Clinical trial results:
A Randomized, Double-Blind, Active-Controlled, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin Versus Sitagliptin in the Treatment of Subjects With Type 2 Diabetes Mellitus With Inadequate Glycemic Control on Metformin and Sulphonylurea Therapy

Due to a system error, the data reported in v1 and v2 are not correct and have been removed from public view.

Summary

EudraCT number	2010-020053-14
Trial protocol	DE AT BE NL DK
Global end of trial date	09 March 2012

Results information

Result version number	v3 (current)
This version publication date	15 July 2016
First version publication date	28 January 2015
Version creation reason	• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	28431754DIA3015

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01137812
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	Archimedsweg 29-2333CM, Leiden, Netherlands, B235-0
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 March 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 March 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of the addition of treatment with canagliflozin compared with the addition of treatment with sitagliptin on HbA1c after 52 weeks.
To assess the safety and tolerability of canagliflozin

Protection of trial subjects:

A company internal Medical Safety Review Committee (MSRC) was established to monitor the safety of participants participating in this study. The MSRC included, but will not be limited to, at least 1 medical expert and at least 1 statistician. The MSRC was composed of individuals from the sponsor organization. The MSRC monitored the progress of the study by reviewing blinded data on a regular basis.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 June 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Austria: 6
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Poland: 46
Country: Number of subjects enrolled	Brazil: 156
Country: Number of subjects enrolled	Canada: 86
Country: Number of subjects enrolled	India: 56
Country: Number of subjects enrolled	Israel: 10
Country: Number of subjects enrolled	Malaysia: 24
Country: Number of subjects enrolled	New Zealand: 24
Country: Number of subjects enrolled	Singapore: 4
Country: Number of subjects enrolled	Korea, Republic of: 19

Country: Number of subjects enrolled	Ukraine: 46
Country: Number of subjects enrolled	United States: 243
Worldwide total number of subjects	756
EEA total number of subjects	88

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	612
From 65 to 84 years	142
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

The study was conducted between 30 June 2010 and 09 March 2012 and recruited participants from 140 study centers located in 17 countries worldwide.

Pre-assignment

Screening details:

A total of 756 participants were randomly allocated to the 2 treatment arms in the study. 755 participants received at least 1 dose of study drug and were included in the modified intent-to-treat (mITT) analysis set and the safety analysis set.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Canagliflozin 300 mg

Arm description:

Canagliflozin 300 milligram (mg) capsule once daily for 52 weeks along with protocol-specified doses of metformin and sulphonylurea.

Arm type	Experimental
Investigational medicinal product name	Canagliflozin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants administered with 300 mg Canagliflozin capsule once a daily.

Arm title	Sitagliptin 100 mg

Arm description:

Sitagliptin 100 mg capsule orally once daily for 52 weeks along with protocol-specified doses of metformin and sulphonylurea.

Arm type	Active comparator
Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants administered with 100 mg sitagliptin capsule once daily.

Number of subjects in period 1[1]	Canagliflozin 300 mg	Sitagliptin 100 mg
Started	377	378
Completed	254	210
Not completed	123	168
Creatinine or eGFR withdrawal criteria	22	14
Consent withdrawn by subject	5	13
Physician decision	2	3
Adverse event, non-fatal	21	14
Death	2	-
Study terminated by sponsor	1	-
Noncompliance with study drug	4	4
Unspecified	19	27
Participant met glycemic withdrawal criteria	40	85
Lost to follow-up	6	8
Protocol deviation	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One subject was randomly assigned to canagliflozin 300 mg group, but not dosed.

Baseline characteristics

Reporting groups	
Reporting group title	Canagliflozin 300 mg
Reporting group description:	
Canagliflozin 300 milligram (mg) capsule once daily for 52 weeks along with protocol-specified doses of metformin and sulphonylurea.	
Reporting group title	Sitagliptin 100 mg
Reporting group description:	
Sitagliptin 100 mg capsule orally once daily for 52 weeks along with protocol-specified doses of metformin and sulphonylurea.	

Reporting group values	Canagliflozin 300 mg	Sitagliptin 100 mg	Total
Number of subjects	377	378	755
Age categorical Units: Subjects			
Less Than and Equal to (<=) 18 years	0	0	0
Between 18 and 65 years	304	307	611
Greater Than and Equal to (>=) 65 years	73	71	144
Age continuous Units: years			
arithmetic mean	56.6	56.7	
standard deviation	± 9.62	± 9.3	-
Gender categorical Units: Subjects			
Female	170	163	333
Male	207	215	422

End points

End points reporting groups

Reporting group title	Canagliflozin 300 mg
Reporting group description:	
Canagliflozin 300 milligram (mg) capsule once daily for 52 weeks along with protocol-specified doses of metformin and sulphonylurea.	
Reporting group title	Sitagliptin 100 mg
Reporting group description:	
Sitagliptin 100 mg capsule orally once daily for 52 weeks along with protocol-specified doses of metformin and sulphonylurea.	

