mean	(0.984)
95% Confidence Interval	-5.273 to -1.413

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	No text entered.

7. Secondary: Percent Change in Triglycerides From Baseline to Week 26 [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Secondary

Measure Title	Percent Change in Triglycerides From Baseline to Week 26
Measure Description	The table below shows the least-squares (LS) mean percent change in triglycerides from Baseline to Week 26 for each treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin or sitagliptin group minus placebo) in the LS mean percent change.
Time Frame	Day 1 (Baseline) and Week 26
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 26 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Placebo/Sitagliptin	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Measured Values

	Placebo/Sitagliptin	**Canagliflozin 100 mg**	**Canagliflozin 300 mg**	**Sitagliptin 100 mg**
Number of Participants Analyzed [units: participants]	**171**	**358**	**341**	**338**
Percent Change in Triglycerides From Baseline to Week 26 [units: Percent change] Least Squares Mean (Standard Error)	**3.2 (3.6)**	**1.6 (2.6)**	**-1.4 (2.6)**	**1.0 (2.7)**

Statistical Analysis 1 for Percent Change in Triglycerides From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	0.702
Least-Squares Mean Difference [4]	-1.6
Standard Error of the mean	(4.2)
95% Confidence Interval	-9.9 to 6.7

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change in Triglycerides From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 300 mg

Method [2]	ANCOVA
P Value [3]	0.274
Least-Squares Mean Difference [4]	-4.7
Standard Error of the mean	(4.3)
95% Confidence Interval	-13.0 to 3.7

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Percent Change in Triglycerides From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Sitagliptin 100 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	-2.3
Standard Error of the mean	(4.3)
95% Confidence Interval	-10.6 to 6.1

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	No text entered.

8. Secondary: Percent Change in High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 26 [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Secondary
Measure Title	Percent Change in High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 26
Measure Description	The table below shows the least-squares (LS) mean percent change in HDL-C from Baseline to Week 26 for each treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin or sitagliptin group minus placebo) in the LS mean percent change.
Time Frame	Day 1 (Baseline) and Week 26
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 26 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Placebo/Sitagliptin	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release.

Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Measured Values

	Placebo/Sitagliptin	Canagliflozin 100 mg	Canagliflozin 300 mg	Sitagliptin 100 mg
Number of Participants Analyzed [units: participants]	**171**	**357**	**336**	**336**
Percent Change in High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 26 [units: Percent change] Least Squares Mean (Standard Error)	**3.7 (1.3)**	**10.4 (0.9)**	**12.1 (1.0)**	**5.0 (1.0)**

Statistical Analysis 1 for Percent Change in High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	6.7
Standard Error of the mean	(1.6)
95% Confidence Interval	3.6 to 9.7

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change in High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Canagliflozin 300 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	8.5
Standard Error of the mean	(1.6)
95% Confidence Interval	5.4 to 11.5

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Percent Change in High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 26

Groups [1]	Placebo/Sitagliptin vs. Sitagliptin 100 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	1.3
Standard Error of the mean	(1.6)
95% Confidence Interval	-1.7 to 4.4

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	No text entered.

9. Secondary: Change in HbA1c From Baseline to Week 52 [Time Frame: Day 1 (Baseline) and Week 52]

Measure Type	Secondary
Measure Title	Change in HbA1c From Baseline to Week 52
Measure Description	The table below shows the least-squares (LS) mean change in HbA1c from Baseline to Week 52 for each active treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin group minus sitagliptin) in the LS mean change.
Time Frame	Day 1 (Baseline) and Week 52
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 52 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Measured Values

	Canagliflozin 100 mg	**Canagliflozin 300 mg**	**Sitagliptin 100 mg**
Number of Participants Analyzed [units: participants]	**365**	**360**	**354**
Change in HbA1c From Baseline to Week 52 [units: Percent] Least Squares Mean (Standard Error)	**-0.73 (0.047)**	**-0.88 (0.047)**	**-0.73 (0.047)**

