



Clinical trial results:

A Study Comparing Dulaglutide With Insulin Glargine on Glycemic Control in Participants With Type 2 Diabetes (T2D) and Moderate or Severe Chronic Kidney Disease (CKD) (AWARD-7)

Summary

EudraCT number	2012-000829-44
Trial protocol	ES HU
Global end of trial date	20 December 2016

Results information

Result version number	v1
This version publication date	31 December 2017
First version publication date	31 December 2017

Trial information

Trial identification

Sponsor protocol code	H9X-MC-GBDX
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01621178
WHO universal trial number (UTN)	-
Other trial identifiers	Trial ID: 13798

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, United States, 46285
Public contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559,

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	20 December 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	20 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to determine the glycemic efficacy and safety of dulaglutide compared to insulin glargine in the treatment of participants with type 2 diabetes and moderate or severe chronic kidney disease.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 July 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects**Subjects enrolled per country**

Country: Number of subjects enrolled	United States: 183
Country: Number of subjects enrolled	Romania: 37
Country: Number of subjects enrolled	Hungary: 55
Country: Number of subjects enrolled	Ukraine: 40
Country: Number of subjects enrolled	Brazil: 141
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Mexico: 53
Country: Number of subjects enrolled	South Africa: 51
Country: Number of subjects enrolled	Spain: 12
Worldwide total number of subjects	577
EEA total number of subjects	109

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)	270
From 65 to 84 years	307
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All randomized participants, except for 1, in the dulaglutide group, were treated with at least 1 dose of study drug and comprised the ITT population. One participant did not receive study drug because after randomization the physician determined that the participant would be unable to successfully comply with the protocol.

Period 1

Period 1 title	Randomization Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
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Arm title	Insulin Glargine
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Arm description:

Insulin glargine was administered subcutaneously (SC) at bedtime per a modified forced-titration treat-to-target algorithm. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Arm type	Active comparator
Investigational medicinal product name	Insulin Glargine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin glargine was administered subcutaneously (SC) at bedtime per a modified forced-titration treat-to-target algorithm. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Arm title	Dulaglutide 0.75 mg
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Arm description:

0.75 milligram (mg) of dulaglutide was administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Arm type	Experimental
Investigational medicinal product name	Dulaglutide 0.75 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dulaglutide 0.75 mg was administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Arm title	Dulaglutide 1.5 mg
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Arm description:

1.5 mg of dulaglutide was administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Arm type	Experimental
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Investigational medicinal product name	Dulaglutide 1.5 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dulaglutide 1.5 mg was administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Number of subjects in period 1	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg
Started	194	190	193
Received at least one dose of study drug	194	190	193
Modified Intent to Treat Population	194	190	193
Completed	194	190	193

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	Yes ^[1]
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Insulin Glargine

Arm description:

Insulin glargine was administered SC at bedtime per a modified forced-titration treat-to-target algorithm. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Arm type	Experimental
Investigational medicinal product name	Insulin Glargine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin glargine was administered SC at bedtime per a modified forced-titration treat-to-target algorithm. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Arm title	Dulaglutide 0.75 mg
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Arm description:

Dulaglutide 0.75 mg administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Arm type	Experimental
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Investigational medicinal product name	Dulaglutide 0.75
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dulaglutide 0.75 mg administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day

Arm title	Dulaglutide 1.5 mg
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Arm description:

Dulaglutide 1.5 mg administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Arm type	Experimental
Investigational medicinal product name	Dulaglutide 1.5 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dulaglutide 1.5 mg administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The baseline period consists of the intent to treat population in period 2. One participant did not receive study drug because after randomization the physician determined that the participant would be unable to successfully comply with the protocol.

Number of subjects in period 2	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg
Started	194	190	193
Received at least one dose of study drug	194	190	192
Modified intent to treat population	186	180	183
Completed	163	160	157
Not completed	31	30	36
Adverse event, serious fatal	6	7	2
Consent withdrawn by subject	14	17	18
Physician decision	5	2	7
Adverse event, non-fatal	5	2	8
Lost to follow-up	1	2	1

Baseline characteristics

Reporting groups

Reporting group title	Insulin Glargine
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Reporting group description:

Insulin glargine was administered SC at bedtime per a modified forced-titration treat-to-target algorithm. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Reporting group title	Dulaglutide 0.75 mg
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Reporting group description:

Dulaglutide 0.75 mg administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Reporting group title	Dulaglutide 1.5 mg
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Reporting group description:

Dulaglutide 1.5 mg administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.

Reporting group values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg
Number of subjects	194	190	193
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)	94	89	87
From 65-84 years	100	101	106
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	101	86	89
Male	93	104	104
Body Weight			
Body weight was analyzed on all randomized participants who received at least 1 dose of study drug.			
Units: kilogram (kg)			
arithmetic mean	88.20	90.88	88.14
standard deviation	± 18.5	± 18.3	± 16.0
Body Mass Index (BMI)			
BMI was analyzed on all randomized participants who received at least 1 dose of study drug.			
Units: kilogram/square meter (kg/m ²)			
arithmetic mean	32	33	32
standard deviation	± 5.3	± 5.5	± 4.8
Hemoglobin A1C (HbA1c) at Baseline			
HbA1c was analyzed on all randomized participants who received at least 1 dose of study drug.			
Units: Percentage of HbA1c			
arithmetic mean	8.56	8.57	8.59
standard deviation	± 0.9	± 1.0	± 0.8

Duration of Diabetes			
Duration of diabetes was analyzed on all randomized participants who received at least 1 dose of study drug.			
Units: years			
arithmetic mean	18	18	18
standard deviation	± 8.7	± 8.8	± 8.7
Duration of Chronic Kidney Disease (CKD) Stage 3 or Higher			
Duration of CKD was analyzed on all randomized participants who received at least 1 dose of study drug.			
Units: years			
arithmetic mean	3.47	4.03	4.18
standard deviation	± 3.9	± 4.8	± 5.6
Estimated Glomerular Filtration Rate (eGFR)			
eGFR was analyzed on all randomized participants who received at least 1 dose of study drug.			
Units: milliliter/minute/1.73 square meter			
arithmetic mean	38.5	38.3	38.1
standard deviation	± 12.9	± 12.3	± 13.2

Reporting group values	Total		
Number of subjects	577		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	270		
From 65-84 years	307		
85 years and over	0		
Gender categorical			
Units: Subjects			
Female	276		
Male	301		
Body Weight			
Body weight was analyzed on all randomized participants who received at least 1 dose of study drug.			
Units: kilogram (kg)			
arithmetic mean			
standard deviation	-		
Body Mass Index (BMI)			
BMI was analyzed on all randomized participants who received at least 1 dose of study drug.			
Units: kilogram/square meter (kg/m ²)			
arithmetic mean			
standard deviation	-		
Hemoglobin A1C (HbA1c) at Baseline			
HbA1c was analyzed on all randomized participants who received at least 1 dose of study drug.			
Units: Percentage of HbA1c			
arithmetic mean			

standard deviation	-		
Duration of Diabetes			
Duration of diabetes was analyzed on all randomized participants who received at least 1 dose of study drug.			
Units: years			
arithmetic mean			
standard deviation	-		
Duration of Chronic Kidney Disease (CKD) Stage 3 or Higher			
Duration of CKD was analyzed on all randomized participants who received at least 1 dose of study drug.			
Units: years			
arithmetic mean			
standard deviation	-		
Estimated Glomerular Filtration Rate (eGFR)			
eGFR was analyzed on all randomized participants who received at least 1 dose of study drug.			
Units: milliliter/minute/1.73 square meter			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Insulin Glargine
Reporting group description: Insulin glargine was administered subcutaneously (SC) at bedtime per a modified forced-titration treat-to-target algorithm. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.	
Reporting group title	Dulaglutide 0.75 mg
Reporting group description: 0.75 milligram (mg) of dulaglutide was administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.	
Reporting group title	Dulaglutide 1.5 mg
Reporting group description: 1.5 mg of dulaglutide was administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.	
Reporting group title	Insulin Glargine
Reporting group description: Insulin glargine was administered SC at bedtime per a modified forced-titration treat-to-target algorithm. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.	
Reporting group title	Dulaglutide 0.75 mg
Reporting group description: Dulaglutide 0.75 mg administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.	
Reporting group title	Dulaglutide 1.5 mg
Reporting group description: Dulaglutide 1.5 mg administered once weekly as a SC injection. Participants were instructed to administer their titrated prandial insulin lispro dose SC with the three most significant meals of the day.	

Primary: Change from Baseline in Hemoglobin A1c (HbA1c)

End point title	Change from Baseline in Hemoglobin A1c (HbA1c)
End point description: HbA1c is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. Least square (LS) means in HbA1c were calculated using a restricted maximum likelihood (REML) based mixed-effects model for repeated measures (MMRM) with the change in HbA1c as the dependent variable and treatment, macroalbuminuria (MA) region, Baseline CKD Severity, week, treatment*week, baseline HbA1c (%), log baseline eGFR (within CKD severity), and participant was the random effect. Covariance structure = Unstructured. Only measurements prior to rescue or study drug discontinuation were used.	
End point type	Primary
End point timeframe: Baseline, 26 Weeks	

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	175 ^[1]	149 ^[2]	138 ^[3]	
Units: percentage of HbA1c				
least squares mean (standard error)	-1.13 (± 0.12)	-1.12 (± 0.12)	-1.19 (± 0.13)	

Notes:

[1] - All randomized participants who received (rec'd) one dose of study drug and had evaluable HbA1c data

[2] - All randomized participants who received one dose of study drug and had evaluable HbA1c data.

[3] - All randomized participants who received one dose of study drug and had evaluable HbA1c data.

Statistical analyses

Statistical analysis title	Dulaglutide 1.5 mg Statistical Analysis
Statistical analysis description:	
All participants were included in the statistical analysis at week 26.	
Comparison groups	Insulin Glargine v Dulaglutide 1.5 mg
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[4]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.15

Notes:

[4] - Non-Inferiority to Glargine with a 0.4% margin.

Statistical analysis title	Dulaglutide 0.75 mg Statistical Analysis
Statistical analysis description:	
All participants were included in the statistical analysis at week 26.	
Comparison groups	Insulin Glargine v Dulaglutide 0.75 mg
Number of subjects included in analysis	324
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[5]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.22

Notes:

[5] - Non-Inferiority to Glargine with a 0.4% margin

Secondary: Percentage of Participants whose HbA1c was <7.0%

End point title	Percentage of Participants whose HbA1c was <7.0%
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End point description:

Percentage of participants whose HbA1c was <7.0% based on last observation carried forward (LOCF). Only measurement prior to rescue or study drug discontinuation were used.

End point type	Secondary
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End point timeframe:

26 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	182 ^[6]	164 ^[7]	152 ^[8]	
Units: percentage of participants				
number (not applicable)	34.6	31.7	37.5	

Notes:

[6] - All randomized participants who received at least 1 dose of study drug and had evaluable HbA1c data.

[7] - All randomized participants who received at least 1 dose of study drug and had evaluable HbA1c data.

[8] - All randomized participants who received at least 1 dose of study drug and had evaluable HbA1c data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants whose HbA1c was <8.0%

End point title	Percentage of Participants whose HbA1c was <8.0%
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End point description:

Percentage of Participants whose HbA1c was <8.0% based on last observation carried forward (LOCF). Only measurement prior to rescue or study drug discontinuation were used.

End point type	Secondary
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End point timeframe:

26 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	182 ^[9]	164 ^[10]	152 ^[11]	
Units: percentage of participants				
number (not applicable)	75.3	72.6	78.3	

Notes:

[9] - All randomized participants who received at least 1 dose of study drug and had evaluable HbA1c data.

[10] - All randomized participants who received at least 1 dose of study drug and had evaluable HbA1c data.

[11] - All randomized participants who received at least 1 dose of study drug and had evaluable HbA1c data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in 8-Point Self-Monitored Plasma Glucose (SMPG)

End point title	Change from Baseline in 8-Point Self-Monitored Plasma Glucose (SMPG)
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End point description:

The daily mean of 8-point SMPG profile at Week 26 is presented. Participants were required to perform two 8-point SMPG profiles over a 1-week period at 3 separate times throughout the study. LS means were calculated using the MMRM model including the corresponding baseline value as a continuous covariate, as well as baseline HbA1c, MA-region, treatment, week, treatment*week, baseline CKD severity, and log baseline eGFR (within CKD severity). The two 8-point SMPG profiles were collected on two non-consecutive days (pre-meal and 2-hour postprandial SMPG x [morning, midday, and evening meals in one day] + bedtime + 5 hours after bedtime). Only measurement prior to rescue or study drug discontinuation were used.

End point type	Secondary
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End point timeframe:

Baseline, 26 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128 ^[12]	107 ^[13]	102 ^[14]	
Units: milligrams/deciliter (mg/dL)				
least squares mean (standard error)	-37.6 (± 3.41)	-31.7 (± 3.53)	-33.7 (± 3.77)	

Notes:

[12] - All randomized participants who received at least 1 dose of study drug & had evaluable HbA1c & SMPG.

[13] - All randomized participants who received at least 1 dose of study drug & had evaluable HbA1c & SMPG.

[14] - All randomized participants who received at least 1 dose of study drug & had evaluable HbA1c & SMPG.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fasting Glucose (FG)

End point title	Change from Baseline in Fasting Glucose (FG)
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End point description:

LS means were calculated using MMRM with the change in FG as the dependent variable and treatment, MA -region, Baseline CKD Severity, week, treatment*week, baseline FG, baseline HbA1c (%), log baseline eGFR (within CKD severity), and participant was the random effect. Covariance structure = Unstructured. Only measurement prior to rescue or study drug discontinuation were used.

End point type	Secondary
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End point timeframe:

Baseline, 26 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	162 ^[15]	145 ^[16]	132 ^[17]	
Units: milligram/deciliter (mg/dL)				
least squares mean (standard deviation)	-19.1 (± 6.00)	17.7 (± 6.14)	23.1 (± 6.50)	

Notes:

[15] - All randomized participants who received at least 1 dose of study drug & had evaluable HbA1c & FG.

[16] - All randomized participants who received at least 1 dose of study drug & had evaluable HbA1c & FG.

[17] - All randomized participants who received at least 1 dose of study drug & had evaluable HbA1c & FG.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean Daily Insulin Lispro Dose

End point title	Change From Baseline in Mean Daily Insulin Lispro Dose
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End point description:

The mean daily insulin was based on a 4-week interval prior to week 26 assessments. LS means were calculated using a REML based mixed-effects model for repeated measures (MMRM) with the change in HbA1c as the dependent variable and treatment, MA-region, Baseline HbA1c, baseline mean daily insulin, baseline CKD Severity, week, treatment*week, baseline HbA1c (%), log baseline eGFR (within CKD severity), and participant was the random effect. Covariance structure = Unstructured. Only measurements prior to rescue or study drug discontinuation were used.

End point type	Secondary
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End point timeframe:

26 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	177 ^[18]	154 ^[19]	141 ^[20]	
Units: Units/day (U/day)				
least squares mean (standard error)	16.64 (± 2.76)	26.16 (± 2.80)	18.12 (± 3.00)	

Notes:

[18] - All randomized participants who rec'd 1 dose of study drug & had evaluable insulin lispro dose data.

[19] - All randomized participants who rec'd 1 dose of study drug & had evaluable insulin lispro dose data.

[20] - All randomized participants who rec'd 1 dose of study drug & had evaluable insulin lispro dose data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Estimated Average Glucose <154 mg/dL

End point title	Percentage of Participants With Estimated Average Glucose <154 mg/dL
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End point description:

Percentage of Participants With Estimated Average Glucose <154 milligram/deciliter (mg/dL) was based on last observation carried forward (LOCF). Only measurements prior to rescue and study

discontinuation were used.

End point type	Secondary
End point timeframe:	
26 Weeks	

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134 ^[21]	118 ^[22]	110 ^[23]	
Units: percentage of participants				
number (not applicable)	64.9	52.5	56.4	

Notes:

[21] - All randomized participants who had 1 dose of study drug & had evaluable estimated average glucose.

[22] - All randomized participants who had 1 dose of study drug & had evaluable estimated average glucose.

[23] - All randomized participants who had 1 dose of study drug & had evaluable estimated average glucose.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Serum Creatinine (sCr)

End point title	Change from Baseline in Serum Creatinine (sCr)
End point description:	
Change from baseline in serum creatinine (sCr) levels after treatment.	
End point type	Secondary
End point timeframe:	
Baseline, 26 Weeks	

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	176 ^[24]	169 ^[25]	163 ^[26]	
Units: mg/dL				
median (inter-quartile range (Q1-Q3))	0.10 (-0.04 to 0.28)	0.02 (-0.15 to 0.15)	0.04 (-0.14 to 0.20)	

Notes:

[24] - All randomized participants who received at least 1 dose of study drug and had evaluable sCr data.

[25] - All randomized participants who received at least 1 dose of study drug and had evaluable sCr data.

[26] - All randomized participants who received at least 1 dose of study drug and had evaluable sCr data..

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in estimated Glomerular Filtration Rate (eGFR)

End point title	Change from Baseline in estimated Glomerular Filtration Rate (eGFR)
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End point description:

The change in estimated glomerular filtration rate (eGFR) by using CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation.

End point type	Secondary
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End point timeframe:

Baseline, 26 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	176 ^[27]	169 ^[28]	163 ^[29]	
Units: milliliter/minute/1.73m ² (mL/min/1.73m ²)				
median (inter-quartile range (Q1-Q3))	-2.5 (-6.0 to 1.0)	-1.0 (-4.5 to 3.0)	-1.0 (-5.5 to 3.0)	

Notes:

[27] - All randomized participants who received at least 1 dose of study drug and had evaluable eGFR data.

[28] - All randomized participants who received at least 1 dose of study drug and had evaluable eGFR data.

[29] - All randomized participants who received at least 1 dose of study drug and had evaluable eGFR data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in estimated Creatinine Clearance (eCrCl)

End point title	Change from Baseline in estimated Creatinine Clearance (eCrCl)
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End point description:

Estimated creatinine clearance (eCrCl) was calculated by Cockcroft-Gault [Cockcroft and Gault 1976] equation using baseline estimated lean body weight.

End point type	Secondary
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End point timeframe:

Baseline, 26 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	176 ^[30]	169 ^[31]	163 ^[32]	
Units: milliliter/minute (ml/min)				
median (inter-quartile range (Q1-Q3))	-2.0 (-4.0 to 0.5)	-1.0 (-3.5 to 2.0)	-0.5 (-4.0 to 2.0)	

Notes:

[30] - All randomized participants who received at least 1 dose of study drug and had evaluable eCrCl data.

[31] - All randomized participants who received at least 1 dose of study drug and had evaluable eCrCl data.

[32] - All randomized participants who received at least 1 dose of study drug and had evaluable eCrCl data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Urinary Albumin to Creatinine Ratio (UACR)

End point title	Change from Baseline in Urinary Albumin to Creatinine Ratio (UACR)
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End point description:

The change from baseline in Urinary Albumin to Creatinine Ratio (UACR).

End point type	Secondary
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End point timeframe:

Baseline, 26 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	181 ^[33]	175 ^[34]	175 ^[35]	
Units: gram/kilogram (g/kg)				
median (inter-quartile range (Q1-Q3))	-1.3 (-71.7 to 62.0)	-11.1 (-147.8 to 33.2)	-10.2 (-180.5 to 53.1)	

Notes:

[33] - All randomized participants who received at least 1 dose of study drug and had evaluable UACR data.

[34] - All randomized participants who received at least 1 dose of study drug and had evaluable UACR data.

[35] - All randomized participants who received at least 1 dose of study drug and had evaluable UACR data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Body Weight

End point title	Change from Baseline in Body Weight
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End point description:

LS means were calculated from a REML based MMRM model: Change from Baseline = treatment , week, treatment*Week, MA-region, Baseline HbA1c (%), Baseline Body Weight (kg), Baseline CKD Severity, Log Baseline eGFR (within CKD severity), where participant enters the model as a random effect. Covariance structure = Unstructured. Only measurement and prior to rescue or study drug discontinuation were used.

End point type	Secondary
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End point timeframe:

Baseline, 26 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	175 ^[36]	151 ^[37]	140 ^[38]	
Units: kilogram (kg)				
least squares mean (standard error)	1.11 (± 0.346)	-2.02 (± 0.357)	-2.81 (± 0.374)	

Notes:

[36] - All randomized participants who rec'd 1 dose of study drug & had evaluable HbA1c & body weight.

[37] - All randomized participants who rec'd 1 dose of study drug & had evaluable HbA1c & body weight.

[38] - All randomized participants who rec'd 1 dose of study drug & had evaluable HbA1c & body weight.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Self-Reported Hypoglycemic Events (HE)

End point title	Percentage of Participants with Self-Reported Hypoglycemic Events (HE)
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End point description:

Hypoglycemic events (HE) were classified as severe (defined as an episode requiring the assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions), documented symptomatic (defined as any time a participant feels that he/she is experiencing symptoms and/or signs associated with hypoglycemia, and has a plasma glucose level of ≤ 3.9 mmol/L (≤ 70 mg/dL), nocturnal (defined as any hypoglycemic event that occurs between bedtime and waking). The number of self-reported hypoglycemic events was summarized cumulatively at 26 weeks. A summary of other nonserious AEs, and all SAEs, regardless of causality, is located in the Reported Adverse Events section. Only measurements prior to rescue and study discontinuation was used.

End point type	Secondary
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End point timeframe:

Baseline through 26 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	194 ^[39]	189 ^[40]	190 ^[41]	
Units: percentage of participants				
number (not applicable)				
Total Hypo	71.6	50.8	43.2	
Documented Symptomatic Hypo	60.3	40.7	31.6	
Severe Hypo	4.1	1.1	0	
Nocturnal Hypo	38.1	15.9	13.2	

Notes:

[39] - All randomized participants who received at least 1 dose of study drug and evaluable HE data.

[40] - All randomized participants who received at least 1 dose of study drug and evaluable HE data.

[41] - All randomized participants who received at least 1 dose of study drug and evaluable HE data.

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Hypoglycemic Events

End point title	Rate of Hypoglycemic Events
End point description: Hypoglycemic events (HE) were classified as total HE rate, documented symptomatic hypoglycemia, severe hypoglycemia, and nocturnal. The 1-year adjusted rate of HEs was summarized cumulatively at 26 weeks. A summary of other nonserious AEs, and all SAEs, regardless of causality, is located in the Reported Adverse Events section. Only measurements prior to rescue and study discontinuation were used.	
End point type	Secondary
End point timeframe: Baseline through 26 Weeks	

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	194 ^[42]	189 ^[43]	190 ^[44]	
Units: Events/Participant/Year				
arithmetic mean (standard deviation)				
Total HE Rate	17.07 (± 27.70)	7.76 (± 20.39)	5.45 (± 12.54)	
Documented Symptomatic HE Rate	11.34 (± 22.04)	4.86 (± 13.37)	4.19 (± 11.58)	
Severe HE Rate	0.10 (± 0.56)	0.03 (± 0.31)	0.00 (± 0.00)	
Nocturnal HE Rate	3.06 (± 7.26)	0.73 (± 2.25)	0.63 (± 2.26)	

Notes:

[42] - All randomized participants who received at least 1 dose of study drug & had evaluable HE rate.

[43] - All randomized participants who received at least 1 dose of study drug & had evaluable HE rate.

[44] - All randomized participants who received at least 1 dose of study drug & had evaluable HE rate.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HbA1c

End point title	Change from Baseline in HbA1c
End point description: HbA1c is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. LS means in HbA1c were calculated using a REML based mixed-effects model for repeated measures (MMRM) with the change in HbA1c as the dependent variable and treatment, MA region, Baseline CKD Severity, week, treatment*week, baseline HbA1c (%), log baseline eGFR (within CKD severity), and participant was the random effect. Covariance structure = Unstructured. Only measurements prior to rescue and study discontinuation were used.	
End point type	Secondary
End point timeframe: Baseline, 52 Weeks	

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153 ^[45]	132 ^[46]	130 ^[47]	
Units: percentage of HbA1c				
least squares mean (standard error)	-1.00 (± 0.12)	-1.10 (± 0.12)	-1.10 (± 0.13)	

Notes:

[45] - All randomized participants who received at least 1 dose of study drug and had evaluable HbA1c data.

[46] - All randomized participants who received at least 1 dose of study drug and had evaluable HbA1c data.

[47] - All randomized participants who received at least 1 dose of study drug and had evaluable HbA1c data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Whose HbA1c is <7.0%

End point title	Percentage of Participants Whose HbA1c is <7.0%
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End point description:

Percentage of participants whose HbA1c was <7.0% based on last observation carried forward (LOCF). Only measurements prior to rescue and study discontinuation were used.

End point type	Secondary
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End point timeframe:

52 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	182 ^[48]	164 ^[49]	152 ^[50]	
Units: percentage of participants				
number (not applicable)	29.1	33.5	32.9	

Notes:

[48] - All randomized participants who had received at least 1 dose of study drug & had evaluable HbA1c.

[49] - All randomized participants who had received at least 1 dose of study drug & had evaluable HbA1c.

[50] - All randomized participants who had received at least 1 dose of study drug & had evaluable HbA1c.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Whose HbA1c is <8.0%

End point title	Percentage of Participants Whose HbA1c is <8.0%
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End point description:

Percentage of participants whose HbA1c was <8.0% based on last observation carried forward (LOCF). Only measurements prior to rescue and study discontinuation were used.

End point type	Secondary
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End point timeframe:

Baseline, 52 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	182 ^[51]	164 ^[52]	152 ^[53]	
Units: percentage of participants				
number (not applicable)	70.3	69.5	69.1	

Notes:

[51] - All randomized participants who received at least 1 dose of study drug & had evaluable HbA1c data.

[52] - All randomized participants who received at least 1 dose of study drug & had evaluable HbA1c data.

[53] - All randomized participants who received at least 1 dose of study drug & had evaluable HbA1c data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 8-Point SMPG

End point title	Change From Baseline in 8-Point SMPG
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End point description:

The daily mean of 8-point SMPG profile at Week 52 is presented. Participants were required to perform two 8-point SMPG profiles over a 1-week period at 5 separate times throughout the study. LS means were calculated using the MMRM model including the corresponding baseline value as a continuous covariate, as well as baseline HbA1c, MA-region, treatment, week, treatment*week, baseline CKD severity, and log baseline eGFR (within CKD severity). The two 8-point SMPG profiles were collected on two non-consecutive days (pre-meal and 2-hour postprandial SMPG x [morning, midday, and evening meals in one day] + bedtime + 5 hours after bedtime). Only measurements prior to rescue and study discontinuation were used.

End point type	Secondary
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End point timeframe:

Baseline, 52 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	118 ^[54]	96 ^[55]	102 ^[56]	
Units: mg/dL				
least squares mean (standard error)	-40.5 (± 3.59)	-30.0 (± 3.75)	-27.2 (± 3.93)	

Notes:

[54] - All randomized participants who had at least 1 dose of study drug & had evaluable HbA1c & SMPG data.

[55] - All randomized participants who had at least 1 dose of study drug & had evaluable HbA1c & SMPG data

[56] - All randomized participants who had at least 1 dose of study drug & had evaluable HbA1c & SMPG data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FG

End point title	Change From Baseline in FG
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End point description:

LS means were calculated using MMRM with the change in FG as the dependent variable and treatment, MA -region, Baseline CKD Severity, week, treatment*week, baseline FG, baseline HbA1c (%), log baseline eGFR (within CKD severity), and participant was the random effect. Covariance structure = Unstructured. Only measurements prior to rescue and study discontinuation used.

End point type	Secondary
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End point timeframe:

Baseline, 52 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	152 ^[57]	132 ^[58]	131 ^[59]	
Units: mg/dL				
least squares mean (standard error)	-6.4 (± 6.38)	20.8 (± 6.58)	28.3 (± 6.87)	

Notes:

[57] - All randomized participants who received 1 dose of study drug and had evaluable HbA1c and FG data.

[58] - All randomized participants who received 1 dose of study drug and had evaluable HbA1c and FG data.

[59] - All randomized participants who recieved 1 dose of study drug and had evaluable HbA1c and FG data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Mean Daily Insulin Lispro Dose

End point title	Change in Mean Daily Insulin Lispro Dose
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End point description:

The mean daily insulin was based on a 4-week interval prior to week 52 assessments. LS means were calculated using a REML based mixed-effects model for repeated measures (MMRM) with the change in HbA1c as the dependent variable and treatment, MA-region, Baseline HbA1c, baseline mean daily insulin, baseline CKD Severity, week, treatment*week, baseline HbA1c (%), log baseline eGFR (within CKD severity), and participant was the random effect. Covariance structure = Unstructured. Only measurements prior to rescue and study discontinuation were used.

End point type	Secondary
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End point timeframe:

Baseline, 52 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159 ^[60]	140 ^[61]	132 ^[62]	
Units: U/day				
least squares mean (standard error)	16.84 (± 2.87)	27.46 (± 2.93)	20.05 (± 3.13)	

Notes:

[60] - All randomized participants who had 1 dose of study drug & evaluable HbA1c & Lispro dose data.

[61] - All randomized participants who had 1 dose of study drug & evaluable HbA1c & Lispro dose data.

[62] - All randomized participants who had 1 dose of study drug & evaluable HbA1c & Lispro dose data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Estimated Average Glucose <154 mg/dL

End point title	Percentage of Participants With Estimated Average Glucose <154 mg/dL
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End point description:

Percentage of Participants With Estimated Average Glucose <154 milligram/deciliter (mg/dL) was based on last observation carried forward (LOCF). Only measurements prior to rescue and study discontinuation were used.

End point type	Secondary
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End point timeframe:

Baseline, 52 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	137 ^[63]	122 ^[64]	116 ^[65]	
Units: percentage of participants				
number (not applicable)	73.7	57.4	50.9	

Notes:

[63] - All randomized participants who had evaluable HbA1c and average self-monitored plasma glucose data.

[64] - All randomized participants who had evaluable HbA1c and average self-monitored plasma glucose data.

[65] - All randomized participants who had evaluable HbA1c and average self-monitored plasma glucose data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in sCr

End point title	Change From Baseline in sCr
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End point description:

Change from baseline in sCr levels after treatment.

End point type	Secondary
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End point timeframe:

Baseline, 52 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	164 ^[66]	160 ^[67]	157 ^[68]	
Units: mg/dL				
median (inter-quartile range (Q1-Q3))	0.12 (-0.05 to 0.38)	0.04 (-0.11 to 0.27)	0.07 (-0.11 to 0.21)	

Notes:

[66] - All randomized participants who had evaluable baseline and post-baseline sCr data.

[67] - All randomized participants had evaluable baseline and post-baseline sCr data.

[68] - All randomized participants who had evaluable baseline and post-baseline sCr data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in eGFR

End point title	Change From Baseline in eGFR
End point description: The change in eGFR by using CKD-EPI equation.	
End point type	Secondary
End point timeframe: Baseline, 52 Weeks	

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	164 ^[69]	160 ^[70]	157 ^[71]	
Units: mL/min/1.73m ²				
median (inter-quartile range (Q1-Q3))	-3.3 (-7.5 to 1.0)	-1.5 (-5.5 to 2.5)	-2.0 (-6.0 to 2.5)	

Notes:

[69] - All randomized participants who and had evaluable baseline and post baseline eGFR data.

[70] - All randomized participants who and had evaluable baseline and post baseline eGFR data.

[71] - All randomized participants who and had evaluable baseline and post baseline eGFR data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in eCrCl

End point title	Change From Baseline in eCrCl
End point description: eCrCl was calculated by Cockcroft-Gault [Cockcroft and Gault 1976] equation using baseline estimated lean body weight.	
End point type	Secondary
End point timeframe: Baseline, 52 Weeks	

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	164 ^[72]	160 ^[73]	157 ^[74]	
Units: mL/min				
median (inter-quartile range (Q1-Q3))	-2.5 (-5.8 to 0.5)	-1.3 (-4.0 to 1.5)	-1.5 (-5.0 to 1.5)	

Notes:

[72] - All randomized participants who study drug and had evaluable baseline and post-baseline eCrCl data.

[73] - All randomized participants who study drug and had evaluable baseline and post-baseline eCrCl data.

[74] - All randomized participants who study drug and had evaluable baseline and post-baseline eCrCl data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in UACR

End point title	Change From Baseline in UACR
End point description:	
The change from baseline in UACR	
End point type	Secondary
End point timeframe:	
Baseline, 52 Weeks	

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	165 ^[75]	162 ^[76]	159 ^[77]	
Units: g/kg				
median (inter-quartile range (Q1-Q3))	3.5 (-56.2 to 138.1)	-3.0 (-88.5 to 87.6)	-11.5 (-158.0 to 42.9)	

Notes:

[75] - All randomized participants who had evaluable baseline and post-baseline UACR data.

[76] - All randomized participants who had evaluable baseline and post-baseline UACR data.

[77] - All randomized participants who had evaluable baseline and post-baseline UACR data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Weight

End point title	Change From Baseline in Body Weight
End point description:	
LS means were calculated from a REML based MMRM model: Change from Baseline = treatment , week, treatment*Week, MA-region, Baseline HbA1c (%), Baseline Body Weight (kg), Baseline CKD Severity, Log Baseline eGFR (within CKD severity), where participant enters the model as a random effect.	

Covariance structure = Unstructured. Only measurements prior to rescue and study discontinuation were used.

End point type	Secondary
End point timeframe:	
Baseline, 52 Weeks	

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158 ^[78]	137 ^[79]	132 ^[80]	
Units: kg				
least squares mean (standard error)	1.57 (± 0.429)	-1.71 (± 0.448)	-2.66 (± 0.467)	

Notes:

[78] - All randomized participants who rec'd 1 dose of study drug & had evaluable HbA1c & body weight.

[79] - All randomized participants who rec'd 1 dose of study drug & had evaluable HbA1c & body weight.

[80] - All randomized participants who rec'd 1 dose of study drug & had evaluable HbA1c & body weight.

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Hypoglycemic Events (HE)

End point title	Rate of Hypoglycemic Events (HE)
End point description:	
HE were classified as total HE rate, documented symptomatic hypoglycemia, severe hypoglycemia, and nocturnal. The 1-year adjusted rate of HEs was summarized cumulatively at 52 weeks. A summary of other nonserious AEs, and all SAEs, regardless of causality, is located in the Reported Adverse Events section. Only measurements prior to rescue and study discontinuation were used.	
End point type	Secondary
End point timeframe:	
Baseline, 52 Weeks	

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	194 ^[81]	189 ^[82]	190 ^[83]	
Units: Events/Participant/Year				
arithmetic mean (standard deviation)				
Total	14.36 (± 22.20)	7.59 (± 17.81)	5.82 (± 13.70)	
Documented Symptomatic	9.62 (± 17.72)	4.34 (± 9.30)	4.44 (± 12.23)	
Severe	0.09 (± 0.37)	0.03 (± 0.21)	0.00 (± 0.00)	
Nocturnal	2.48 (± 5.10)	0.76 (± 0.09)	0.70 (± 2.29)	

Notes:

[81] - All randomized participants who received at least 1 dose of study drug & had evaluable HE data.

[82] - All randomized participants who received at least 1 dose of study drug & had evaluable HE data.

[83] - All randomized participants who received at least 1 dose of study drug & had evaluable HE data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Allergic/Hypersensitivity Reactions

End point title	Percentage of Participants with Allergic/Hypersensitivity Reactions
End point description: Percentage of Participants with Allergic/Hypersensitivity Reactions: Angioedema Standardized MedDRA Query (SMQ), Anaphylactic Reaction SMQ, or Severe Cutaneous Adverse Reactions SMQ	
End point type	Secondary
End point timeframe: Baseline through 52 Weeks	

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	194 ^[84]	190 ^[85]	192 ^[86]	
Units: events				
number (not applicable)				
Angioedema SMQ	1	2	2	
Angiodema	0	0	1	
Eyelid edema	0	1	0	
Face edema	0	1	1	
Urticaria	1	0	0	
Anaphylactic Reaction SMQ	1	0	0	
Circulatory Collapse	1	0	0	
Severe Cutaneous Adverse Reactions SMQ	0	0	0	

Notes:

[84] - All randomized participants who received at least one dose of study drug.

[85] - All randomized participants who received at least one dose of study drug.

[86] - All randomized participants who received at least one dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Self-Reported Hypoglycemic Events (HE)

End point title	Percentage of Participants with Self-Reported Hypoglycemic Events (HE)
End point description: Hypoglycemic events (HE) were classified as severe (defined as an episode requiring the assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions), documented symptomatic (defined as any time a participant feels that he/she is experiencing symptoms and/or signs associated with hypoglycemia, and has a plasma glucose level of ≤ 3.9 mmol/L (≤ 70 mg/dL), nocturnal (defined as any hypoglycemic event that occurs between bedtime and waking). The number of self-reported hypoglycemic events was summarized cumulatively at 52 weeks. A summary of other nonserious AEs, and all SAEs, regardless of causality, is located in the Reported Adverse Events section. Only measurements prior to rescue and study discontinuation was used.	
End point type	Secondary

End point timeframe:

Baseline, 52 Weeks

End point values	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	194 ^[87]	189 ^[88]	190 ^[89]	
Units: percentage of participants				
Total HE	75	60	50	
Documented Symptomatic HE	63	48	41	
Severe HE	6	3	0	
Nocturnal HE	48	24	21	

Notes:

[87] - All randomized participants who received at least 1 dose of study drug and had evaluable HE data.

[88] - All randomized participants who received at least 1 dose of study drug and had evaluable HE data.

[89] - All randomized participants who received at least 1 dose of study drug and had evaluable HE data.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

H9X-MC-GBDX

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Insulin Glargine
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Reporting group description: -

Reporting group title	Dulaglutide 0.75 mg
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Reporting group description: -

Reporting group title	Dulaglutide 1.5 mg
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Reporting group description: -

Serious adverse events	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	56 / 194 (28.87%)	48 / 190 (25.26%)	41 / 192 (21.35%)
number of deaths (all causes)	6	9	3
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
bladder neoplasm			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastric cancer			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
Vascular disorders			
circulatory collapse			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
deep vein thrombosis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
hypertensive crisis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
hypotension			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
peripheral arterial occlusive disease			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peripheral ischaemia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

peripheral vascular disorder alternative dictionary used: MedDRA 19.1 subjects affected / exposed	0 / 194 (0.00%)	2 / 190 (1.05%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
chest pain alternative dictionary used: MedDRA 19.1 subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	3 / 192 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
death alternative dictionary used: MedDRA 19.1 subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
ischaemic ulcer alternative dictionary used: MedDRA 19.1 subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
non-cardiac chest pain alternative dictionary used: MedDRA 19.1 subjects affected / exposed	1 / 194 (0.52%)	1 / 190 (0.53%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
oedema peripheral alternative dictionary used: MedDRA 19.1 subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pacemaker generated arrhythmia alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
pyrexia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
sudden death			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Immune system disorders			
drug hypersensitivity			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
acute pulmonary oedema			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
aspiration			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
colpocoele			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed ^[1]	1 / 101 (0.99%)	0 / 86 (0.00%)	0 / 88 (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
dyspnoea			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
epistaxis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
pleural effusion			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
pulmonary embolism			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory distress			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
respiratory failure			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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

Investigations			
blood creatinine increased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 194 (1.03%)	3 / 190 (1.58%)	3 / 192 (1.56%)
occurrences causally related to treatment / all	0 / 3	0 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
glomerular filtration rate decreased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
haemoglobin decreased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
red blood cell sedimentation rate increased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
Injury, poisoning and procedural complications			
accidental overdose			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
ankle fracture			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
concussion			

alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
fall			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 194 (1.03%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
foot fracture			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
postpericardiotomy syndrome			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
road traffic accident			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tendon rupture			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
toxicity to various agents			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
wrist fracture			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 194 (1.03%)	1 / 190 (0.53%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
acute myocardial infarction			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	4 / 194 (2.06%)	6 / 190 (3.16%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 4	1 / 6	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
angina pectoris			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
angina unstable			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	3 / 194 (1.55%)	2 / 190 (1.05%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrial fibrillation			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
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 arrest			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
cardiac failure			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	1 / 190 (0.53%)	3 / 192 (1.56%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
cardiac failure acute			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
cardiac failure congestive			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 194 (1.03%)	2 / 190 (1.05%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
coronary artery disease			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	1 / 190 (0.53%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
coronary artery occlusion			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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

heart valve incompetence alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
ischaemic cardiomyopathy alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
myocardial infarction alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	1 / 190 (0.53%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
myocardial ischaemia alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
palpitations alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
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			
carotid artery stenosis alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
cerebrovascular accident alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
cervical radiculopathy			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
iiird nerve paralysis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
ischaemic stroke			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myoclonus			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
presyncope			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
sciatica			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	1 / 190 (0.53%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
transient ischaemic attack			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
Eye disorders			
retinal artery occlusion			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
visual acuity reduced			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
abdominal pain lower			

alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
colitis ischaemic			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diarrhoea			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastritis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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 haemorrhage			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
nausea			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatitis acute			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vomiting			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
cholecystitis acute			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	2 / 190 (1.05%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
portal vein thrombosis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
Skin and subcutaneous tissue disorders			
diabetic foot			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
skin ulcer			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 194 (1.03%)	5 / 190 (2.63%)	3 / 192 (1.56%)
occurrences causally related to treatment / all	0 / 2	1 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
chronic kidney disease			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 194 (1.03%)	0 / 190 (0.00%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
end stage renal disease			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 194 (1.03%)	2 / 190 (1.05%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haematuria			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
prerenal failure			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal injury			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
tubulointerstitial nephritis alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
urethral haemorrhage alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
Musculoskeletal and connective tissue disorders			
musculoskeletal chest pain alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
osteoarthritis alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pain in extremity alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
rhabdomyolysis alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 194 (0.00%)	2 / 190 (1.05%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Infections and infestations			
abdominal abscess			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
appendicitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
cellulitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	3 / 194 (1.55%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
clostridium difficile colitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
diverticulitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
gastroenteritis			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	1 / 194 (0.52%)	1 / 190 (0.53%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastroenteritis viral			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
groin abscess			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
localised infection			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
osteomyelitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	1 / 190 (0.53%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
pneumonia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	3 / 194 (1.55%)	3 / 190 (1.58%)	0 / 192 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia haemophilus			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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

pneumonia legionella alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
pseudomembranous colitis alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyelonephritis alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sepsis alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
tonsillitis alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	0 / 192 (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
tracheobronchitis alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
urinary tract infection alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	3 / 194 (1.55%)	2 / 190 (1.05%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
wound infection			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
dehydration			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fluid retention			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	1 / 190 (0.53%)	0 / 192 (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
hyperglycaemia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 194 (0.00%)	0 / 190 (0.00%)	2 / 192 (1.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypoglycaemia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	13 / 194 (6.70%)	6 / 190 (3.16%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	14 / 17	5 / 7	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hyponatraemia			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	1 / 194 (0.52%)	0 / 190 (0.00%)	1 / 192 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Colpocele is a gender-specific SAE in females and is the correct N presented.

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

Non-serious adverse events	Insulin Glargine	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	130 / 194 (67.01%)	134 / 190 (70.53%)	144 / 192 (75.00%)
Investigations			
blood creatinine increased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	90 / 194 (46.39%)	71 / 190 (37.37%)	74 / 192 (38.54%)
occurrences (all)	124	102	106
glomerular filtration rate decreased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	26 / 194 (13.40%)	20 / 190 (10.53%)	17 / 192 (8.85%)
occurrences (all)	29	25	22
weight increased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	16 / 194 (8.25%)	9 / 190 (4.74%)	9 / 192 (4.69%)
occurrences (all)	18	9	10
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	20 / 194 (10.31%)	13 / 190 (6.84%)	14 / 192 (7.29%)
occurrences (all)	20	13	14
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	10 / 194 (5.15%)	11 / 190 (5.79%)	8 / 192 (4.17%)
occurrences (all)	12	12	11
Blood and lymphatic system disorders			

anaemia alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	10 / 194 (5.15%) 10	3 / 190 (1.58%) 3	5 / 192 (2.60%) 5
General disorders and administration site conditions oedema peripheral alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	15 / 194 (7.73%) 16	12 / 190 (6.32%) 13	10 / 192 (5.21%) 10
Gastrointestinal disorders constipation alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all) diarrhoea alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all) nausea alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all) vomiting alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	6 / 194 (3.09%) 6 14 / 194 (7.22%) 17 9 / 194 (4.64%) 9 9 / 194 (4.64%) 9	10 / 190 (5.26%) 10 30 / 190 (15.79%) 37 27 / 190 (14.21%) 38 16 / 190 (8.42%) 22	12 / 192 (6.25%) 13 31 / 192 (16.15%) 49 38 / 192 (19.79%) 52 26 / 192 (13.54%) 42
Respiratory, thoracic and mediastinal disorders cough alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	15 / 194 (7.73%) 17	7 / 190 (3.68%) 7	7 / 192 (3.65%) 8
Musculoskeletal and connective tissue disorders back pain alternative dictionary used: MedDRA 19.1			

subjects affected / exposed occurrences (all)	7 / 194 (3.61%) 8	8 / 190 (4.21%) 8	10 / 192 (5.21%) 10
Infections and infestations			
influenza			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	10 / 194 (5.15%)	15 / 190 (7.89%)	12 / 192 (6.25%)
occurrences (all)	10	18	12
nasopharyngitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	12 / 194 (6.19%)	9 / 190 (4.74%)	11 / 192 (5.73%)
occurrences (all)	15	12	12
sinusitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	11 / 194 (5.67%)	4 / 190 (2.11%)	2 / 192 (1.04%)
occurrences (all)	13	4	2
upper respiratory tract infection			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	20 / 194 (10.31%)	13 / 190 (6.84%)	8 / 192 (4.17%)
occurrences (all)	26	15	9
urinary tract infection			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	19 / 194 (9.79%)	10 / 190 (5.26%)	13 / 192 (6.77%)
occurrences (all)	25	12	16
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	3 / 194 (1.55%)	5 / 190 (2.63%)	11 / 192 (5.73%)
occurrences (all)	3	6	11
hyperkalaemia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	13 / 194 (6.70%)	8 / 190 (4.21%)	12 / 192 (6.25%)
occurrences (all)	15	10	14

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