Primary: Change From Baseline in Glycosylated Hemoglobin (HbA1c) at Week 52

End point title	Change From Baseline in Glycosylated Hemoglobin (HbA1c) at Week 52
End point description:	
Level of HbA1c is an indicator for the average level of blood glucose over the previous 3 months. Here "n" defines the number of participants who analysed for this end point.	
End point type	Primary
End point timeframe:	
Day 1 (Baseline), Week 52	

End point values	Canagliflozin 300 mg	Sitagliptin 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	377	378		
Units: percent				
arithmetic mean (standard deviation)				
Baseline (n = 374, 365)	8.12 (± 0.91)	8.13 (± 0.916)		
Change at week 52 (n= 374, 365)	-1 (± 0.94)	-0.63 (± 1.022)		

Statistical analyses

Statistical analysis title	Week 52: Change From Baseline in HbA1c
Statistical analysis description:	
If the hypothesis of non-inferiority of canagliflozin to sitagliptin at Week 52 was demonstrated (ie, upper bound of the 95% Confidence Interval of the treatment difference [canagliflozin minus sitagliptin] was less than 0.3) and the upper bound was less than 0.0, the superiority of the canagliflozin dose relative to sitagliptin would be concluded.	
Comparison groups	Sitagliptin 100 mg v Canagliflozin 300 mg

Number of subjects included in analysis	755
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Least-Squares Mean Difference
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.064

Notes:

[1] - Power calculation: assuming a difference between canagliflozin and sitagliptin of 0.0% and a common standard deviation of 1.0%, and using a 2-sample, 1-sided t-test with a Type I error rate of 0.025, it was estimated that 234 patients per group would provide approximately 90% power to demonstrate non-inferiority with the non-inferiority margin of 0.3, comparing canagliflozin with sitagliptin.

Secondary: Percentage of Participants With HbA1c Less Than (<) 7% at Week 52

End point title	Percentage of Participants With HbA1c Less Than (<) 7% at Week 52

End point description:

Level of HbA1c is an indicator for the average level of blood glucose over the previous 3 months.

End point type	Secondary

End point timeframe:

Week 52

End point values	Canagliflozin 300 mg	Sitagliptin 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	374	365		
Units: Percentage of Participants				
number (not applicable)	47.6	35.3		

Statistical analyses

Statistical analysis title	Week 52: Percentage of Participants With HbA1c <7%
Comparison groups	Canagliflozin 300 mg v Sitagliptin 100 mg
Number of subjects included in analysis	739
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	2.48

Secondary: Change From Baseline in Fasting Plasma Glucose (FPG) at Week 52

End point title	Change From Baseline in Fasting Plasma Glucose (FPG) at Week 52
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and Week 52	

End point values	Canagliflozin 300 mg	Sitagliptin 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	377	378		
Units: milligram(s)/decilitre				
arithmetic mean (standard deviation)				
Baseline	9.42 (± 2.639)	9.09 (± 2.423)		
Change at week 52	-1.72 (± 2.452)	-0.19 (± 2.881)		

Statistical analyses

Statistical analysis title	Week 52: Change From Baseline in FPG
Comparison groups	Canagliflozin 300 mg v Sitagliptin 100 mg
Number of subjects included in analysis	755
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least-Squares Mean Difference
Point estimate	-1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.658
upper limit	-1.012

Secondary: Percent Change From Baseline in Body Weight at Week 52

End point title	Percent Change From Baseline in Body Weight at Week 52
End point description:	
Here 'n' signifies the number of participants analysed for this endpoint.	
End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	Canagliflozin 300 mg	Sitagliptin 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	377	378		
Units: percentage change				
arithmetic mean (standard deviation)				
Baseline (n= 375, 367)	87.58 (± 23.159)	89.61 (± 23.147)		
Percentage change at week 52 (n= 375, 367)	-2.6 (± 3.7)	0.2 (± 3.6)		

Statistical analyses

Statistical analysis title	Week 52: Percent Change in Body Weight
Comparison groups	Canagliflozin 300 mg v Sitagliptin 100 mg
Number of subjects included in analysis	755
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least-Squares Mean Difference
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	-2.2
Variability estimate	Standard error of the mean
Dispersion value	0.3

Secondary: Change From Baseline in Systolic Blood Pressure (SBP) at Week 52

End point title	Change From Baseline in Systolic Blood Pressure (SBP) at Week 52
End point description:	
End point type	Secondary

End point timeframe: Baseline, Week 52

End point values	Canagliflozin 300 mg	Sitagliptin 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	367		
Units: millimeter of mercury (mm Hg)				
least squares mean (standard error)	-5.06 (± 0.656)	0.85 (± 0.666)		

Statistical analyses

Statistical analysis title	Week 52: Change From Baseline in SBP
Comparison groups	Canagliflozin 300 mg v Sitagliptin 100 mg
Number of subjects included in analysis	742
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least-Squares Mean Difference
Point estimate	-5.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.642
upper limit	-4.175
Variability estimate	Standard error of the mean
Dispersion value	0.883

Secondary: Percent Change From Baseline in Triglycerides at Week 52	
End point title	Percent Change From Baseline in Triglycerides at Week 52
End point description: Here 'n' signifies the number of participants analysed for this endpoint.	
End point type	Secondary
End point timeframe: Baseline, Week 52	

End point values	Canagliflozin 300 mg	Sitagliptin 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	377	378		
Units: Percentage change				
arithmetic mean (standard deviation)				
Baseline (n= 365, 353)	2.06 (± 1.389)	1.9 (± 1.327)		
Percentage change from Baseline (n = 365, 353)	7.8 (± 60.6)	11.6 (± 44.1)		

Statistical analyses

Statistical analysis title	Week 52: Percent Change in Triglycerides
Comparison groups	Canagliflozin 300 mg v Sitagliptin 100 mg
Number of subjects included in analysis	755
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.554
Method	ANCOVA
Parameter estimate	Least-Squares Mean Difference
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.8
upper limit	5.3
Variability estimate	Standard error of the mean
Dispersion value	3.9

Secondary: Percent Change From Baseline in High-density Lipoprotein Cholesterol (HDL-C) at Week 52

End point title	Percent Change From Baseline in High-density Lipoprotein Cholesterol (HDL-C) at Week 52
End point description:	
Here 'n' signifies the number of participants analysed for this endpoint.	
End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	Canagliflozin 300 mg	Sitagliptin 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	377	378		
Units: percentage change				
arithmetic mean (standard deviation)				
Baseline (n = 364, 353)	1.18 (± 0.308)	1.18 (± 0.308)		
Percentage change from baseline (n = 364, 353)	8.2 (± 16.9)	1.3 (± 17.2)		

Statistical analyses

Statistical analysis title	Week 52: Percent Change in HDL-C
Comparison groups	Canagliflozin 300 mg v Sitagliptin 100 mg
Number of subjects included in analysis	755
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least-Squares Mean Difference
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.6
upper limit	9.3
Variability estimate	Standard error of the mean
Dispersion value	1.2

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline upto 30 days after the last dose of study drug (Week 52) or early withdrawal	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups	
Reporting group title	Canagliflozin 300 mg
Reporting group description:	
Canagliflozin 300 milligram (mg) capsule once daily for 52 weeks along with protocol-specified doses of metformin and sulphonylurea.	
Reporting group title	Sitagliptin 100 mg
Reporting group description:	
Sitagliptin 100 mg capsule orally once daily for 52 weeks along with protocol-specified doses of metformin and sulphonylurea.	

Serious adverse events	Canagliflozin 300 mg	Sitagliptin 100 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 377 (6.37%)	21 / 378 (5.56%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal cancer stage unspecified			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			

subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arterial thrombosis limb			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	2 / 377 (0.53%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory arrest			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			

subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia, obstructive			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus lesion			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic rupture			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			

subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	2 / 377 (0.53%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 377 (0.00%)	2 / 378 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			

Cerebrovascular accident			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical cord compression			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gallbladder oedema			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Leukocytoclastic vasculitis			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	1 / 377 (0.27%)	0 / 378 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leptospirosis			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 377 (0.00%)	2 / 378 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	0 / 377 (0.00%)	1 / 378 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Canagliflozin 300 mg	Sitagliptin 100 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	157 / 377 (41.64%)	159 / 378 (42.06%)	
Nervous system disorders			
Headache			
subjects affected / exposed	29 / 377 (7.69%)	27 / 378 (7.14%)	
occurrences (all)	46	32	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	17 / 377 (4.51%)	26 / 378 (6.88%)	
occurrences (all)	21	32	
Infections and infestations			
Influenza			
subjects affected / exposed	22 / 377 (5.84%)	15 / 378 (3.97%)	
occurrences (all)	26	21	
Nasopharyngitis			

subjects affected / exposed	33 / 377 (8.75%)	38 / 378 (10.05%)	
occurrences (all)	40	44	
Upper respiratory tract infection			
subjects affected / exposed	33 / 377 (8.75%)	21 / 378 (5.56%)	
occurrences (all)	38	28	
Urinary tract infection			
subjects affected / exposed	15 / 377 (3.98%)	19 / 378 (5.03%)	
occurrences (all)	16	21	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	66 / 377 (17.51%)	75 / 378 (19.84%)	
occurrences (all)	223	259	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 July 2010	The overall reason for the amendment was to modify the exclusion criterion for the estimated glomerular filtration rate (eGFR) in order to expand participant eligibility yet remain consistent with the use of metformin per the local label.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported