Clinical trial results:
A Phase III, Randomized, Double-Blind, Multicenter Study to Evaluate the Efficacy and Safety of the Combination of Ertugliflozin (MK-8835/PF-04971729) with Sitagliptin Compared with Ertugliflozin Alone and Sitagliptin Alone, in the Treatment of Subjects with T2DM With Inadequate Glycemic Control on Metformin Monotherapy

Summary

EudraCT number	2013-003698-82
Trial protocol	HU CZ IT GB FI SK BG PL
Global end of trial date	26 May 2016

Results information

Result version number	v1
This version publication date	12 May 2017
First version publication date	12 May 2017

Trial information

Trial identification

Sponsor protocol code	8835-005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02099110
WHO universal trial number (UTN)	-
Other trial identifiers	MK-8835-005: Merck protocol number, B1521015: Pfizer protocol number

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	26 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a study of co-administration of ertugliflozin (MK-8835/PF-04971729) and sitagliptin given together or alone along with metformin in participants with type 2 diabetes mellitus (T2DM) and inadequate glycemic control on metformin monotherapy. The primary hypothesis of this study is that ertugliflozin 5 mg or 15 mg daily plus sitagliptin 100 mg daily provides greater hemoglobin A1C (A1C) - lowering compared with sitagliptin 100 mg daily alone.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Participants who meet pre-specified glycemic criteria and who are rescued will receive oral tablets of open-label glimepiride or insulin glargine injected subcutaneously at dose strengths determined by the investigator.

Background therapy:

For participants requiring metformin dose adjustment, metformin will be titrated over a period of up-to 4 weeks before the required dose-stabilization period (≥8 weeks) begins. While receiving blinded investigational product during the double-blind treatment period, participants will also receive metformin >= 1500 mg/day, tablets, oral, for 52 weeks.

Evidence for comparator: -

Actual start date of recruitment	22 April 2014
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	Argentina: 89
Country: Number of subjects enrolled	Bulgaria: 41
Country: Number of subjects enrolled	Canada: 38
Country: Number of subjects enrolled	Chile: 40
Country: Number of subjects enrolled	Colombia: 10
Country: Number of subjects enrolled	Czech Republic: 35
Country: Number of subjects enrolled	Finland: 7
Country: Number of subjects enrolled	Hungary: 36
Country: Number of subjects enrolled	Israel: 35

Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Malaysia: 27
Country: Number of subjects enrolled	Mexico: 71
Country: Number of subjects enrolled	New Zealand: 21
Country: Number of subjects enrolled	Philippines: 45
Country: Number of subjects enrolled	Poland: 87
Country: Number of subjects enrolled	Romania: 84
Country: Number of subjects enrolled	Russian Federation: 96
Country: Number of subjects enrolled	Slovakia: 58
Country: Number of subjects enrolled	Thailand: 9
Country: Number of subjects enrolled	Ukraine: 64
Country: Number of subjects enrolled	United States: 338
Worldwide total number of subjects	1233
EEA total number of subjects	350

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)	1034
From 65 to 84 years	199
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were randomized at 204 sites in 21 countries.

Pre-assignment

Screening details:

Male and female participants with Type 2 diabetes mellitus of at least 18 years of age were enrolled in this trial.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ertugliflozin 5 mg

Arm description:

Ertugliflozin 5 mg once daily, placebo to ertugliflozin once daily, placebo to sitagliptin once daily, and metformin >= 1500 mg/day, all for 52 weeks

Arm type	Experimental
Investigational medicinal product name	Ertugliflozin
Investigational medicinal product code	
Other name	MK-8835, PF-04971729
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ertugliflozin, 5 mg, once daily, orally for 52 weeks

Investigational medicinal product name	Placebo to ertugliflozin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to ertugliflozin once daily for 52 weeks

Investigational medicinal product name	Placebo to sitagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to sitagliptin once daily for 52 weeks

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	Glucophage Glucophage XR
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

For participants requiring metformin dose adjustment, metformin will be titrated over a period of up-to 4 weeks before the required dose-stabilization period (≥8 weeks) begins. While receiving blinded investigational product during the double-blind treatment period, participants will also receive metformin >= 1500 mg/day, tablets, oral, for 52 weeks.

Investigational medicinal product name	Insulin Glargine Rescue Medication
Investigational medicinal product code	
Other name	Lantus
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Open-label insulin glargine, subcutaneous injection, as required as a rescue medication; dose determined per the investigator's discretion

Investigational medicinal product name	Glimepiride Rescue Medication
Investigational medicinal product code	
Other name	AMARYL
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Open-label glimepiride tablets, oral, as required as a rescue medication, dose determined per the investigator's discretion

Arm title	Ertugliflozin 15 mg

Arm description:

Ertugliflozin 15 mg once daily, placebo to sitagliptin once daily, and metformin >= 1500 mg/day, all for 52 weeks

Arm type	Experimental
Investigational medicinal product name	Ertugliflozin
Investigational medicinal product code	
Other name	MK-8835, PF-04971729
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ertugliflozin 15 mg once daily, for 52 weeks

Investigational medicinal product name	Placebo to sitagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to sitagliptin once daily for 52 weeks

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	Glucophage Glucophage XR
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

For participants requiring metformin dose adjustment, metformin will be titrated over a period of up-to 4 weeks before the required dose-stabilization period (≥8 weeks) begins. While receiving blinded investigational product during the double-blind treatment period, participants will also receive metformin >= 1500 mg/day, tablets, oral, for 52 weeks.

Investigational medicinal product name	Insulin Glargine Rescue Medication
Investigational medicinal product code	
Other name	Lantus
Pharmaceutical forms	Solution for injection

Routes of administration	Subcutaneous use

Dosage and administration details:

Open-label insulin glargine, subcutaneous injection, as required as a rescue medication; dose determined per the investigator's discretion

Investigational medicinal product name	Glimepiride Rescue Medication
Investigational medicinal product code	
Other name	AMARYL
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Open-label glimepiride tablets, oral, as required as a rescue medication, dose determined per the investigator's discretion

Arm title	Sitagliptin 100 mg

Arm description:

Sitagliptin 100 mg once daily, placebo to ertugliflozin once daily, and metformin >= 1500 mg/day, all for 52 weeks

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

Dosage and administration details:

Sitagliptin 100 mg once daily, for 52 weeks

Investigational medicinal product name	Placebo to ertugliflozin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to ertugliflozin once daily for 52 weeks

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	Glucophage Glucophage XR
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

For participants requiring metformin dose adjustment, metformin will be titrated over a period of up-to 4 weeks before the required dose-stabilization period (≥8 weeks) begins. While receiving blinded investigational product during the double-blind treatment period, participants will also receive metformin >= 1500 mg/day, tablets, oral, for 52 weeks.

Investigational medicinal product name	Insulin Glargine Rescue Medication
Investigational medicinal product code	
Other name	Lantus
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Open-label insulin glargine, subcutaneous injection, as required as a rescue medication; dose determined per the investigator's discretion

Investigational medicinal product name	Glimepiride Rescue Medication
Investigational medicinal product code	
Other name	AMARYL
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Open-label glimepiride tablets, oral, as required as a rescue medication, dose determined per the investigator's discretion

Arm title	Ertugliflozin 5 mg + Sitagliptin 100 mg

Arm description:

Ertugliflozin 5 mg once daily, sitagliptin 100 mg once daily, placebo to ertugliflozin once daily, and metformin >= 1500 mg/day, all for 52 weeks

Arm type	Experimental
Investigational medicinal product name	Ertugliflozin
Investigational medicinal product code	
Other name	MK-8835, PF-04971729
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ertugliflozin 5 mg once daily for 52 weeks

Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	JANUVIA®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Sitagliptin 100 mg once daily, for 52 weeks

Investigational medicinal product name	Placebo to ertugliflozin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to ertugliflozin once daily for 52 weeks

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	Glucophage Glucophage XR
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

For participants requiring metformin dose adjustment, metformin will be titrated over a period of up-to 4 weeks before the required dose-stabilization period (≥8 weeks) begins. While receiving blinded investigational product during the double-blind treatment period, participants will also receive metformin >= 1500 mg/day, tablets, oral, for 52 weeks.

Investigational medicinal product name	Insulin Glargine Rescue Medication
Investigational medicinal product code	
Other name	Lantus
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Open-label insulin glargine, subcutaneous injection, as required as a rescue medication; dose determined per the investigator's discretion

Investigational medicinal product name	Glimepiride Rescue Medication
Investigational medicinal product code	
Other name	AMARYL
Pharmaceutical forms	Tablet

Routes of administration	Oral use

Dosage and administration details:

Open-label glimepiride tablets, oral, as required as a rescue medication, dose determined per the investigator's discretion

Arm title	Ertugliflozin 15 mg + Sitagliptin 100 mg

Arm description:

Ertugliflozin 15 mg once daily, sitagliptin 100 mg once daily, and metformin >= 1500 mg/day, all for 52 weeks

Arm type	Experimental
Investigational medicinal product name	Ertugliflozin
Investigational medicinal product code	
Other name	MK-8835, PF-04971729
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ertugliflozin 15 mg once daily, for 52 weeks

Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	JANUVIA®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Sitagliptin 100 mg once daily, for 52 weeks

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	Glucophage Glucophage XR
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

For participants requiring metformin dose adjustment, metformin will be titrated over a period of up-to 4 weeks before the required dose-stabilization period (≥8 weeks) begins. While receiving blinded investigational product during the double-blind treatment period, participants will also receive metformin >= 1500 mg/day, tablets, oral, for 52 weeks.