Statistical Analysis 1 for Change in HbA1c From Baseline to Week 52

Groups [1]	Canagliflozin 100 mg vs. Sitagliptin 100 mg
Non-Inferiority/Equivalence Test [2]	Yes

Method [3]	ANCOVA
Least-Squares Mean Difference [4]	0.00
Standard Error of the mean	(0.061)
95% Confidence Interval	-0.119 to 0.122

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Assuming a discontinuation rate of 35% at Week 52, with a 2:2:2:1 treatment assignment ratio for canagliflozin 100 mg, canagliflozin 300 mg, sitagliptin 100 mg, or placebo, it was estimated that 360 subjects would need to be randomly assigned to each of the 3 active treatment groups and approximately 180 subjects to the placebo group to demonstrate non-inferiority with a non-inferiority margin of 0.3%.
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change in HbA1c From Baseline to Week 52

Groups [1]	Canagliflozin 300 mg vs. Sitagliptin 100 mg
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANCOVA
Least-Squares Mean Difference [4]	-0.15
Standard Error of the mean	(0.062)
95% Confidence Interval	-0.273 to -0.031

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Assuming a discontinuation rate of 35% at Week 52, with a 2:2:2:1 treatment assignment ratio for canagliflozin 100 mg, canagliflozin 300 mg, sitagliptin 100 mg, or placebo, it was estimated that 360 subjects would need to be randomly assigned to each of the 3 active treatment groups and approximately 180 subjects to the placebo group to demonstrate non-inferiority with a non-inferiority margin of 0.3%.
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

10. Secondary: Change in Fasting Plasma Glucose (FPG) From Baseline to Week 52 [Time Frame: Day 1 (Baseline) and Week 52]

Measure Type	Secondary
Measure Title	Change in Fasting Plasma Glucose (FPG) From Baseline to Week 52
Measure Description	The table below shows the least-squares (LS) mean change in FPG from Baseline to Week 52 for each active treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin group minus sitagliptin) in the LS mean change.
Time Frame	Day 1 (Baseline) and Week 52
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 52 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Measured Values

	Canagliflozin 100 mg	Canagliflozin 300 mg	Sitagliptin 100 mg
Number of Participants Analyzed [units: participants]	**365**	**360**	**354**
Change in Fasting Plasma Glucose (FPG) From Baseline to Week 52 [units: mg/dL] Least Squares Mean (Standard Error)	**-26.2 (1.814)**	**-35.2 (1.833)**	**-17.7 (1.848)**

Statistical Analysis 1 for Change in Fasting Plasma Glucose (FPG) From Baseline to Week 52

Groups [1]	Canagliflozin 100 mg vs. Sitagliptin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-8.55
Standard Error of the mean	(2.394)
95% Confidence Interval	-13.25 to -3.857

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change in Fasting Plasma Glucose (FPG) From Baseline to Week 52

Groups [1]	Canagliflozin 300 mg vs. Sitagliptin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-17.5
Standard Error of the mean	(2.404)
95% Confidence Interval	-22.24 to -12.81

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

11. Secondary: Percent Change in Body Weight From Baseline to Week 52 [Time Frame: Day 1 (Baseline) and Week 52]

Measure Type	Secondary
Measure Title	Percent Change in Body Weight From Baseline to Week 52
Measure Description	The table below shows the least-squares (LS) mean percent change in body weight from Baseline to Week 52 for each active treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin group minus sitagliptin) in the LS mean percent change.
Time Frame	Day 1 (Baseline) and Week 52
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 52 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Measured Values

	Canagliflozin 100 mg	**Canagliflozin 300 mg**	**Sitagliptin 100 mg**
Number of Participants Analyzed [units: participants]	**365**	**360**	**355**
Percent Change in Body Weight From Baseline to Week 52 [units: Percent change] Least Squares Mean (Standard Error)	**-3.8 (0.2)**	**-4.2 (0.2)**	**-1.3 (0.2)**

Statistical Analysis 1 for Percent Change in Body Weight From Baseline to Week 52

Groups [1]	Canagliflozin 100 mg vs. Sitagliptin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-2.4
Standard Error of the mean	(0.3)
95% Confidence Interval	-3.0 to -1.8

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change in Body Weight From Baseline to Week 52

Groups [1]	Canagliflozin 300 mg vs. Sitagliptin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-2.9
Standard Error of the mean	(0.3)
95% Confidence Interval	-3.4 to -2.3

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

12. Secondary: Change in Systolic Blood Pressure (SBP) From Baseline to Week 52 [Time Frame: Day 1 (Baseline) and Week 52]

Measure Type	Secondary
Measure Title	Change in Systolic Blood Pressure (SBP) From Baseline to Week 52
Measure Description	The table below shows the least-squares (LS) mean change in SBP from Baseline to Week 52 for each active treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin group minus sitagliptin) in the LS mean change.
Time Frame	Day 1 (Baseline) and Week 52
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 52 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Measured Values

	Canagliflozin 100 mg	**Canagliflozin 300 mg**	**Sitagliptin 100 mg**
Number of Participants Analyzed [units: participants]	**365**	**360**	**355**
Change in Systolic Blood Pressure (SBP) From Baseline to Week 52 [units: mmHg] Least Squares Mean (Standard Error)	**-3.53 (0.615)**	**-4.65 (0.618)**	**-0.66 (0.625)**

Statistical Analysis 1 for Change in Systolic Blood Pressure (SBP) From Baseline to Week 52

Groups [1]	Canagliflozin 100 mg vs. Sitagliptin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-2.87
Standard Error of the mean	(0.812)
95% Confidence Interval	-4.464 to -1.276

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change in Systolic Blood Pressure (SBP) From Baseline to Week 52

Groups [1]	Canagliflozin 300 mg vs. Sitagliptin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-3.99
Standard Error of the mean	(0.815)
95% Confidence Interval	-5.589 to -2.389

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

13. Secondary: Percent Change in Triglycerides From Baseline to Week 52 [Time Frame: Day 1 (Baseline) and Week 52]

Measure Type	Secondary
Measure Title	Percent Change in Triglycerides From Baseline to Week 52
Measure Description	The table below shows the least-squares (LS) mean percent change in triglycerides from Baseline to Week 52 for each active treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin group minus sitagliptin) in the LS mean percent change.
Time Frame	Day 1 (Baseline) and Week 52
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 52 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Measured Values

	Canagliflozin 100 mg	Canagliflozin 300 mg	Sitagliptin 100 mg
Number of Participants Analyzed [units: participants]	**359**	**343**	**339**
Percent Change in Triglycerides From Baseline to Week 52 [units: Percent change] Least Squares Mean (Standard Error)	**1.9 (2.4)**	**2.7 (2.4)**	**-0.4 (2.5)**

Statistical Analysis 1 for Percent Change in Triglycerides From Baseline to Week 52

Groups [1]	Canagliflozin 100 mg vs. Sitagliptin 100 mg
Method [2]	ANCOVA
P Value [3]	0.466
Least-Squares Mean Difference [4]	2.3
Standard Error of the mean	(3.2)
95% Confidence Interval	-3.9 to 8.5

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change in Triglycerides From Baseline to Week 52

Groups [1]	Canagliflozin 300 mg vs. Sitagliptin 100 mg
Method [2]	ANCOVA
P Value [3]	0.323
Least-Squares Mean Difference [4]	3.2
Standard Error of the mean	(3.2)
95% Confidence Interval	-3.1 to 9.4

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:

	No text entered.

14. Secondary: Percent Change in High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 52 [Time Frame: Day 1 (Baseline) and Week 52]

Measure Type	Secondary
Measure Title	Percent Change in High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 52
Measure Description	The table below shows the least-squares (LS) mean percent change in HDL-C from Baseline to Week 52 for each active treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin group minus sitagliptin) in the LS mean percent change.
Time Frame	Day 1 (Baseline) and Week 52
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Analysis used mITT analysis set (all randomized patients who received at least 1 dose of study drug). Last-observation-carried-forward method used for missing Week 52 values. Measurements taken pre-rescue used as last observation in patients receiving glycemic rescue therapy. Table includes only patients with both baseline and post baseline values.

Reporting Groups

	Description
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release.
Sitagliptin 100 mg	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release.

Measured Values

	Canagliflozin 100 mg	**Canagliflozin 300 mg**	**Sitagliptin 100 mg**
Number of Participants Analyzed [units: participants]	**359**	**343**	**338**
Percent Change in High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 52 [units: Percent change] Least Squares Mean (Standard Error)	**11.2 (1.0)**	**13.3 (1.1)**	**6.0 (1.1)**

Statistical Analysis 1 for Percent Change in High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 52

Groups [1]	Canagliflozin 100 mg vs. Sitagliptin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	5.2
Standard Error of the mean	(1.4)
95% Confidence Interval	2.5 to 8.0

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change in High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 52

Groups [1]	Canagliflozin 300 mg vs. Sitagliptin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	7.3
Standard Error of the mean	(1.4)
95% Confidence Interval	4.5 to 10.1

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Adverse events were reported for the duration of the study; each patient participated in the study for approximately 52 weeks.
Additional Description	The total number of adverse events listed in the "Other (non-Serious) Adverse Event" table are based upon a cut-off of greater than or equal to 5 percent of patients experiencing the adverse event in any treatment arm.

Reporting Groups

	Description
Placebo/Sitagliptin: Baseline to Week 26	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 26.
Canagliflozin 100 mg: Baseline to Week 26	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 26.
Canagliflozin 300 mg: Baseline to Week 26	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 26.
Sitagliptin 100 mg: Baseline to Week 26	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 26.
Placebo/Sitagliptin: Baseline to Week 52	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 52.
Canagliflozin 100 mg: Baseline to Week 52	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 52.
Canagliflozin 300 mg: Baseline to Week 52	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 52.
Sitagliptin 100mg: Baseline to Week 52	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 52.

Serious Adverse Events

	Placebo/Sitagliptin: Baseline to Week	Canagliflozin 100 mg: Baseline to	Canagliflozin 300 mg: Baseline to	Sitagliptin 100 mg: Baseline to	Placebo/Sitagliptin: Baseline to Week	Canagliflozin 100 mg: Baseline to	Canagliflozin 300 mg: Baseline to	Sitagliptin 100mg: Baseline to

	26	Week 26	Week 26	Week 26	52	Week 52	Week 52	Week 52
Total, serious adverse events								
# participants affected / at risk	4/183 (2.19%)	12/368 (3.26%)	10/367 (2.72%)	8/366 (2.19%)	7/183 (3.83%)	15/368 (4.08%)	12/367 (3.27%)	18/366 (4.92%)
Cardiac disorders								
Acute coronary syndrome * 1 [3]								
# participants affected / at risk	1/183 (0.55%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	1/183 (0.55%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)
Angina unstable * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Coronary artery disease * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	1/366 (0.27%)
Stress cardiomyopathy * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Supraventricular tachycardia * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)
Acute myocardial infarction * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Atrial fibrillation * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)
Cardiac arrest * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Cardiomyopathy * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)
Myocardial infarction * 1 [3]								

# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)
Ear and labyrinth disorders								
Vertigo * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)
Eye disorders								
Cataract nuclear * 1 [4]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)
Gastrointestinal disorders								
Abdominal pain * 1 [5]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)
Constipation * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)
Inguinal hernia * 1 [3]								
# participants affected / at risk	1/183 (0.55%)	1/368 (0.27%)	1/367 (0.27%)	0/366 (0.00%)	1/183 (0.55%)	1/368 (0.27%)	1/367 (0.27%)	0/366 (0.00%)
Umbilical hernia * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)
Abdominal hernia * 1 [5]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Diverticulum * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
General disorders								
Hernia obstructive * 1 [6]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)
Hepatobiliary disorders								

Cholangitis [*1] [3]								
# participants affected / at risk	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)
Cholecystitis acute [*1] [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)
Cholecystitis [*1] [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)
Infections and infestations								
Cellulitis [*1] [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)	1/183 (0.55%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Gastroenteritis [*1] [3]								
# participants affected / at risk	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	1/366 (0.27%)
Pneumonia [*1] [3]								
# participants affected / at risk	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)
Pyothorax [*1] [7]								
# participants affected / at risk	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)
Sepsis [*1] [3]								
# participants affected / at risk	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)	1/183 (0.55%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)
Subcutaneous abscess [*1] [3]								
# participants affected / at risk	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)
Urinary tract infection [*1] [3]								
# participants affected / at risk	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	1/368 (0.27%)	1/367 (0.27%)	0/366 (0.00%)
Dengue fever [*1] [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)

Infectious pleural effusion * 1 [7]								
# participants affected / at risk	**0/183 (0.00%)**	**0/368 (0.00%)**	**0/367 (0.00%)**	**0/366 (0.00%)**	**0/183 (0.00%)**	**1/368 (0.27%)**	**0/367 (0.00%)**	**0/366 (0.00%)**
Lobar pneumonia * 1 [3]								
# participants affected / at risk	**0/183 (0.00%)**	**0/368 (0.00%)**	**0/367 (0.00%)**	**0/366 (0.00%)**	**0/183 (0.00%)**	**0/368 (0.00%)**	**0/367 (0.00%)**	**1/366 (0.27%)**
Septic shock * 1 [3]								
# participants affected / at risk	**0/183 (0.00%)**	**0/368 (0.00%)**	**0/367 (0.00%)**	**0/366 (0.00%)**	**0/183 (0.00%)**	**0/368 (0.00%)**	**0/367 (0.00%)**	**1/366 (0.27%)**
Injury, poisoning and procedural complications								
Burns second degree * 1 [3]								
# participants affected / at risk	**0/183 (0.00%)**	**1/368 (0.27%)**	**0/367 (0.00%)**	**0/366 (0.00%)**	**0/183 (0.00%)**	**1/368 (0.27%)**	**0/367 (0.00%)**	**0/366 (0.00%)**
Cervical vertebral fracture * 1 [3]								
# participants affected / at risk	**0/183 (0.00%)**	**1/368 (0.27%)**	**0/367 (0.00%)**	**0/366 (0.00%)**	**0/183 (0.00%)**	**1/368 (0.27%)**	**0/367 (0.00%)**	**0/366 (0.00%)**
Incisional hernia * 1 [3]								
# participants affected / at risk	**1/183 (0.55%)**	**0/368 (0.00%)**	**0/367 (0.00%)**	**0/366 (0.00%)**	**1/183 (0.55%)**	**0/368 (0.00%)**	**0/367 (0.00%)**	**0/366 (0.00%)**
Incisional hernia, obstructive * 1 [6]								
# participants affected / at risk	**0/183 (0.00%)**	**0/368 (0.00%)**	**0/367 (0.00%)**	**0/366 (0.00%)**	**0/183 (0.00%)**	**0/368 (0.00%)**	**0/367 (0.00%)**	**1/366 (0.27%)**
Multiple drug overdose * 1 [3]								
# participants affected / at risk	**0/183 (0.00%)**	**0/368 (0.00%)**	**0/367 (0.00%)**	**0/366 (0.00%)**	**0/183 (0.00%)**	**0/368 (0.00%)**	**1/367 (0.27%)**	**0/366 (0.00%)**
Thermal burn * 1 [3]								
# participants affected / at risk	**0/183 (0.00%)**	**0/368 (0.00%)**	**0/367 (0.00%)**	**0/366 (0.00%)**	**0/183 (0.00%)**	**0/368 (0.00%)**	**0/367 (0.00%)**	**1/366 (0.27%)**
Metabolism and nutrition disorders								
Diabetic ketoacidosis * 1 [3]								

# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Musculoskeletal and connective tissue disorders								
Plantar fasciitis * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)
Spinal column stenosis * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Intervertebral disc protrusion * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)								
Breast cancer in situ * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)
Gastric cancer * 1 [3]								
# participants affected / at risk	1/183 (0.55%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	1/183 (0.55%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)
Malignant mesenchymoma * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Meningioma * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)
Bronchial carcinoma * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)
Colorectal cancer * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)

Large cell lung cancer stage III * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Prostate cancer * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)
Nervous system disorders								
Brain oedema * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)
Coma * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)
Ischaemic stroke * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)
Transient ischaemic attack * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	1/368 (0.27%)	0/367 (0.00%)	0/366 (0.00%)
Cerebrovascular accident * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Trigeminal neuralgia * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	1/183 (0.55%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)
Pregnancy, puerperium and perinatal conditions								
High risk pregnancy * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)
Renal and urinary disorders								
Renal failure acute * 1 [3]								
#								

# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Respiratory, thoracic and mediastinal disorders								
Asthma * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Respiratory failure * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)
Vascular disorders								
Arterial thrombosis * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)	0/183 (0.00%)	0/368 (0.00%)	1/367 (0.27%)	0/366 (0.00%)
Hypertensive crisis * 1 [3]								
# participants affected / at risk	0/183 (0.00%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)	1/183 (0.55%)	0/368 (0.00%)	0/367 (0.00%)	1/366 (0.27%)

* Events were collected by non-systematic assessment
1 Term from vocabulary, MEDDRA 14.0/15.0
[3] Source vocabulary is MEDDRA 14.0 for Week 26 and MEDDRA 15.0 for Week 52.
[4] Source vocabulary is MEDDRA 14.0 for Week 26 and MEDDRA 15.0 for Week 52. NOTE: event was reassessed as non-serious in the Week 52 study report.
[5] Source vocabulary is MEDDRA 14.0 for Week 26 and MEDDRA 15.0 for Week 52. In the Week 26 study report, this event was coded as "abdominal pain"; it was subsequently re-coded in the Week 52 study report as "abdominal hernia".
[6] Source vocabulary is MEDDRA 14.0 for Week 26 and MEDDRA 15.0 for Week 52. In the Week 26 study report, this event was coded as "hernia obstructive"; it was subsequently re-coded in the Week 52 study report as "incisional hernia, obstructive".
[7] Source vocabulary is MEDDRA 14.0 for Week 26 and MEDDRA 15.0 for Week 52. In the Week 26 study report, this event was coded as "pyothorax"; it was subsequently re-coded in the Week 52 study report as "infectious pleural effusion".

Other Adverse Events

Hide Other Adverse Events

Time Frame	Adverse events were reported for the duration of the study; each patient participated in the study for approximately 52 weeks.
Additional Description	The total number of adverse events listed in the "Other (non-Serious) Adverse Event" table are based upon a cut-off of greater than or equal to 5 percent of patients experiencing the adverse event in any treatment arm.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Placebo/Sitagliptin: Baseline to Week 26	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 26.
Canagliflozin 100 mg: Baseline to Week 26	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 26.
Canagliflozin 300 mg: Baseline to Week 26	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of

	metformin immediate release. Data are presented for Baseline to Week 26.
Sitagliptin 100 mg: Baseline to Week 26	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 26.
Placebo/Sitagliptin: Baseline to Week 52	Each patient received matching placebo once daily for 26 weeks and were then switched from placebo to 100 mg of sitagliptin once daily until Week 52. Placebo and sitagliptin were given with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 52.
Canagliflozin 100 mg: Baseline to Week 52	Each patient received 100 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 52.
Canagliflozin 300 mg: Baseline to Week 52	Each patient received 300 mg of canagliflozin once daily for 52 weeks with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 52.
Sitagliptin 100mg: Baseline to Week 52	Each patient received 100 mg of sitagliptin once daily for 52 weeks with protocol-specified doses of metformin immediate release. Data are presented for Baseline to Week 52.

Other Adverse Events

	Placebo/Sitagliptin: Baseline to Week 26	Canagliflozin 100 mg: Baseline to Week 26	Canagliflozin 300 mg: Baseline to Week 26	Sitagliptin 100 mg: Baseline to Week 26	Placebo/Sitagliptin: Baseline to Week 52	Canagliflozin 100 mg: Baseline to Week 52	Canagliflozin 300 mg: Baseline to Week 52	S 100m to
Total, other (not including serious) adverse events								
# participants affected / at risk	**31/183 (16.94%)**	**55/368 (14.95%)**	**45/367 (12.26%)**	**42/366 (11.48%)**	**55/183 (30.05%)**	**108/368 (29.35%)**	**101/367 (27.52%)**	**109/3**
Gastrointestinal disorders								
Diarrhoea * 1 [3]								
# participants affected / at risk	**12/183 (6.56%)**	**12/368 (3.26%)**	**18/367 (4.90%)**	**16/366 (4.37%)**	**13/183 (7.10%)**	**15/368 (4.08%)**	**23/367 (6.27%)**	**23/3**
Infections and infestations								
Nasopharyngitis * 1 [3]								
# participants affected / at risk	**13/183 (7.10%)**	**15/368 (4.08%)**	**10/367 (2.72%)**	**14/366 (3.83%)**	**13/183 (7.10%)**	**18/368 (4.89%)**	**16/367 (4.36%)**	**22/3**
Upper respiratory tract infection * 1 [3]								
# participants affected / at risk	**6/183 (3.28%)**	**5/368 (1.36%)**	**18/367 (4.90%)**	**18/366 (4.92%)**	**10/183 (5.46%)**	**12/368 (3.26%)**	**23/367 (6.27%)**	**22/3**
Urinary tract infection * 1 [3]								
# participants affected / at risk	**4/183 (2.19%)**	**18/368 (4.89%)**	**13/367 (3.54%)**	**12/366 (3.28%)**	**12/183 (6.56%)**	**27/368 (7.34%)**	**17/367 (4.63%)**	**22/3**
Musculoskeletal and connective tissue disorders								
Arthralgia * 1 [3]								
# participants affected / at risk	**9/183 (4.92%)**	**7/368 (1.90%)**	**4/367 (1.09%)**	**11/366 (3.01%)**	**11/183 (6.01%)**	**10/368 (2.72%)**	**9/367 (2.45%)**	**17/3**
Back pain * 1 [3]								
# participants affected / at	**6/183 (3.28%)**	**8/368 (2.17%)**	**12/367 (3.27%)**	**4/366 (1.09%)**	**10/183 (5.46%)**	**13/368 (3.53%)**	**15/367 (4.09%)**	**10/3**

risk								
Nervous system disorders								
Headache * 1 [3]								
# participants affected / at risk	**12/183 (6.56%)**	**12/368 (3.26%)**	**10/367 (2.72%)**	**16/366 (4.37%)**	**13/183 (7.10%)**	**19/368 (5.16%)**	**13/367 (3.54%)**	**19/3**
Renal and urinary disorders								
Pollakiuria * 1 [3]								
# participants affected / at risk	**1/183 (0.55%)**	**21/368 (5.71%)**	**10/367 (2.72%)**	**2/366 (0.55%)**	**1/183 (0.55%)**	**21/368 (5.71%)**	**11/367 (3.00%)**	**2/3**

* Events were collected by non-systematic assessment
1 Term from vocabulary, MEDDRA 14.0/15.0
[3] Source vocabulary is MEDDRA 14.0 for Week 26 and MEDDRA 15.0 for Week 52.

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is: ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☑ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed. **Restriction Description:** A copy of the manuscript must be provided to the sponsor for review at least 60 days before submission for publication or presentation. If requested in writing, such publication will be withheld for up to an additional 60 days.

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Watts NB, Bilezikian JP, Usiskin K, Edwards R, Desai M, Law G, Meininger G. Effects of Canagliflozin on Fracture Risk in Patients With Type 2 Diabetes Mellitus. J Clin Endocrinol Metab. 2016 Jan;101(1):157-66. doi: 10.1210/jc.2015-3167. Epub 2015 Nov 18.

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