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Trial record **1 of 1** for: 28431754DIA3010
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A Safety and Efficacy Study of Canagliflozin in Older Patients (55 to 80 Years of Age) With Type 2 Diabetes Mellitus

This study has been completed.

Sponsor:
Janssen Research & Development, LLC

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

ClinicalTrials.gov Identifier:
NCT01106651

First received: April 1, 2010
Last updated: October 27, 2014
Last verified: October 2014
History of Changes

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Results First Received: April 1, 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
	Drug: Canagliflozin 100 mg Drug: Canagliflozin 300 mg

Interventions:	Drug: Antihyperglycemic agent(s) Drug: Placebo

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 in older patients with type 2 diabetes mellitus with inadequate control on their current diabetes treatment regimen. The study began on 07 June 2010 and ended on 23 May 2013. Patients were recruited from 90 study centers located in 17 countries worldwide.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
716 patients were randomly allocated to the 3 treatment arms. 714 patients received at least 1 dose of study drug and were included in the modified intent-to-treat (mITT) analysis set and safety analysis set. Participant flow is presented for Baseline to Week 104 (Overall Study).

Reporting Groups

	Description
Placebo	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Participant Flow: Overall Study

	Placebo	**Canagliflozin 100 mg**	**Canagliflozin 300 mg**

STARTED	**237**	**241**	**236**
COMPLETED	**158**	**184**	**178**
NOT COMPLETED	**79**	**57**	**58**
Adverse Event	**17**	**9**	**23**
Lost to Follow-up	**8**	**2**	**6**
Physician Decision	**4**	**3**	**1**
Protocol Violation	**1**	**2**	**1**
Withdrawal by Subject	**14**	**7**	**4**
Noncompliance with study drug	**1**	**0**	**2**
Not specified	**34**	**31**	**21**
Death	**0**	**3**	**0**

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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable

	antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Total	Total of all reporting groups

Baseline Measures

	Placebo	Canagliflozin 100 mg	Canagliflozin 300 mg	Total
Number of Participants [units: participants]	**237**	**241**	**236**	**714**
Age [units: participants]				
<=18 years	**0**	**0**	**0**	**0**
Between 18 and 65 years	**151**	**141**	**149**	**441**
>=65 years	**86**	**100**	**87**	**273**
Age [units: years] Mean (Standard Deviation)	**63.2 (6.21)**	**64.3 (6.46)**	**63.4 (5.99)**	**63.6 (6.24)**
Gender [units: participants]				
Female	**94**	**117**	**107**	**318**
Male	**143**	**124**	**129**	**396**
Region of Enrollment [units: participants]				
AUSTRALIA	**6**	**6**	**11**	**23**
CANADA	**24**	**32**	**28**	**84**
COLOMBIA	**18**	**15**	**20**	**53**

FRANCE	**2**	**2**	**3**	**7**
GREECE	**1**	**1**	**1**	**3**
HONG KONG	**1**	**1**	**2**	**4**
INDIA	**8**	**3**	**11**	**22**
NEW ZEALAND	**16**	**10**	**11**	**37**
POLAND	**11**	**12**	**14**	**37**
ROMANIA	**8**	**10**	**7**	**25**
SOUTH AFRICA	**9**	**12**	**10**	**31**
SPAIN	**2**	**3**	**8**	**13**
SWEDEN	**4**	**4**	**2**	**10**
SWITZERLAND	**2**	**2**	**0**	**4**
UKRAINE	**3**	**8**	**3**	**14**
UNITED KINGDOM	**19**	**22**	**8**	**49**
UNITED STATES	**103**	**98**	**97**	**298**

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 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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo	**Canagliflozin 100 mg**	**Canagliflozin 300 mg**
Number of Participants Analyzed [units: participants]	**232**	**239**	**229**
Change in HbA1c From Baseline to Week 26 [units: Percent] Least Squares Mean (Standard Error)	**-0.03 (0.063)**	**-0.60 (0.063)**	**-0.73 (0.064)**

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

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-0.57
Standard Error of the mean	(0.069)
95% Confidence Interval	-0.708 to -0.436

[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 HbA1c From Baseline to Week 26

Groups [1]	Placebo vs. Canagliflozin 300 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-0.70

Standard Error of the mean	(0.070)
95% Confidence Interval	-0.841 to -0.566

[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.