Investigational medicinal product name	Insulin Glargine Rescue Medication
Investigational medicinal product code	
Other name	Lantus
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Open-label insulin glargine, subcutaneous injection, as required as a rescue medication; dose determined per the investigator's discretion

Investigational medicinal product name	Glimepiride Rescue Medication
Investigational medicinal product code	
Other name	AMARYL
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Open-label glimepiride tablets, oral, as required as a rescue medication, dose determined per the investigator's discretion

Number of subjects in period 1	Ertugliflozin 5 mg	Ertugliflozin 15 mg	Sitagliptin 100 mg
Started	250	248	247
Treated	250	248	247
Completed	226	217	219
Not completed	24	31	28
Physician decision	3	-	1
Consent withdrawn by subject	7	11	13
Screen Failure	-	-	-
Non-Compliance with Study Drug	2	-	-
Adverse event, non-fatal	3	5	2
Death	-	1	-
Participant Moved	1	1	1
Lost to follow-up	6	12	11
Protocol deviation	2	1	-

Number of subjects in period 1	Ertugliflozin 5 mg + Sitagliptin 100 mg	Ertugliflozin 15 mg + Sitagliptin 100 mg
Started	243	245
Treated	243	244
Completed	221	218
Not completed	22	27
Physician decision	2	1
Consent withdrawn by subject	9	13
Screen Failure	-	1
Non-Compliance with Study Drug	-	1
Adverse event, non-fatal	3	2
Death	-	-
Participant Moved	-	2
Lost to follow-up	5	6
Protocol deviation	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Ertugliflozin 5 mg
Reporting group description:	
Ertugliflozin 5 mg once daily, placebo to ertugliflozin once daily, placebo to sitagliptin once daily, and metformin >= 1500 mg/day, all for 52 weeks	
Reporting group title	Ertugliflozin 15 mg
Reporting group description:	
Ertugliflozin 15 mg once daily, placebo to sitagliptin once daily, and metformin >= 1500 mg/day, all for 52 weeks	
Reporting group title	Sitagliptin 100 mg
Reporting group description:	
Sitagliptin 100 mg once daily, placebo to ertugliflozin once daily, and metformin >= 1500 mg/day, all for 52 weeks	
Reporting group title	Ertugliflozin 5 mg + Sitagliptin 100 mg
Reporting group description:	
Ertugliflozin 5 mg once daily, sitagliptin 100 mg once daily, placebo to ertugliflozin once daily, and metformin >= 1500 mg/day, all for 52 weeks	
Reporting group title	Ertugliflozin 15 mg + Sitagliptin 100 mg
Reporting group description:	
Ertugliflozin 15 mg once daily, sitagliptin 100 mg once daily, and metformin >= 1500 mg/day, all for 52 weeks	

Reporting group values	Ertugliflozin 5 mg	Ertugliflozin 15 mg	Sitagliptin 100 mg
Number of subjects	250	248	247
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	214	205	205
From 65-84 years	35	43	42
85 years and over	1	0	0
Age Continuous Units: years			
arithmetic mean	55.1	55.3	54.8
standard deviation	± 10.1	± 9.5	± 10.7
Gender Categorical Units: Subjects			
Female	123	114	93
Male	127	134	154
Hemoglobin A1C % n=244, 247, 242, 237, 241 Units: Percent glycated hemoglobin			
arithmetic mean	8.57	8.57	8.5

standard deviation	± 1.05	± 1.01	± 1.03
Fasting Plasma Glucose (FPG) n=250, 247, 246, 240, 241			
Units: mg/dL			
arithmetic mean	184.1	179.5	177.4
standard deviation	± 52.2	± 45.6	± 46.6

Reporting group values	Ertugliflozin 5 mg + Sitagliptin 100 mg	Ertugliflozin 15 mg + Sitagliptin 100 mg	Total
Number of subjects	243	245	1233
Age Categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	199	211	1034
From 65-84 years	44	34	198
85 years and over	0	0	1
Age Continuous			
Units: years			
arithmetic mean	55.2	55.1	
standard deviation	± 10.4	± 9.8	-
Gender Categorical			
Units: Subjects			
Female	120	118	568
Male	123	127	665
Hemoglobin A1C % n=244, 247, 242, 237, 241			
Units: Percent glycated hemoglobin			
arithmetic mean	8.56	8.56	
standard deviation	± 0.99	± 0.97	-
Fasting Plasma Glucose (FPG) n=250, 247, 246, 240, 241			
Units: mg/dL			
arithmetic mean	183.8	177.2	
standard deviation	± 44.3	± 49.4	-