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 (ie, each canagliflozin group minus placebo) in the percentage.
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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo	Canagliflozin 100 mg	Canagliflozin 300 mg
Number of Participants Analyzed [units: participants]	**232**	**239**	**229**
Percentage of Patients With HbA1c <7% at Week 26 [units: Percentage of patients]	**28.0**	**47.7**	**58.5**

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

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	Regression, Logistic
P Value [3]	<0.001
Odds Ratio (OR) [4]	2.96

95% Confidence Interval	1.93 to 4.56

[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 vs. Canagliflozin 300 mg
Method [2]	Regression, Logistic
P Value [3]	<0.001
Odds Ratio (OR) [4]	4.48
95% Confidence Interval	2.89 to 6.95

[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 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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo	Canagliflozin 100 mg	Canagliflozin 300 mg
Number of Participants Analyzed [units: participants]	**231**	**239**	**229**
Change in Fasting Plasma Glucose (FPG) From Baseline to Week 26 [units: mg/dL] Least Squares Mean (Standard Error)	**7.39 (2.875)**	**-18.1 (2.860)**	**-20.3 (2.920)**

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

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-25.5
Standard Error of the mean	(3.147)
95% Confidence Interval	-31.68 to -19.32

[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 vs. Canagliflozin 300 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-27.7
Standard Error of the mean	(3.179)
95% Confidence Interval	-33.97 to -21.49

[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.

4. 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 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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo	Canagliflozin 100 mg	Canagliflozin 300 mg
Number of Participants Analyzed [units: participants]	**234**	**240**	**229**
Percent Change in Body Weight From Baseline to Week 26 [units: Percent change] Least Squares Mean (Standard Error)	**-0.1 (0.3)**	**-2.4 (0.3)**	**-3.1 (0.3)**

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

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-2.3
Standard Error of the mean	(0.3)
95% Confidence Interval	-2.8 to -1.7

[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 Body Weight From Baseline to Week 26

Groups [1]	Placebo vs. Canagliflozin 300 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-3.0
Standard Error of the mean	(0.3)
95% Confidence Interval	-3.5 to -2.4

[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.

5. Secondary: Change in Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Secondary
Measure Title	Change in Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition
Measure Description	The table below shows the least-squares (LS) mean change in total fat from Baseline to Week 26 for each treatment group in patients randomized to the subset of patients undergoing specific DXA analysis for body composition. The statistical analyses show the treatment differences (ie, each canagliflozin 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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo		

		Canagliflozin 100 mg	Canagliflozin 300 mg
Number of Participants Analyzed [units: participants]	**50**	**56**	**60**
Change in Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition [units: kg] Least Squares Mean (Standard Error)	**-0.28 (0.336)**	**-1.87 (0.332)**	**-2.38 (0.323)**

Statistical Analysis 1 for Change in Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-1.59
Standard Error of the mean	(0.379)
95% Confidence Interval	-2.339 to -0.842

[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 Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition

Groups [1]	Placebo vs. Canagliflozin 300 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-2.10
Standard Error of the mean	(0.371)
95% Confidence Interval	-2.833 to -1.368

[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.

6. Secondary: Change in Region Percent Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray

Absorptiometry (DXA) Analysis for Body Composition [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Secondary
Measure Title	Change in Region Percent Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition
Measure Description	Region percent total fat = body fat as a percentage of (body fat + lean body mass + bone mass content). The table below shows the least-squares (LS) mean change in region percent total fat from Baseline to Week 26 for each treatment group in patients randomized to the subset of patients undergoing specific dual-energy X-ray absorptiometry (DXA) analysis for body composition. The statistical analyses show the treatment differences (ie, each canagliflozin 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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo	Canagliflozin 100 mg	Canagliflozin 300 mg
Number of Participants Analyzed [units: participants]	**50**	**56**	**60**
Change in Region Percent Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition [units: Percent] Least Squares Mean (Standard Error)	**0.00 (0.270)**	**-1.03 (0.268)**	**-1.18 (0.261)**

Statistical Analysis 1 for Change in Region Percent Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-1.03
Standard Error of the mean	(0.305)
95% Confidence Interval	-1.633 to -0.428

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Region percent total fat
[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 Region Percent Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition

Groups [1]	Placebo vs. Canagliflozin 300 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-1.18
Standard Error of the mean	(0.300)
95% Confidence Interval	-1.772 to -0.587

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Region percent total fat
[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.

7. Secondary: Change in Tissue Percent Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Secondary
Measure Title	Change in Tissue Percent Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition
Measure Description	Tissue percent total fat = body fat as a percentage of body fat + lean body mass. The table below shows the least-squares (LS) mean change in tissue percent total fat from Baseline to Week 26 for each treatment group in patients randomized to the subset of patients undergoing specific DXA analysis for body composition. The statistical analyses show the treatment differences (ie, each canagliflozin 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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo	Canagliflozin 100 mg	Canagliflozin 300 mg
Number of Participants Analyzed [units: participants]	**50**	**56**	**60**
Change in Tissue Percent Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition [units: Percent] Least Squares Mean (Standard Error)	**0.02 (0.280)**	**-1.04 (0.278)**	**-1.18 (0.270)**

Statistical Analysis 1 for Change in Tissue Percent Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	0.001
Least-Squares Mean Difference [4]	-1.05
Standard Error of the mean	(0.316)
95% Confidence Interval	-1.677 to -0.430

[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 Tissue Percent Total Fat From Baseline to Week 26 in a Subset of Patients Undergoing Specific Dual-energy X-ray Absorptiometry (DXA) Analysis for Body Composition

Groups [1]	Placebo vs. Canagliflozin 300 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-1.20
Standard Error of the mean	(0.311)
95% Confidence Interval	-1.812 to -0.584

[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.

8. 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 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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo	Canagliflozin 100 mg	Canagliflozin 300 mg
Number of Participants Analyzed [units: participants]	**234**	**240**	**229**
Change in Systolic Blood Pressure (SBP) From Baseline to Week 26 [units: mmHg] Least Squares Mean (Standard Error)	**1.10 (1.039)**	**-3.52 (1.035)**	**-6.79 (1.056)**

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

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-4.63
Standard Error of the mean	(1.134)
95% Confidence Interval	-6.854 to -2.401

[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 vs. Canagliflozin 300 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	-7.89
Standard Error of the mean	(1.147)
95% Confidence Interval	-10.14 to -5.641

[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.

9. 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 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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo	**Canagliflozin 100 mg**	**Canagliflozin 300 mg**
Number of Participants Analyzed [units: participants]	**206**	**227**	**222**

Percent Change in Triglycerides From Baseline to Week 26 [units: Percent change] Least Squares Mean (Standard Error)	**7.7 (3.4)**	**2.8 (3.3)**	**8.4 (3.4)**

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

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	0.194
Least-Squares Mean Difference [4]	-4.8
Standard Error of the mean	(3.7)
95% Confidence Interval	-12.1 to 2.5

[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 26

Groups [1]	Placebo vs. Canagliflozin 300 mg

Method [2]	ANCOVA
P Value [3]	0.846
Least-Squares Mean Difference [4]	0.7
Standard Error of the mean	(3.7)
95% Confidence Interval	-6.6 to 8.1

[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.

10. 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 or each treatment group. The statistical analyses show the treatment differences (ie, each canagliflozin 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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo	**Canagliflozin 100 mg**	**Canagliflozin 300 mg**
Number of Participants Analyzed [units: participants]	**206**	**225**	**222**
Percent Change in High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 26 [units: Percent change] Least Squares Mean (Standard Error)	**1.5 (1.2)**	**6.8 (1.2)**	**6.2 (1.2)**

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

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	ANCOVA
P Value [3]	<0.001
Least-Squares Mean Difference [4]	5.3
Standard Error of the mean	(1.4)
95% Confidence Interval	2.6 to 7.9

[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 High-density Lipoprotein Cholesterol (HDL-C) From Baseline to Week 26

Groups [1]	Placebo vs. Canagliflozin 300 mg
Method [2]	ANCOVA
P Value [3]	<0.001

Least-Squares Mean Difference [4]	4.7
Standard Error of the mean	(1.4)
95% Confidence Interval	2.0 to 7.4

[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.

11. Secondary: Percent Change in Lumbar Spine Bone Mineral Density (BMD) From Baseline to Week 26 [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Secondary
Measure Title	Percent Change in Lumbar Spine Bone Mineral Density (BMD) From Baseline to Week 26
Measure Description	The table below shows the least-squares (LS) mean percent change from Baseline to Week 26 in lumbar spine BMD for each treatment group as assessed by dual-energy X-ray absorptiometry (DXA). The statistical analyses show the treatment differences (ie, each canagliflozin group minus placebo) in LS mean percent change.
Time Frame	Day 1 (Baseline) and Week 26
Safety Issue	Yes

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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo	**Canagliflozin 100 mg**	**Canagliflozin 300 mg**
Number of Participants Analyzed [units: participants]	**185**	**206**	**192**
Percent Change in Lumbar Spine Bone Mineral Density (BMD) From Baseline to Week 26 [units: Percent change] Least Squares Mean (Standard Error)	**0.5 (0.3)**	**0.7 (0.3)**	**0.2 (0.3)**

Statistical Analysis 1 for Percent Change in Lumbar Spine Bone Mineral Density (BMD) From Baseline to Week 26

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	0.2
Standard Error of the mean	(0.3)
95% Confidence Interval	-0.4 to 0.8

[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]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change in Lumbar Spine Bone Mineral Density (BMD) From Baseline to Week 26

Groups [1]	Placebo vs. Canagliflozin 300 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	-0.3
Standard Error of the mean	(0.3)
95% Confidence Interval	-0.9 to 0.3

[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]	Other relevant estimation information:
	No text entered.

12. Secondary: Percent Change in Distal Forearm Bone Mineral Density (BMD) From Baseline to Week 26 [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Secondary
Measure Title	Percent Change in Distal Forearm Bone Mineral Density (BMD) From Baseline to Week 26
Measure Description	The table below shows the least-squares (LS) mean percent change from Baseline to Week 26 in distal forearm BMD for each treatment group as assessed by dual-energy X-ray absorptiometry (DXA). The statistical analyses show the treatment differences (ie, each canagliflozin group minus placebo) in LS mean percent change.
Time Frame	Day 1 (Baseline) and Week 26
Safety Issue	Yes

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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo	**Canagliflozin 100 mg**	**Canagliflozin 300 mg**
Number of Participants Analyzed [units: participants]	**187**	**208**	**187**
Percent Change in Distal Forearm Bone Mineral Density (BMD) From Baseline to Week 26 [units: Percent change] Least Squares Mean (Standard Error)	**-0.5 (0.3)**	**-0.7 (0.3)**	**-0.8 (0.3)**

Statistical Analysis 1 for Percent Change in Distal Forearm Bone Mineral Density (BMD) From Baseline to Week 26

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	-0.3
Standard Error of the mean	(0.3)
95% Confidence Interval	-0.9 to 0.4

[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.

Statistical Analysis 2 for Percent Change in Distal Forearm Bone Mineral Density (BMD) From Baseline to Week 26

Groups [1]	Placebo vs. Canagliflozin 300 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	-0.4
Standard Error of the mean	(0.3)
95% Confidence Interval	-1.0 to 0.3

[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]	Other relevant estimation information:
	No text entered.

13. Secondary: Percent Change in Femoral Neck Bone Mineral Density (BMD) From Baseline to Week 26 [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Secondary
Measure Title	Percent Change in Femoral Neck Bone Mineral Density (BMD) From Baseline to Week 26
Measure Description	The table below shows the least-squares (LS) mean percent change from Baseline to Week 26 in femoral neck BMD for each treatment group as assessed by dual-energy X-ray absorptiometry (DXA). The statistical analyses show the

	treatment differences (ie, each canagliflozin group minus placebo) in LS mean percent change.
Time Frame	Day 1 (Baseline) and Week 26
Safety Issue	Yes

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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo	Canagliflozin 100 mg	Canagliflozin 300 mg
Number of Participants Analyzed [units: participants]	**183**	**209**	**190**
Percent Change in Femoral Neck Bone Mineral Density (BMD) From Baseline to Week 26 [units: Percent change] Least Squares Mean (Standard Error)	**-1.0 (0.3)**	**-0.7 (0.3)**	**-0.6 (0.3)**

Statistical Analysis 1 for Percent Change in Femoral Neck Bone Mineral Density (BMD) From Baseline to Week 26

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	0.3
Standard Error of the mean	(0.3)
95% Confidence Interval	-0.3 to 1.0

[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]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change in Femoral Neck Bone Mineral Density (BMD) From Baseline to Week 26

Groups [1]	Placebo vs. Canagliflozin 300 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	0.4
Standard Error of the mean	(0.3)
95% Confidence Interval	-0.3 to 1.1

[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.

14. Secondary: Percent Change in Total Hip Bone Mineral Density (BMD) From Baseline to Week 26 [Time Frame: Day 1 (Baseline) and Week 26]

Measure Type	Secondary
Measure Title	Percent Change in Total Hip Bone Mineral Density (BMD) From Baseline to Week 26
Measure Description	The table below shows the least-squares (LS) mean percent change from Baseline to Week 26 in total hip BMD for each treatment group as assessed by dual-energy X-ray absorptiometry (DXA). The statistical analyses show the treatment differences (ie, each canagliflozin group minus placebo) in LS mean percent change.
Time Frame	Day 1 (Baseline) and Week 26
Safety Issue	Yes

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	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 100 mg	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.
Canagliflozin 300 mg	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry.

Measured Values

	Placebo	**Canagliflozin 100 mg**	**Canagliflozin 300 mg**
Number of Participants Analyzed [units: participants]	**183**	**209**	**190**
Percent Change in Total Hip Bone Mineral Density (BMD) From Baseline to Week 26 [units: Percent change] Least Squares Mean (Standard Error)	**-0.5 (0.2)**	**-0.9 (0.2)**	**-1.0 (0.2)**

Statistical Analysis 1 for Percent Change in Total Hip Bone Mineral Density (BMD) From Baseline to Week 26

Groups [1]	Placebo vs. Canagliflozin 100 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	-0.4
Standard Error of the mean	(0.2)
95% Confidence Interval	-0.8 to -0.0

[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]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percent Change in Total Hip Bone Mineral Density (BMD) From Baseline to Week 26

Groups [1]	Placebo vs. Canagliflozin 300 mg
Method [2]	ANCOVA
Least-Squares Mean Difference [3]	-0.5
Standard Error of the mean	(0.2)
95% Confidence Interval	-0.9 to -0.1

[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.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Adverse event data was collected for the duration of the study (104 weeks).

Additional Description	The total number of adverse events listed in the "Other (non-Serious) Adverse Events" 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. MEDDRA 14.0 used for Week 26 results/ MEDDRA 16.0 used for Week 104 results.

Reporting Groups

	Description
Placebo: Baseline to Week 26	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry. 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 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry. 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 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry. Data are presented for Baseline to Week 26.
Placebo: Baseline to Week 104	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry. Data are presented for Baseline to Week 104.
Canagliflozin 100 mg: Baseline to Week 104	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry. Data are presented for Baseline to Week 104
Canagliflozin 300 mg: Baseline to Week 104	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry. Data are presented for Baseline to Week 104

Serious Adverse Events

	Placebo: Baseline to Week 26	Canagliflozin 100 mg: Baseline to Week 26	Canagliflozin 300 mg: Baseline to Week 26	Placebo: Baseline to Week 104	Canagliflozin 100 mg: Baseline to Week 104	Canagliflozin 300 mg: Baseline to Week 104

Total, serious adverse events						
# participants affected / at risk	**12/237 (5.06%)**	**10/241 (4.15%)**	**8/236 (3.39%)**	**41/237 (17.30%)**	**40/241 (16.60%)**	**43/236 (18.22%)**
Cardiac disorders						
Angina pectoris [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Atrial fibrillation [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**	**2/237 (0.84%)**	**1/241 (0.41%)**	**3/236 (1.27%)**
Bradycardia [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Cardiac failure congestive [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Coronary artery disease [*1]						
# participants affected / at risk	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**3/237 (1.27%)**	**3/241 (1.24%)**	**3/236 (1.27%)**
Myocardial infarction [*1]						
# participants affected / at risk	**2/237 (0.84%)**	**0/241 (0.00%)**	**1/236 (0.42%)**	**2/237 (0.84%)**	**1/241 (0.41%)**	**2/236 (0.85%)**
Myocarditis [*1]						
# participants affected / at risk	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Acute myocardial						

infarction [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**2/236 (0.85%)**
Angina unstable [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**2/237 (0.84%)**	**0/241 (0.00%)**	**2/236 (0.85%)**
Intracardiac thrombus [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Sick sinus syndrome [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Eye disorders						
Diplopia [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Gastrointestinal disorders						
Haematochezia [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Intestinal infarction [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Umbilical hernia, obstructive [*1]						
# participants affected / at risk	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Abdominal hernia						

obstructive [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Abdominal pain upper [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Colitis [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Gastrointestinal angiodysplasia haemorrhagic [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Gastrointestinal haemorrhage [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Gastrooesophageal reflux disease [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Inguinal hernia, obstructive [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Intestinal obstruction [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**1/241 (0.41%)**	**1/236 (0.42%)**

Lower gastrointestinal haemorrhage [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**2/236 (0.85%)**
Pancreatitis [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Pouchitis [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Small intestinal obstruction [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
General disorders						
Non-cardiac chest pain [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**2/237 (0.84%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Hepatobiliary disorders						
Bile duct obstruction [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Cholecystitis [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Cholecystitis acute [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**

Cholelithiasis [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Immune system disorders						
Drug hypersensitivity [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Infections and infestations						
Pneumonia [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**2/236 (0.85%)**	**2/237 (0.84%)**	**0/241 (0.00%)**	**3/236 (1.27%)**
Urinary tract infection [*1]						
# participants affected / at risk	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Urosepsis [*1]						
# participants affected / at risk	**2/237 (0.84%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**2/237 (0.84%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Appendicitis perforated [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Cholecystitis infective [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**2/241 (0.83%)**	**0/236 (0.00%)**
Gastroenteritis [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Otitis media [*1]						
# participants affected	**0/237 (0.00%)**					

/ at risk		0/241 (0.00%)	0/236 (0.00%)	0/237 (0.00%)	0/241 (0.00%)	1/236 (0.42%)
Sepsis [*1]						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	1/237 (0.42%)	0/241 (0.00%)	1/236 (0.42%)
Subcutaneous abscess [*1]						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	0/237 (0.00%)	0/241 (0.00%)	1/236 (0.42%)
Injury, poisoning and procedural complications						
Ankle fracture [*1]						
# participants affected / at risk	0/237 (0.00%)	1/241 (0.41%)	0/236 (0.00%)	0/237 (0.00%)	2/241 (0.83%)	0/236 (0.00%)
Cervical vertebral fracture [*1]						
# participants affected / at risk	1/237 (0.42%)	0/241 (0.00%)	0/236 (0.00%)	1/237 (0.42%)	0/241 (0.00%)	0/236 (0.00%)
Hand fracture [*1]						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	1/237 (0.42%)	0/241 (0.00%)	0/236 (0.00%)
Hip fracture [*1]						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	0/237 (0.00%)	0/241 (0.00%)	1/236 (0.42%)
Joint dislocation [*1]						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	1/237 (0.42%)	0/241 (0.00%)	0/236 (0.00%)
Laceration [*1]						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	0/237 (0.00%)	1/241 (0.41%)	0/236 (0.00%)

Meniscus injury [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Muscle rupture [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Procedural pain [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Investigations						
Blood pressure increased [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Metabolism and nutrition disorders						
Hypoglycaemia [*1]						
# participants affected / at risk	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Diabetic ketoacidosis [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Musculoskeletal and connective tissue disorders						
Osteoarthritis [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**1/241 (0.41%)**	**2/236 (0.85%)**
Cartilage atrophy [*1]						

# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	1/237 (0.42%)	0/241 (0.00%)	0/236 (0.00%)
Cervical spinal stenosis * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	0/237 (0.00%)	0/241 (0.00%)	1/236 (0.42%)
Foot deformity * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	1/237 (0.42%)	0/241 (0.00%)	0/236 (0.00%)
Muscular weakness * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	0/237 (0.00%)	0/241 (0.00%)	1/236 (0.42%)
Musculoskeletal chest pain * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	1/237 (0.42%)	1/241 (0.41%)	0/236 (0.00%)
Spinal column stenosis * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	1/237 (0.42%)	0/241 (0.00%)	0/236 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Bronchioloalveolar carcinoma * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	1/236 (0.42%)	0/237 (0.00%)	0/241 (0.00%)	1/236 (0.42%)
Metastases to central nervous system * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	1/236 (0.42%)	0/237 (0.00%)	0/241 (0.00%)	1/236 (0.42%)

Prostate cancer [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**2/241 (0.83%)**	**0/236 (0.00%)**
Squamous cell carcinoma [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Adrenal adenoma [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Angiosarcoma [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Benign salivary gland neoplasm [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Breast cancer [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**2/236 (0.85%)**
Colon cancer [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Hodgkin's disease [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Papillary thyroid cancer [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**2/236 (0.85%)**

Thyroid neoplasm [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Nervous system disorders						
Carotid artery stenosis [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Cerebrovascular accident [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**3/241 (1.24%)**	**1/236 (0.42%)**
Presyncope [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Cauda equina syndrome [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Hepatic encephalopathy [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Hypoaesthesia [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Hypoglycaemic coma [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Hypoglycaemic seizure [*1]						

# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	1/237 (0.42%)	0/241 (0.00%)	0/236 (0.00%)
Loss of consciousness * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	1/237 (0.42%)	0/241 (0.00%)	0/236 (0.00%)
Migraine with aura * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	1/237 (0.42%)	0/241 (0.00%)	0/236 (0.00%)
Syncope * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	0/237 (0.00%)	1/241 (0.41%)	0/236 (0.00%)
Transient ischaemic attack * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	0/237 (0.00%)	1/241 (0.41%)	0/236 (0.00%)
Psychiatric disorders						
Post-traumatic stress disorder * 1						
# participants affected / at risk	0/237 (0.00%)	1/241 (0.41%)	0/236 (0.00%)	0/237 (0.00%)	1/241 (0.41%)	0/236 (0.00%)
Renal and urinary disorders						
Renal colic * 1						
# participants affected / at risk	1/237 (0.42%)	0/241 (0.00%)	0/236 (0.00%)	2/237 (0.84%)	0/241 (0.00%)	0/236 (0.00%)
Renal impairment * 1						
# participants affected / at risk	1/237 (0.42%)	0/241 (0.00%)	1/236 (0.42%)	1/237 (0.42%)	0/241 (0.00%)	1/236 (0.42%)
Calculus ureteric * 1						

# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	0/237 (0.00%)	1/241 (0.41%)	0/236 (0.00%)
Nephrolithiasis [*1]						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	0/237 (0.00%)	3/241 (1.24%)	1/236 (0.42%)
Reproductive system and breast disorders						
Balanoposthitis [*1]						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	0/237 (0.00%)	0/241 (0.00%)	1/236 (0.42%)
Benign prostatic hyperplasia [*1]						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	0/237 (0.00%)	0/241 (0.00%)	1/236 (0.42%)
Genital prolapse [*1]						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	0/237 (0.00%)	0/241 (0.00%)	1/236 (0.42%)
Respiratory, thoracic and mediastinal disorders						
Chronic obstructive pulmonary disease [*1]						
# participants affected / at risk	0/237 (0.00%)	1/241 (0.41%)	0/236 (0.00%)	0/237 (0.00%)	2/241 (0.83%)	0/236 (0.00%)
Respiratory failure [*1]						
# participants affected / at risk	0/237 (0.00%)	1/241 (0.41%)	0/236 (0.00%)	0/237 (0.00%)	1/241 (0.41%)	0/236 (0.00%)
Asthma [*1]						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	1/237 (0.42%)	0/241 (0.00%)	0/236 (0.00%)

Hypoventilation [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Nasal septum deviation [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Pulmonary embolism [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Pulmonary fibrosis [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**1/237 (0.42%)**	**0/241 (0.00%)**	**0/236 (0.00%)**
Sinus polyp [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Skin and subcutaneous tissue disorders						
Psoriasis [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Vascular disorders						
Deep vein thrombosis [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Embolism arterial [*1]						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**1/241 (0.41%)**	**0/236 (0.00%)**
Haematoma [*1]						

# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**
Peripheral vascular disorder * 1						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**0/237 (0.00%)**	**0/241 (0.00%)**	**1/236 (0.42%)**

* Events were collected by non-systematic assessment

1 Term from vocabulary, MEDDRA 14.0 / 16.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	Adverse event data was collected for the duration of the study (104 weeks).
Additional Description	The total number of adverse events listed in the "Other (non-Serious) Adverse Events" 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. MEDDRA 14.0 used for Week 26 results/ MEDDRA 16.0 used for Week 104 results.

Frequency Threshold

Threshold above which other adverse events are reported	5

Reporting Groups

	Description
Placebo: Baseline to Week 26	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry. 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 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry. 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 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry. Data are presented for Baseline to Week 26.
Placebo: Baseline to Week 104	Each patient received matching placebo once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry. Data are presented for Baseline to Week 104.
Canagliflozin 100 mg: Baseline to Week 104	Each patient received 100 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry. Data are presented for Baseline to Week 104
Canagliflozin 300 mg: Baseline to Week 104	Each patient received 300 mg of canagliflozin once daily for 104 weeks in addition to being on a stable antihyperglycemic (AHA) regimen at the time of study entry. Data are presented for Baseline to Week 104

Other Adverse Events

	Placebo: Baseline to Week 26	Canagliflozin 100 mg: Baseline to Week 26	Canagliflozin 300 mg: Baseline to Week 26	Placebo: Baseline to Week 104	Canagliflozin 100 mg: Baseline to Week 104	Canagliflozin 300 mg: Baseline to Week 104
Total, other (not including serious) adverse events						
# participants affected / at risk	**99/237 (41.77%)**	**92/241 (38.17%)**	**98/236 (41.53%)**	**166/237 (70.04%)**	**169/241 (70.12%)**	**169/236 (71.61%)**
Gastrointestinal disorders						
Diarrhoea [*1]						
# participants affected / at risk	**14/237 (5.91%)**	**10/241 (4.15%)**	**11/236 (4.66%)**	**24/237 (10.13%)**	**14/241 (5.81%)**	**24/236 (10.17%)**
Constipation [*1]						

# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	8/237 (3.38%)	18/241 (7.47%)	13/236 (5.51%)
Nausea * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	16/237 (6.75%)	11/241 (4.56%)	13/236 (5.51%)
General disorders						
Oedema peripheral * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	17/237 (7.17%)	6/241 (2.49%)	2/236 (0.85%)
Infections and infestations						
Influenza * 1						
# participants affected / at risk	5/237 (2.11%)	14/241 (5.81%)	9/236 (3.81%)	18/237 (7.59%)	25/241 (10.37%)	18/236 (7.63%)
Nasopharyngitis * 1						
# participants affected / at risk	19/237 (8.02%)	23/241 (9.54%)	19/236 (8.05%)	36/237 (15.19%)	45/241 (18.67%)	44/236 (18.64%)
Upper respiratory tract infection * 1						
# participants affected / at risk	11/237 (4.64%)	13/241 (5.39%)	10/236 (4.24%)	29/237 (12.24%)	23/241 (9.54%)	25/236 (10.59%)
Urinary tract infection * 1						
# participants						

affected / at risk	9/237 (3.80%)	14/241 (5.81%)	17/236 (7.20%)	21/237 (8.86%)	32/241 (13.28%)	35/236 (14.83%)
Bronchitis * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	8/237 (3.38%)	15/241 (6.22%)	11/236 (4.66%)
Sinusitis * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	13/237 (5.49%)	9/241 (3.73%)	6/236 (2.54%)
Vulvovaginal mycotic infection * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	1/237 (0.42%)	13/241 (5.39%)	11/236 (4.66%)
Metabolism and nutrition disorders						
Hypoglycaemia * 1						
# participants affected / at risk	34/237 (14.35%)	25/241 (10.37%)	23/236 (9.75%)	47/237 (19.83%)	37/241 (15.35%)	36/236 (15.25%)
Hyperglycaemia * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	19/237 (8.02%)	6/241 (2.49%)	6/236 (2.54%)
Musculoskeletal and connective tissue disorders						
Arthralgia * 1						

# participants affected / at risk	12/237 (5.06%)	4/241 (1.66%)	5/236 (2.12%)	24/237 (10.13%)	21/241 (8.71%)	9/236 (3.81%)
Back pain * 1						
# participants affected / at risk	8/237 (3.38%)	6/241 (2.49%)	12/236 (5.08%)	19/237 (8.02%)	24/241 (9.96%)	28/236 (11.86%)
Muscle spasms * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	13/237 (5.49%)	4/241 (1.66%)	6/236 (2.54%)
Pain in extremity * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	11/237 (4.64%)	16/241 (6.64%)	11/236 (4.66%)
Nervous system disorders						
Headache * 1						
# participants affected / at risk	15/237 (6.33%)	8/241 (3.32%)	13/236 (5.51%)	25/237 (10.55%)	14/241 (5.81%)	22/236 (9.32%)
Dizziness * 1						
# participants affected / at risk	0/237 (0.00%)	0/241 (0.00%)	0/236 (0.00%)	13/237 (5.49%)	9/241 (3.73%)	6/236 (2.54%)
Psychiatric disorders						
Insomnia * 1						
# participants						

affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**6/237 (2.53%)**	**5/241 (2.07%)**	**12/236 (5.08%)**
Renal and urinary disorders						
Pollakiuria * 1						
# participants affected / at risk	**6/237 (2.53%)**	**6/241 (2.49%)**	**12/236 (5.08%)**	**10/237 (4.22%)**	**11/241 (4.56%)**	**15/236 (6.36%)**
Respiratory, thoracic and mediastinal disorders						
Cough * 1						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**22/237 (9.28%)**	**17/241 (7.05%)**	**18/236 (7.63%)**
Oropharyngeal pain * 1						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**15/237 (6.33%)**	**11/241 (4.56%)**	**7/236 (2.97%)**
Vascular disorders						
Hypertension * 1						
# participants affected / at risk	**0/237 (0.00%)**	**0/241 (0.00%)**	**0/236 (0.00%)**	**12/237 (5.06%)**	**5/241 (2.07%)**	**7/236 (2.97%)**

* Events were collected by non-systematic assessment

1 Term from vocabulary, MEDDRA 14.0 / 16.0

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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Weir MR, Kline I, Xie J, Edwards R, Usiskin K. Effect of canagliflozin on serum electrolytes in patients with type 2 diabetes in relation to estimated glomerular filtration rate (eGFR). Curr Med Res Opin. 2014 Sep;30(9):1759-68. doi: 10.1185/03007995.2014.919907. Epub 2014 May 22.

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