End points

End points reporting groups

Reporting group title	Ertugliflozin 5 mg
Reporting group description:	
Ertugliflozin 5 mg once daily, placebo to ertugliflozin once daily, placebo to sitagliptin once daily, and metformin >= 1500 mg/day, all for 52 weeks	
Reporting group title	Ertugliflozin 15 mg
Reporting group description:	
Ertugliflozin 15 mg once daily, placebo to sitagliptin once daily, and metformin >= 1500 mg/day, all for 52 weeks	
Reporting group title	Sitagliptin 100 mg
Reporting group description:	
Sitagliptin 100 mg once daily, placebo to ertugliflozin once daily, and metformin >= 1500 mg/day, all for 52 weeks	
Reporting group title	Ertugliflozin 5 mg + Sitagliptin 100 mg
Reporting group description:	
Ertugliflozin 5 mg once daily, sitagliptin 100 mg once daily, placebo to ertugliflozin once daily, and metformin >= 1500 mg/day, all for 52 weeks	
Reporting group title	Ertugliflozin 15 mg + Sitagliptin 100 mg
Reporting group description:	
Ertugliflozin 15 mg once daily, sitagliptin 100 mg once daily, and metformin >= 1500 mg/day, all for 52 weeks	
Subject analysis set title	Ertugliflozin 5 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Ertugliflozin 5 mg once daily, placebo to ertugliflozin once daily, placebo to sitagliptin once daily, and metformin >= 1500 mg/day, all for 52 weeks	
Subject analysis set title	Ertugliflozin 15 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Ertugliflozin 15 mg once daily, placebo to sitagliptin once daily, and metformin >= 1500 mg/day, all for 52 weeks	
Subject analysis set title	Sitagliptin 100 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Sitagliptin 100 mg once daily, placebo to ertugliflozin once daily, and metformin >= 1500 mg/day, all for 52 weeks	
Subject analysis set title	Ertugliflozin 5 mg + Sitagliptin 100 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Ertugliflozin 5 mg once daily, sitagliptin 100 mg once daily, placebo to ertugliflozin once daily, and metformin >= 1500 mg/day, all for 52 weeks	
Subject analysis set title	Ertugliflozin 15 mg + Sitagliptin 100 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Ertugliflozin 15 mg once daily, sitagliptin 100 mg once daily, and metformin >= 1500 mg/day, all for 52 weeks	

Primary: Change from Baseline in Hemoglobin A1C (A1C) at Week 26 Excluding Data After Initiation of Rescue Therapy

End point title	Change from Baseline in Hemoglobin A1C (A1C) at Week 26 Excluding Data After Initiation of Rescue Therapy

End point description:

Hemoglobin A1C is blood marker used to report average blood glucose levels over prolonged periods of time and is reported as a percentage (% glycated hemoglobin). Thus, this change from baseline reflects the Week 26 A1C minus the Week 0 A1C. The population analyzed included all randomized, treated participants who had at least 1 baseline or post-baseline A1C measurement. Rescue Therapy: Participants who met pre-specified glycemic criteria were rescued with oral tablets of open-label glimepiride or insulin glargine injected subcutaneously at dose strengths determined by the investigator.

End point type	Primary

End point timeframe:

Baseline and Week 26

End point values	Ertugliflozin 5 mg	Ertugliflozin 15 mg	Sitagliptin 100 mg	Ertugliflozin 5 mg + Sitagliptin 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	250	248	247	243
Units: Percent glycated hemoglobin				
least squares mean (confidence interval 95%)	-1.02 (-1.14 to -0.9)	-1.08 (-1.2 to -0.96)	-1.05 (-1.17 to -0.93)	-1.49 (-1.61 to -1.36)

End point values	Ertugliflozin 15 mg + Sitagliptin 100 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	244			
Units: Percent glycated hemoglobin				
least squares mean (confidence interval 95%)	-1.52 (-1.64 to -1.4)			

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Based on Constrained Longitudinal Data Analysis (cLDA) model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.

Comparison groups	Ertugliflozin 5 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg
Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-0.46

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	-0.3

Statistical analysis title	Difference in the Least Squares Means
Statistical analysis description:	
Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.	
Comparison groups	Sitagliptin 100 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	-0.27

Statistical analysis title	Difference in the Least Squares Means
Statistical analysis description:	
Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.	
Comparison groups	Ertugliflozin 15 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	-0.27

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.

Comparison groups	Sitagliptin 100 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	-0.3

Primary: Percentage of Participants Who Experienced an Adverse Event (AE)

End point title	Percentage of Participants Who Experienced an Adverse Event (AE)

End point description:

An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. The population analyzed included all randomized, treated participants.

End point type	Primary

End point timeframe:

Up to 54 weeks

End point values	Ertugliflozin 5 mg	Ertugliflozin 15 mg	Sitagliptin 100 mg	Ertugliflozin 5 mg + Sitagliptin 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	250	248	247	243
Units: Percentage of Participants				
number (not applicable)	62	57.7	57.5	58.8

End point values	Ertugliflozin 15 mg + Sitagliptin 100 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	244			
Units: Percentage of Participants				
number (not applicable)	55.7			

Statistical analyses

Statistical analysis title	Difference in % of Participants
Statistical analysis description: Difference in % of Participants	
Comparison groups	Ertugliflozin 5 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg
Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen
Parameter estimate	Difference in % vs Ertugliflozin 5 mg
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	5.5

Statistical analysis title	Difference in % vs Ertugliflozin 15 mg
Statistical analysis description: Difference in % vs Ertugliflozin 15 mg	
Comparison groups	Ertugliflozin 15 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen
Parameter estimate	Difference in % vs Ertugliflozin 5 mg
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	6.8

Statistical analysis title	Difference in % vs Sitagliptin 100 mg
Statistical analysis description: Difference in % vs Sitagliptin 100 mg	
Comparison groups	Sitagliptin 100 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg

Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen
Parameter estimate	Difference in % vs Sitagliptin 100 mg
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.4
upper limit	10.1

Statistical analysis title	Difference in % vs Sitagliptin 100 mg
Statistical analysis description: Difference in % vs Sitagliptin 100 mg	
Comparison groups	Sitagliptin 100 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen
Parameter estimate	Difference in % vs Sitagliptin 100 mg
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.5
upper limit	7

Primary: Percentage of Participants Who Discontinued Study Medication due to an AE

End point title	Percentage of Participants Who Discontinued Study Medication due to an AE
End point description: An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. The population analyzed included all randomized, treated participants.	
End point type	Primary
End point timeframe: Up to 52 weeks	

End point values	Ertugliflozin 5 mg	Ertugliflozin 15 mg	Sitagliptin 100 mg	Ertugliflozin 5 mg + Sitagliptin 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	250	248	247	243
Units: Percentage of Participants				
number (not applicable)	3.2	3.2	2.8	3.3

End point values	Ertugliflozin 15 mg + Sitagliptin 100 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	244			
Units: Percentage of Participants				
number (not applicable)	3.7			

Statistical analyses

Statistical analysis title	Difference in % of Participants
Statistical analysis description: Difference in % of Participants	
Comparison groups	Ertugliflozin 5 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg
Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in % vs Ertugliflozin 5 mg
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	3.6

Statistical analysis title	Difference in % of Participants
Statistical analysis description: Difference in % of Participants	
Comparison groups	Ertugliflozin 15 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in % vs Ertugliflozin 15 mg
Point estimate	0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	4

Statistical analysis title	Difference in % of Participants
Statistical analysis description: Difference in % of Participants	
Comparison groups	Sitagliptin 100 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in % vs Sitagliptin 100 mg
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	3.9

Statistical analysis title	Difference in % of Participants
Statistical analysis description: Difference in % of Participants	
Comparison groups	Sitagliptin 100 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in % vs Sitagliptin 100 mg
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	4.4

Secondary: Change from Baseline in Body Weight at Week 26 Excluding Data After Initiation of Rescue Therapy

End point title	Change from Baseline in Body Weight at Week 26 Excluding Data After Initiation of Rescue Therapy

End point description:

The change in body weight from baseline reflects the Week 26 body weight minus the Week 0 body weight. The population analyzed included all randomized, treated participants who had at least 1 baseline or post-baseline weight measurement. Rescue Therapy: Participants who met pre-specified glycemic criteria were rescued with oral tablets of open-label glimepiride or insulin glargine injected

subcutaneously at dose strengths determined by the investigator.

End point type	Secondary

End point timeframe:

Baseline and Week 26

End point values	Ertugliflozin 5 mg	Ertugliflozin 15 mg	Sitagliptin 100 mg	Ertugliflozin 5 mg + Sitagliptin 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	250	248	247	243
Units: kilograms				
least squares mean (confidence interval 95%)	-2.69 (-3.13 to -2.25)	-3.74 (-4.18 to -3.29)	-0.67 (-1.12 to -0.22)	-2.52 (-2.97 to -2.07)

End point values	Ertugliflozin 15 mg + Sitagliptin 100 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	244			
Units: kilograms				
least squares mean (confidence interval 95%)	-2.94 (-3.39 to -2.49)			

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.

Comparison groups	Sitagliptin 100 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-1.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.48
upper limit	-1.22

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.

Comparison groups	Sitagliptin 100 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-2.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	-1.64

Secondary: Change from Baseline in Fasting Plasma Glucose at Week 26 Excluding Data After Initiation of Rescue Therapy

End point title	Change from Baseline in Fasting Plasma Glucose at Week 26 Excluding Data After Initiation of Rescue Therapy

End point description:

Blood glucose was measured on a fasting basis. Blood was drawn at predose on Day 1 and after 26 weeks of treatment to determine change in plasma glucose levels (i.e., FPG at Week 26 minus FPG at baseline). The population analyzed included all randomized, treated participants who had at least 1 baseline or post-baseline FPG measurement. Rescue Therapy: Participants who met pre-specified glycemic criteria were rescued with oral tablets of open-label glimepiride or insulin glargine injected subcutaneously at dose strengths determined by the investigator.

End point type	Secondary

End point timeframe:

Baseline and Week 26

End point values	Ertugliflozin 5 mg	Ertugliflozin 15 mg	Sitagliptin 100 mg	Ertugliflozin 5 mg + Sitagliptin 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	250	248	247	243
Units: mg/dL				
least squares mean (confidence interval 95%)	-35.73 (-40.04 to -31.42)	-36.91 (-41.21 to -32.62)	-25.56 (-29.93 to -21.19)	-43.96 (-48.29 to -39.63)

End point values	Ertugliflozin 15 mg + Sitagliptin 100 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	244			
Units: mg/dL				
least squares mean (confidence interval 95%)	-48.7 (-53.01 to -44.39)			

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means
Statistical analysis description:	
Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.	
Comparison groups	Ertugliflozin 5 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg
Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-8.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.82
upper limit	-2.65

Statistical analysis title	Difference in the Least Squares Means
Statistical analysis description:	
Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.	
Comparison groups	Sitagliptin 100 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-18.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.03
upper limit	-12.77

Statistical analysis title	Difference in the Least Squares Means
Statistical analysis description:	
Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.	
Comparison groups	Ertugliflozin 15 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-11.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.35
upper limit	-6.23

Statistical analysis title	Difference in the Least Squares Means
Statistical analysis description:	
Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.	
Comparison groups	Sitagliptin 100 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-23.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.76
upper limit	-17.53

Secondary: Change from Baseline in Sitting Systolic Blood Pressure at Week 26 Excluding Data After Initiation of Rescue Therapy

End point title	Change from Baseline in Sitting Systolic Blood Pressure at Week 26 Excluding Data After Initiation of Rescue Therapy

End point description:

This change from baseline reflects the Week 26 sitting systolic blood pressure (SBP) minus the Week 0 sitting SBP. The population analyzed included all randomized, treated participants who had at least 1 baseline or post-baseline SBP measurement. Rescue Therapy: Participants who met pre-specified glycemic criteria were rescued with oral tablets of open-label glimepiride or insulin glargine injected

subcutaneously at dose strengths determined by the investigator.

End point type	Secondary

End point timeframe:

Baseline and Week 26

End point values	Ertugliflozin 5 mg	Ertugliflozin 15 mg	Sitagliptin 100 mg	Ertugliflozin 5 mg + Sitagliptin 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	250	248	247	243
Units: mmHg				
least squares mean (confidence interval 95%)	-3.89 (-5.28 to -2.5)	-3.69 (-5.08 to -2.3)	-0.66 (-2.07 to 0.76)	-3.42 (-4.82 to -2.03)

End point values	Ertugliflozin 15 mg + Sitagliptin 100 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	244			
Units: mmHg				
least squares mean (confidence interval 95%)	-3.67 (-5.06 to -2.29)			

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.

Comparison groups	Sitagliptin 100 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	Constrained Longitudinal Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-2.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.69
upper limit	-0.83

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.

Comparison groups	Sitagliptin 100 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-3.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.94
upper limit	-1.09

Secondary: Percentage of Participants Achieving a Hemoglobin A1C of <7% at Week 26 Excluding Data After Initiation of Rescue Therapy

End point title	Percentage of Participants Achieving a Hemoglobin A1C of <7% at Week 26 Excluding Data After Initiation of Rescue Therapy

End point description:

Hemoglobin A1C is blood marker used to report average blood glucose levels over prolonged periods of time and is reported as a percentage (%). The population analyzed included all randomized, treated participants who had at least 1 baseline or post-baseline A1C measurement. Rescue Therapy: Participants who met pre-specified glycemic criteria were rescued with oral tablets of open-label glimepiride or insulin glargine injected subcutaneously at dose strengths determined by the investigator.

End point type	Secondary

End point timeframe:

Week 26

End point values	Ertugliflozin 5 mg	Ertugliflozin 15 mg	Sitagliptin 100 mg	Ertugliflozin 5 mg + Sitagliptin 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	250	248	247	243
Units: Percent				
number (not applicable)	26.4	31.9	32.8	52.3

End point values	Ertugliflozin 15 mg +			

	Sitagliptin 100 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	244			
Units: Percent				
number (not applicable)	49.2			

Statistical analyses

Statistical analysis title	Odds Ratio

Statistical analysis description:

Logistic regression with multiple imputations based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.

Comparison groups	Ertugliflozin 5 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg
Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Odds ratio (OR)
Point estimate	4.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.68
upper limit	6.4

Statistical analysis title	Odds Ratio

Statistical analysis description:

Logistic regression with multiple imputations based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.

Comparison groups	Ertugliflozin 15 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Odds ratio (OR)
Point estimate	2.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.68
upper limit	3.83

Statistical analysis title	Odds Ratio

Statistical analysis description:

Logistic regression with multiple imputations based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.

Comparison groups	Sitagliptin 100 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Odds ratio (OR)
Point estimate	2.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.92
upper limit	4.54

Statistical analysis title	Odds Ratio

Statistical analysis description:

Logistic regression with multiple imputations based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.

Comparison groups	Sitagliptin 100 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Odds ratio (OR)
Point estimate	2.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.69
upper limit	3.89

Secondary: Change from Baseline in β-cell Responsivity Static Component (Φs) (10-9min-1) From the 8-Point Meal Tolerance Test (MMTT at Week 26

End point title	Change from Baseline in β-cell Responsivity Static Component (Φs) (10-9min-1) From the 8-Point Meal Tolerance Test (MMTT at Week 26

End point description:

Measurements of plasma glucose, insulin and C-peptide collected, and urine samples were used to

assess parameters of insulin sensitivity and β-cell function. The oral C-peptide minimal model was used to assess the responsiveness of beta-cells to glucose challenge. The model utilizes the fact that C-peptide and insulin are secreted in an equal-molar fashion. The model parameters, i.e. α, β, k, (and h) were estimated in Simulation, Analysis, and Modeling Software for tracer and pharmacokinetic studies (SAAM II) using least squares approach. The endpoint Φs (β-cell responsivity static component) is a function of α and is calculated inside SAAM II, by specifying the formula in the Equation section of the STU file: - Φs = β /0.05551, the unit is 10-9min-1. A higher number indicates greater β-cell responsivity. The population analyzed included all randomized, treated participants who had at least 1 baseline or post-baseline Φs measurement.

End point type	Secondary

End point timeframe:

Baseline and Week 26, 30 minutes before and immediately prior to administration of the standard meal and 15, 30, 60, 90, 120 and 180 minutes following the start of the administration of the meal

End point values	Ertugliflozin 5 mg	Ertugliflozin 15 mg	Sitagliptin 100 mg	Ertugliflozin 5 mg + Sitagliptin 100 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	66	67	63	55
Units: 10^-9 min^-1				
least squares mean (confidence interval 95%)	8.62 (1.28 to 15.96)	9.71 (2.29 to 17.13)	21.11 (13.55 to 28.67)	16.24 (8.36 to 24.11)

End point values	Ertugliflozin 15 mg + Sitagliptin 100 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: 10^-9 min^-1				
least squares mean (confidence interval 95%)	11.51 (3.76 to 19.26)			

Statistical analyses

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.

Comparison groups	Ertugliflozin 5 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.155
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	7.61

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	18.13

Statistical analysis title	Difference in the Least Squares Means
Statistical analysis description:	
Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.	
Comparison groups	Ertugliflozin 15 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.734
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	1.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.66
upper limit	12.27

Statistical analysis title	Difference in the Least Squares Means
Statistical analysis description:	
Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.	
Comparison groups	Sitagliptin 100 mg v Ertugliflozin 5 mg + Sitagliptin 100 mg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.369
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-4.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.54
upper limit	5.8

Statistical analysis title	Difference in the Least Squares Means

Statistical analysis description:

Based on cLDA model with fixed effects for treatment, time, baseline eGFR (continuous), and the interaction of time by treatment. Time was treated as a categorical variable.

Comparison groups	Sitagliptin 100 mg v Ertugliflozin 15 mg + Sitagliptin 100 mg
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.075
Method	Constrained Longitudinal Data Analysis
Parameter estimate	Difference in the Least Squares Means
Point estimate	-9.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.17
upper limit	0.98

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 54 weeks

Adverse event reporting additional description:

The safety population was the All-Subjects-As-Treated (ASaT) Population. The ASaT Population consisted of all randomized participants who took at least one dose of trial treatment. Participants were included in the treatment group corresponding to the trial treatment they actually took for the analysis of safety data.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Ertugliflozin 5 mg

Reporting group description:

Ertugliflozin 5 mg once daily, placebo to ertugliflozin once daily, placebo to sitagliptin once daily, and metformin >= 1500 mg/day, all for 52 weeks

Reporting group title	Ertugliflozin 15 mg

Reporting group description:

Ertugliflozin 15 mg once daily, placebo to sitagliptin once daily, and metformin >= 1500 mg/day, all for 52 weeks

Reporting group title	Sitagliptin 100 mg

Reporting group description:

Sitagliptin 100 mg once daily, placebo to ertugliflozin once daily, and metformin >= 1500 mg/day, all for 52 weeks

Reporting group title	Ertugliflozin 5 mg + Sitagliptin 100 mg

Reporting group description:

Ertugliflozin 5 mg once daily, sitagliptin 100 mg once daily, placebo to ertugliflozin once daily, and metformin >= 1500 mg/day, all for 52 weeks

Reporting group title	Ertugliflozin 15 mg + Sitagliptin 100 mg

Reporting group description:

Ertugliflozin 15 mg once daily, sitagliptin 100 mg once daily, and metformin >= 1500 mg/day, all for 52 weeks

Serious adverse events	Ertugliflozin 5 mg	Ertugliflozin 15 mg	Sitagliptin 100 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 250 (4.80%)	5 / 248 (2.02%)	9 / 247 (3.64%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Nodal marginal zone B-cell lymphoma stage III			

subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic neoplasm			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity			
subjects affected / exposed	0 / 250 (0.00%)	1 / 248 (0.40%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 250 (0.00%)	1 / 248 (0.40%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood potassium decreased			

subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood sodium decreased			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	2 / 247 (0.81%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial fibrillation			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	1 / 247 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Microvascular coronary artery disease			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	1 / 247 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 250 (0.00%)	1 / 248 (0.40%)	1 / 247 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sciatica			
subjects affected / exposed	0 / 250 (0.00%)	1 / 248 (0.40%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Syncope			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	0 / 250 (0.00%)	1 / 248 (0.40%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral hernia			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pancreatitis			
subjects affected / exposed	1 / 250 (0.40%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	1 / 247 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 250 (0.80%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	1 / 247 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	1 / 247 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nephrolithiasis			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis orbital			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	1 / 247 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	0 / 250 (0.00%)	1 / 248 (0.40%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	1 / 247 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonia			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	1 / 247 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obesity			
subjects affected / exposed	0 / 250 (0.00%)	0 / 248 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Ertugliflozin 5 mg + Sitagliptin 100 mg	Ertugliflozin 15 mg + Sitagliptin 100 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 243 (3.70%)	12 / 244 (4.92%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Nodal marginal zone B-cell lymphoma stage III			
subjects affected / exposed	1 / 243 (0.41%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			

subjects affected / exposed	0 / 243 (0.00%)	2 / 244 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatic neoplasm			
subjects affected / exposed	0 / 243 (0.00%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood potassium decreased			
subjects affected / exposed	1 / 243 (0.41%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood sodium decreased			

subjects affected / exposed	1 / 243 (0.41%)	0 / 244 (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			
Head injury			
subjects affected / exposed	0 / 243 (0.00%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	0 / 243 (0.00%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 243 (0.41%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 243 (0.00%)	2 / 244 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 243 (0.00%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac failure chronic			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 243 (0.00%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microvascular coronary artery disease			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 243 (0.41%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 243 (0.41%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 243 (0.41%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 243 (0.41%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral hernia			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Small intestinal obstruction			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 243 (0.00%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	0 / 243 (0.00%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 243 (0.00%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 243 (0.41%)	0 / 244 (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			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 243 (0.00%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 243 (0.00%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis orbital			
subjects affected / exposed	1 / 243 (0.41%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	0 / 243 (0.00%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal sepsis			
subjects affected / exposed	0 / 243 (0.00%)	1 / 244 (0.41%)	
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 / 243 (0.00%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pulmonary tuberculosis			
subjects affected / exposed	0 / 243 (0.00%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 243 (0.41%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 243 (0.00%)	1 / 244 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	1 / 243 (0.41%)	0 / 244 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ertugliflozin 5 mg	Ertugliflozin 15 mg	Sitagliptin 100 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 250 (14.40%)	43 / 248 (17.34%)	28 / 247 (11.34%)
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 250 (2.40%)	13 / 248 (5.24%)	6 / 247 (2.43%)
occurrences (all)	6	14	7
Urinary tract infection			
subjects affected / exposed	20 / 250 (8.00%)	19 / 248 (7.66%)	13 / 247 (5.26%)
occurrences (all)	24	23	13
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	12 / 250 (4.80%)	13 / 248 (5.24%)	11 / 247 (4.45%)
occurrences (all)	25	29	22

Non-serious adverse events	Ertugliflozin 5 mg + Sitagliptin 100 mg	Ertugliflozin 15 mg + Sitagliptin 100 mg	

Total subjects affected by non-serious adverse events subjects affected / exposed	31 / 243 (12.76%)	38 / 244 (15.57%)	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 12 / 243 (4.94%) 14 14 / 243 (5.76%) 18	 12 / 244 (4.92%) 13 8 / 244 (3.28%) 12	
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	 9 / 243 (3.70%) 17	 20 / 244 (8.20%) 42	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported