



Clinical trial results:

A Phase 2 Study of Once-Weekly LY3298176 Compared with Placebo and Dulaglutide in Patients with Type 2 Diabetes Mellitus

Summary

EudraCT number	2016-004179-33
Trial protocol	SK PL
Global end of trial date	01 August 2018

Results information

Result version number	v1 (current)
This version publication date	30 August 2019
First version publication date	30 August 2019

Trial information

Trial identification

Sponsor protocol code	I8F-MC-GPGB
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03131687
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16335

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	01 August 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy of the study drug tirzepatide in participants with type 2 diabetes mellitus.

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	24 May 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Puerto Rico: 16
Country: Number of subjects enrolled	United States: 234
Country: Number of subjects enrolled	Poland: 31
Country: Number of subjects enrolled	Slovakia: 35
Worldwide total number of subjects	316
EEA total number of subjects	66

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)	258
From 65 to 84 years	58
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

Two additional patients were randomized in the US but chose not to take study drug and are not included in the number of patients enrolled. Thus, 318 patients were randomized but 316 took study drug and all data presented are for patients who took at least 1 dose of study drug (316 patients).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Tirzepatide placebo and dulaglutide placebo administered subcutaneously (SC) once weekly.

Arm type	Placebo
Investigational medicinal product name	Tirzepatide Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Tirzepatide placebo administered subcutaneously (SC) once weekly.

Investigational medicinal product name	Dulaglutide Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Dulaglutide placebo administered subcutaneously (SC) once weekly.

Arm title	1 mg Tirzepatide
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Arm description:

1 milligrams (mg) tirzepatide administered SC once weekly.

Dulaglutide placebo administered SC once weekly.

Arm type	Experimental
Investigational medicinal product name	tirzepatide
Investigational medicinal product code	
Other name	LY3298176
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 mg tirzepatide administered SC once weekly

Investigational medicinal product name	Dulaglutide Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
Dulaglutide placebo administered SC once weekly.	
Arm title	5 mg Tirzepatide
Arm description:	
5 mg tirzepatide administered SC once weekly.	
Dulaglutide placebo administered SC once weekly.	
Arm type	Experimental
Investigational medicinal product name	tirzepatide
Investigational medicinal product code	
Other name	LY3298176
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
5 mg tirzepatide administered SC once weekly	
Investigational medicinal product name	Dulaglutide placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
Dulaglutide placebo administered SC once weekly.	
Arm title	10 mg Tirzepatide
Arm description:	
10 mg tirzepatide administered SC once weekly.	
Dulaglutide placebo administered SC once weekly.	
Arm type	Experimental
Investigational medicinal product name	tirzepatide
Investigational medicinal product code	
Other name	LY3298176
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
10 mg tirzepatide administered SC once weekly.	
Investigational medicinal product name	Dulaglutide Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
Dulaglutide placebo administered SC once weekly.	
Arm title	15 mg Tirzepatide
Arm description:	
15 mg tirzepatide administered SC once weekly.	
Dulaglutide placebo administered SC once weekly.	
Arm type	Experimental

Investigational medicinal product name	tirzepatide
Investigational medicinal product code	
Other name	LY3298176
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 15 mg tirzepatide administered SC once weekly.	
Investigational medicinal product name	Dulaglutide Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details: Dulaglutide placebo administered SC once weekly.	
Arm title	1.5 mg Dulaglutide
Arm description: 1.5 mg Dulaglutide administered SC once weekly. Tirzepatide placebo administered SC once weekly.	
Arm type	Active comparator
Investigational medicinal product name	Dulaglutide
Investigational medicinal product code	
Other name	LY2189265
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details: 1.5 mg Dulaglutide administered SC once weekly.	
Investigational medicinal product name	Tirzepatide Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: Tirzepatide placebo administered SC once weekly	

Number of subjects in period 1	Placebo	1 mg Tirzepatide	5 mg Tirzepatide
Started	51	52	55
Received at least one dose of study drug	51	52	55
Completed	45	44	52
Not completed	6	8	3
Consent withdrawn by subject	3	3	3
Adverse event, non-fatal	-	1	-
Death	1	-	-
Lost to follow-up	1	4	-
Participant Started New Diabetic Drug	1	-	-

Number of subjects in period 1	10 mg Tirzepatide	15 mg Tirzepatide	1.5 mg Dulaglutide
Started	51	53	54
Received at least one dose of study drug	51	53	54
Completed	48	45	49
Not completed	3	8	5
Consent withdrawn by subject	1	2	1
Adverse event, non-fatal	1	2	2
Death	-	-	-
Lost to follow-up	1	4	2
Participant Started New Diabetic Drug	-	-	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Tirzepatide placebo and dulaglutide placebo administered subcutaneously (SC) once weekly.	
Reporting group title	1 mg Tirzepatide
Reporting group description: 1 milligrams (mg) tirzepatide administered SC once weekly. Dulaglutide placebo administered SC once weekly.	
Reporting group title	5 mg Tirzepatide
Reporting group description: 5 mg tirzepatide administered SC once weekly. Dulaglutide placebo administered SC once weekly.	
Reporting group title	10 mg Tirzepatide
Reporting group description: 10 mg tirzepatide administered SC once weekly. Dulaglutide placebo administered SC once weekly.	
Reporting group title	15 mg Tirzepatide
Reporting group description: 15 mg tirzepatide administered SC once weekly. Dulaglutide placebo administered SC once weekly.	
Reporting group title	1.5 mg Dulaglutide
Reporting group description: 1.5 mg Dulaglutide administered SC once weekly. Tirzepatide placebo administered SC once weekly.	

Reporting group values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide
Number of subjects	51	52	55
Age categorical			
Units: Subjects			

Age continuous			
All randomized participants who received at least one dose of study drug.			
Units: years			
arithmetic mean	56.6	57.4	57.9
standard deviation	± 8.85	± 8.85	± 8.22
Gender categorical			
All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Female	22	23	21
Male	29	29	34
Ethnicity (NIH/OMB)			
All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Hispanic or Latino	27	25	22
Not Hispanic or Latino	19	23	23
Unknown or Not Reported	5	4	10
Race (NIH/OMB)			
All randomized participants who received at least one dose of study drug.			

Units: Subjects			
American Indian or Alaska Native	5	4	1
Asian	1	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	5	6
White	41	42	46
More than one race	2	1	2
Unknown or Not Reported	0	0	0
Region of Enrollment			
All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Puerto Rico	4	4	3
United States	36	37	38
Poland	6	7	4
Slovakia	5	4	10
Hemoglobin A1C (HbA1c) at Baseline			
Measure Description: HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time.			
Units: Percentage of HbA1c			
arithmetic mean	8.04	8.21	8.17
standard deviation	± 0.861	± 0.905	± 0.961
Reporting group values	10 mg Tirzepatide	15 mg Tirzepatide	1.5 mg Dulaglutide
Number of subjects	51	53	54
Age categorical			
Units: Subjects			

Age continuous			
All randomized participants who received at least one dose of study drug.			
Units: years			
arithmetic mean	56.5	56.0	58.7
standard deviation	± 9.92	± 7.58	± 7.81
Gender categorical			
All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Female	21	31	30
Male	30	22	24
Ethnicity (NIH/OMB)			
All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Hispanic or Latino	26	23	19
Not Hispanic or Latino	20	27	27
Unknown or Not Reported	5	3	8
Race (NIH/OMB)			
All randomized participants who received at least one dose of study drug.			
Units: Subjects			
American Indian or Alaska Native	2	2	1
Asian	1	1	2
Native Hawaiian or Other Pacific Islander	1	1	0
Black or African American	7	6	4

White	37	43	44
More than one race	2	0	2
Unknown or Not Reported	1	0	1
Region of Enrollment			
All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Puerto Rico	3	1	1
United States	37	43	43
Poland	6	6	2
Slovakia	5	3	8
Hemoglobin A1C (HbA1c) at Baseline			
Measure Description: HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time.			
Units: Percentage of HbA1c			
arithmetic mean	8.15	8.13	8.13
standard deviation	± 1.072	± 1.061	± 1.954

Reporting group values	Total		
Number of subjects	316		
Age categorical			
Units: Subjects			

Age continuous			
All randomized participants who received at least one dose of study drug.			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Female	148		
Male	168		
Ethnicity (NIH/OMB)			
All randomized participants who received at least one dose of study drug.			
Units: Subjects			
Hispanic or Latino	142		
Not Hispanic or Latino	139		
Unknown or Not Reported	35		
Race (NIH/OMB)			
All randomized participants who received at least one dose of study drug.			
Units: Subjects			
American Indian or Alaska Native	15		
Asian	5		
Native Hawaiian or Other Pacific Islander	2		
Black or African American	30		
White	253		
More than one race	9		
Unknown or Not Reported	2		
Region of Enrollment			
All randomized participants who received at least one dose of study drug.			
Units: Subjects			

Puerto Rico	16		
United States	234		
Poland	31		
Slovakia	35		
Hemoglobin A1C (HbA1c) at Baseline			
Measure Description: HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time.			
Units: Percentage of HbA1c			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Tirzepatide placebo and dulaglutide placebo administered subcutaneously (SC) once weekly.	
Reporting group title	1 mg Tirzepatide
Reporting group description: 1 milligrams (mg) tirzepatide administered SC once weekly. Dulaglutide placebo administered SC once weekly.	
Reporting group title	5 mg Tirzepatide
Reporting group description: 5 mg tirzepatide administered SC once weekly. Dulaglutide placebo administered SC once weekly.	
Reporting group title	10 mg Tirzepatide
Reporting group description: 10 mg tirzepatide administered SC once weekly. Dulaglutide placebo administered SC once weekly.	
Reporting group title	15 mg Tirzepatide
Reporting group description: 15 mg tirzepatide administered SC once weekly. Dulaglutide placebo administered SC once weekly.	
Reporting group title	1.5 mg Dulaglutide
Reporting group description: 1.5 mg Dulaglutide administered SC once weekly. Tirzepatide placebo administered SC once weekly.	

Primary: Change From Baseline to Week 26 in Hemoglobin A1c (HbA1c) Bayesian Dose Response

End point title	Change From Baseline to Week 26 in Hemoglobin A1c (HbA1c) Bayesian Dose Response
End point description: HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time. This was a Bayesian dose response analysis of HbA1c (%) change from baseline. At baseline: Mean (SD = Standard Deviation) of baseline HbA1c (%). After baseline: Posterior Mean (SD = Posterior Standard Deviation) of HbA1c (%) change from baseline. Analysis Population Description (APD): All randomized participants who received at least one dose of study drug and had a baseline and postbaseline excluding data after rescue drug initiation. The Least Squares Mean is Posterior mean.	
End point type	Primary
End point timeframe: Baseline, Week 26	

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	45	52	47
Units: Percentage of HbA1c				
least squares mean (standard deviation)	-0.06 (± 0.14)	-1.06 (± 0.11)	-1.73 (± 0.08)	-1.89 (± 0.08)

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	49		
Units: Percentage of HbA1c				
least squares mean (standard deviation)	-1.94 (± 0.09)	-1.21 (± 0.14)		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide Bayesian Dose Response
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Statistical analysis description:

Statistics are estimated from a Bayesian hierarchical logistic dose response model along with a titrated integrated two-component prediction model to estimate missing values.

The confidence interval is 80% credible set for difference.

Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Posterior Mean Difference
Point estimate	-1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.22
upper limit	-0.79
Variability estimate	Standard deviation
Dispersion value	0.17

Statistical analysis title	Placebo, 5 mg Tirzepatide Bayesian Dose Response
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Statistical analysis description:

Statistics are estimated from a Bayesian hierarchical logistic dose response model along with a titrated integrated two-component prediction model to estimate missing values.

The confidence interval is 80% credible set for difference.

Comparison groups	Placebo v 5 mg Tirzepatide
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Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Posterior Mean Difference
Point estimate	-1.67
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.88
upper limit	-1.46
Variability estimate	Standard deviation
Dispersion value	0.17

Statistical analysis title	Placebo, 10 mg Tirzepatide Bayesian Dose Response
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Statistical analysis description:

Statistics are estimated from a Bayesian hierarchical logistic dose response model along with a titrated integrated two-component prediction model to estimate missing values.

The confidence interval is 80% credible set for difference.

Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Posterior Mean Difference
Point estimate	-1.83
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-2.04
upper limit	-1.61
Variability estimate	Standard deviation
Dispersion value	0.17

Statistical analysis title	Placebo, 15 mg Tirzepatide Bayesian Dose Response
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Statistical analysis description:

Statistics are estimated from a Bayesian hierarchical logistic dose response model along with a titrated integrated two-component prediction model to estimate missing values.

The confidence interval is 80% credible set for difference.

Comparison groups	Placebo v 15 mg Tirzepatide
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Posterior Mean Difference
Point estimate	-1.89

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-2.11
upper limit	-1.67
Variability estimate	Standard deviation
Dispersion value	0.17

Secondary: Change From Baseline to Week 12 in Hemoglobin A1c (HbA1c) Bayesian Dose Response

End point title	Change From Baseline to Week 12 in Hemoglobin A1c (HbA1c) Bayesian Dose Response
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End point description:

HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time. This was a Bayesian dose response analysis of HbA1c (%) change from baseline. At baseline: Mean (SD = Standard Deviation) of baseline HbA1c (%). After baseline: Posterior Mean (SD = Posterior Standard Deviation) of HbA1c (%) change from baseline.

APD: All randomized participants who received at least one dose of study drug and had a baseline and postbaseline value excluding data after rescue drug initiation.

The Least Squares Mean is Posterior mean.

End point type	Secondary
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End point timeframe:

Baseline, Week 12

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	45	52	48
Units: Percentage of HbA1c				
least squares mean (standard deviation)	-0.05 (± 0.13)	-0.94 (± 0.10)	-1.54 (± 0.07)	-1.68 (± 0.08)

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	51		
Units: Percentage of HbA1c				
least squares mean (standard deviation)	-1.72 (± 0.08)	-1.08 (± 0.13)		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide Bayesian Dose Response
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Statistical analysis description:

Statistics are estimated from a Bayesian hierarchical logistic dose response model along with a titrated

integrated two-component prediction model to estimate missing values.

The confidence interval is 80% credible set for difference.

Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Posterior Mean Difference
Point estimate	-0.89
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.08
upper limit	-0.71
Variability estimate	Standard deviation
Dispersion value	0.15

Statistical analysis title	Placebo, 5 mg Tirzepatide Bayesian Dose Response
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Statistical analysis description:

Statistics are estimated from a Bayesian hierarchical logistic dose response model along with a titrated integrated two-component prediction model to estimate missing values.

The confidence interval is 80% credible set for difference.

Comparison groups	Placebo v 5 mg Tirzepatide
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Posterior Mean Difference
Point estimate	-1.49
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.68
upper limit	-1.3
Variability estimate	Standard deviation
Dispersion value	0.15

Statistical analysis title	Placebo, 10 mg Tirzepatide Bayesian Dose Response
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Statistical analysis description:

Statistics are estimated from a Bayesian hierarchical logistic dose response model along with a titrated integrated two-component prediction model to estimate missing values.

The confidence interval is 80% credible set for difference.

Comparison groups	Placebo v 10 mg Tirzepatide
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Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Posterior Mean Difference
Point estimate	-1.62
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.82
upper limit	-1.43
Variability estimate	Standard deviation
Dispersion value	0.15

Statistical analysis title	Placebo, 15 mg Tirzepatide Bayesian Dose Response
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Statistical analysis description:

Statistics are estimated from a Bayesian hierarchical logistic dose response model along with a titrated integrated two-component prediction model to estimate missing values.

The confidence interval is 80% credible set for difference.

Comparison groups	Placebo v 15 mg Tirzepatide
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Posterior Mean Difference
Point estimate	-1.67
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.86
upper limit	-1.47
Variability estimate	Standard deviation
Dispersion value	0.15

Secondary: Change From Baseline to Week 26 in HbA1c

End point title	Change From Baseline to Week 26 in HbA1c
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End point description:

HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time. The Least Squares (LS) mean was estimated from a mixed-effects model with repeated measures (MMRM) that included the independent variables: Baseline + Baseline BMI Group + Baseline Metformin Flag + Treatment + Time + Treatment*Time.

APD: All randomized participants who received at least one dose of study drug who had a baseline and postbaseline value excluding data after study drug discontinuation or rescue drug initiation.

End point type	Secondary
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End point timeframe:

Baseline, Week 26

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	44	47	43
Units: Percentage of HbA1c				
least squares mean (standard error)	0.1 (± 0.16)	-0.7 (± 0.16)	-1.6 (± 0.15)	-2.0 (± 0.16)

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	47		
Units: Percentage of HbA1c				
least squares mean (standard error)	-2.4 (± 0.17)	-1.1 (± 0.15)		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide MMRM
Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.4

Statistical analysis title	Placebo, 5 mg Tirzepatide MMRM
Comparison groups	Placebo v 5 mg Tirzepatide
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-1.3

Statistical analysis title	Placebo, 10 mg Tirzepatide MMRM
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	-1.6

Statistical analysis title	Placebo, 15 mg Tirzepatide MMRM
Comparison groups	Placebo v 15 mg Tirzepatide
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	-2

Secondary: Change From Baseline to Week 12 in HbA1c

End point title	Change From Baseline to Week 12 in HbA1c
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End point description:

HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time. The Least Squares (LS) mean was estimated from a mixed-effects model with repeated measures (MMRM) that included the independent variables: Baseline + Baseline BMI Group + Baseline Metformin Flag + Treatment + Time + Treatment*Time.

APD: All randomized participants who received at least one dose of study drug who had a baseline and

postbaseline value excluding data after study drug discontinuation or rescue drug initiation.

End point type	Secondary
End point timeframe:	
Baseline, Week 12	

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	44	49	47
Units: Percentage of HbA1c				
least squares mean (standard error)	-0.1 (± 0.13)	-0.9 (± 0.13)	-1.7 (± 0.13)	-2.0 (± 0.13)

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	49		
Units: Percentage of HbA1c				
least squares mean (standard error)	-2.1 (± 0.15)	-1.2 (± 0.13)		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide MMRM
Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.4

Statistical analysis title	Placebo, 5 mg Tirzepatide MMRM
Comparison groups	Placebo v 5 mg Tirzepatide

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1.3

Statistical analysis title	Placebo, 10 mg Tirzepatide MMRM
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	-1.5

Statistical analysis title	Placebo, 15 mg Tirzepatide MMRM
Comparison groups	Placebo v 15 mg Tirzepatide
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-1.7

Secondary: Change From Baseline in Body Weight

End point title	Change From Baseline in Body Weight
End point description:	
Least Squares (LS) mean was determined by mixed-model repeated measures (MMRM) model with independent variables: Baseline + Baseline HbA1C Group + Baseline BMI Group + Baseline Metformin Flag + Treatment + Time + Treatment*Time.	
APD: All randomized participants who received at least one dose of study drug and had a baseline and postbaseline value excluding data after study drug discontinuation or rescue drug initiation.	
End point type	Secondary
End point timeframe:	
Baseline, Week 26	

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	44	48	44
Units: kilograms (kg)				
least squares mean (standard error)	-0.4 (± 0.81)	-0.9 (± 0.80)	-4.8 (± 0.77)	-8.7 (± 0.80)

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	47		
Units: kilograms (kg)				
least squares mean (standard error)	-11.3 (± 0.88)	-2.7 (± 0.78)		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide MMRM
Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.655
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	1.7

Statistical analysis title	Placebo, 5 mg Tirzepatide MMRM
Comparison groups	Placebo v 5 mg Tirzepatide
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	-2.3

Statistical analysis title	Placebo, 10 mg Tirzepatide MMRM
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.5
upper limit	-6

Statistical analysis title	Placebo, 15 mg Tirzepatide MMRM
Comparison groups	Placebo v 15 mg Tirzepatide
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-10.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.3
upper limit	-8.6

Secondary: Percentage of Participants With 5% or Greater Body Weight Loss From Baseline

End point title	Percentage of Participants With 5% or Greater Body Weight Loss From Baseline
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End point description:

Percentage of participants with 5% or greater body weight loss from baseline last observation carried forward (LOCF) analyses using Logistic regression model with Baseline value + Baseline HbA1C Group + Baseline BMI Group + Baseline Metformin + Treatment as factors.

APD: All randomized participants who received at least one dose of study drug excluding data after study drug discontinuation or rescue drug initiation.

End point type	Secondary
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End point timeframe:

Week 26

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	55	51
Units: percentage of participants				
number (not applicable)	0	13.5	47.3	70.6

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	54		
Units: percentage of participants				
number (not applicable)	62.3	22.2		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide
Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.053
Method	Regression, Logistic

Statistical analysis title	Placebo, 5 mg Tirzepatide
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Comparison groups	Placebo v 5 mg Tirzepatide
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	Regression, Logistic

Statistical analysis title	Placebo, 10 mg Tirzepatide
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Logistic

Statistical analysis title	Placebo, 15 mg Tirzepatide
Comparison groups	15 mg Tirzepatide v Placebo
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Logistic

Secondary: Percentage of Participants With 10% or Greater Body Weight Loss From Baseline

End point title	Percentage of Participants With 10% or Greater Body Weight Loss From Baseline
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End point description:

Percentage of participants with 10% or greater body weight loss from baseline LOCF analyses using Logistic regression model with Baseline value + Baseline HbA1C Group + Baseline BMI Group + Baseline Metformin + Treatment as factors.

APD: All randomized participants who received at least one dose of study drug excluding data after study drug discontinuation or rescue drug initiation.

End point type	Secondary
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End point timeframe:

Week 26

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	55	51
Units: percentage of participants				
number (not applicable)	0	5.8	16.4	39.2

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	54		
Units: percentage of participants				
number (not applicable)	37.7	9.3		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide
Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.193
Method	Regression, Logistic

Statistical analysis title	Placebo, 5 mg Tirzepatide
Comparison groups	Placebo v 5 mg Tirzepatide
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.036
Method	Regression, Logistic

Statistical analysis title	Placebo, 10 mg Tirzepatide
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003
Method	Regression, Logistic

Statistical analysis title	Placebo, 15 mg Tirzepatide
Comparison groups	Placebo v 15 mg Tirzepatide
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003
Method	Regression, Logistic

Secondary: Percentage of Participants Reaching the HbA1c Target of $\leq 6.5\%$

End point title	Percentage of Participants Reaching the HbA1c Target of $\leq 6.5\%$
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End point description:

Percentage of participants with HbA1c $\leq 6.5\%$ at Week 26 using a logistic regression model for endpoint used last observation carried forward (LOCF) method including baseline value, baseline BMI Group, baseline Metformin and treatment as factors.

APD: All randomized participants who received at least one dose of study drug excluding data after study drug discontinuation or rescue drug initiation.

End point type	Secondary
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End point timeframe:

Week 26

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	55	50
Units: percentage of participants				
number (not applicable)	2.0	15.4	63.6	82.0

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	54		
Units: percentage of participants				
number (not applicable)	58.5	38.9		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide
Comparison groups	Placebo v 1 mg Tirzepatide

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.03
Method	Regression, Logistic

Statistical analysis title	Placebo, 5 mg Tirzepatide
Comparison groups	Placebo v 5 mg Tirzepatide
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Logistic

Statistical analysis title	Placebo, 10 mg Tirzepatide
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Logistic

Statistical analysis title	Placebo, 15 mg Tirzepatide
Comparison groups	Placebo v 15 mg Tirzepatide
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Logistic

Secondary: Percentage of Participants Reaching the HbA1c Target of <7.0%

End point title	Percentage of Participants Reaching the HbA1c Target of <7.0%
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End point description:

Percentage of participants with HbA1c <7.0% at Week 26 using a logistic regression model for endpoint used last observation carried forward (LOCF) method including baseline value, baseline BMI Group, baseline Metformin and treatment as factors.

APD: All randomized participants who received at least one dose of study drug excluding data after study drug discontinuation or rescue drug initiation.

End point type	Secondary
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End point timeframe:

Week 26

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	55	50
Units: percentage of participants				
number (not applicable)	11.8	32.7	69.1	90.0

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	54		
Units: percentage of participants				
number (not applicable)	77.4	51.9		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide
Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.008
Method	Regression, Logistic

Statistical analysis title	Placebo, 5 mg Tirzepatide
Comparison groups	Placebo v 5 mg Tirzepatide
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Logistic

Statistical analysis title	Placebo, 10 mg Tirzepatide
Comparison groups	Placebo v 10 mg Tirzepatide

Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Logistic

Statistical analysis title	Placebo, 15 mg Tirzepatide
Comparison groups	Placebo v 15 mg Tirzepatide
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Logistic

Secondary: Change From Baseline in Fasting Blood Glucose

End point title	Change From Baseline in Fasting Blood Glucose
End point description:	
Least Squares (LS) mean was determined by mixed-model repeated measures (MMRM) model with covariates: Baseline + Baseline HbA1C Group + Baseline BMI Group + Baseline Metformin Flag + Treatment + Time + Treatment*Time.	
APD: All randomized participants who received at least one dose of study drug who had a baseline and postbaseline value excluding data after study drug discontinuation or rescue drug initiation.	
End point type	Secondary
End point timeframe:	
Baseline, Week 26	

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	44	48	44
Units: milligrams per deciliter (mg/dL)				
least squares mean (standard error)	15.5 (± 6.66)	-6.8 (± 6.43)	-40.7 (± 6.23)	-60.7 (± 6.36)

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	46		
Units: milligrams per deciliter (mg/dL)				
least squares mean (standard error)	-57.5 (± 7.10)	-21.2 (± 6.40)		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide
Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.01
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-22.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.4
upper limit	-5.3

Statistical analysis title	Placebo, 5 mg Tirzepatide
Comparison groups	Placebo v 5 mg Tirzepatide
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-56.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-72.9
upper limit	-39.5

Statistical analysis title	Placebo, 10 mg Tirzepatide
Comparison groups	Placebo v 10 mg Tirzepatide

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-76.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-93.3
upper limit	-59.2

Statistical analysis title	Placebo, 15 mg Tirzepatide
Comparison groups	15 mg Tirzepatide v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-90.9
upper limit	-55.2

Secondary: Change From Baseline in High-Density Lipoprotein Cholesterol (HDL-C)

End point title	Change From Baseline in High-Density Lipoprotein Cholesterol (HDL-C)
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End point description:

LS means were calculated using MMRM model with independent variables: Baseline, Baseline HbA1C Group, Baseline BMI Group, Baseline Metformin Flag, Treatment, time, treatment*time.

APD: All randomized participants who received at least one dose of study drug and had a baseline and postbaseline value.

End point type	Secondary
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End point timeframe:

Baseline, Week 26

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	46	53	48
Units: Millimoles Per Litre (mmol/L)				
least squares mean (standard error)	0.0 (± 0.03)	-0.0 (± 0.03)	0.0 (± 0.03)	0.0 (± 0.03)

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	51		
Units: Millimoles Per Litre (mmol/L)				
least squares mean (standard error)	0.1 (± 0.03)	0.0 (± 0.03)		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide
Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.396
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0

Statistical analysis title	Placebo, 5 mg Tirzepatide
Comparison groups	Placebo v 5 mg Tirzepatide
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.903
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1

Statistical analysis title	Placebo, 10 mg Tirzepatide
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.536
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1

Statistical analysis title	Placebo, 15 mg Tirzepatide
Comparison groups	Placebo v 15 mg Tirzepatide
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.325
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.1

Secondary: Change From Baseline in Total Cholesterol

End point title	Change From Baseline in Total Cholesterol
End point description:	
LS means were calculated using MMRM model with independent variables: Baseline, Baseline HbA1C Group, Baseline BMI Group, Baseline Metformin Flag, Treatment, Time, Treatment*Time.	
APD: All randomized participants who received at least one dose of study drug and had a baseline and postbaseline value.	
End point type	Secondary
End point timeframe:	
Baseline, Week 26	

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	46	53	48
Units: Millimoles Per Litre (mmol/L)				
least squares mean (standard error)	0.3 (± 0.13)	0.2 (± 0.13)	-0.1 (± 0.12)	-0.3 (± 0.12)

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	51		
Units: Millimoles Per Litre (mmol/L)				
least squares mean (standard error)	-0.3 (± 0.13)	-0.2 (± 0.12)		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide
Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.565
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.2

Statistical analysis title	Placebo, 5 mg Tirzepatide
Comparison groups	5 mg Tirzepatide v Placebo
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.01
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.1

Statistical analysis title	Placebo, 10 mg Tirzepatide
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.2

Statistical analysis title	Placebo, 15 mg Tirzepatide
Comparison groups	Placebo v 15 mg Tirzepatide
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.3

Secondary: Change From Baseline in Triglycerides

End point title	Change From Baseline in Triglycerides
End point description:	
LS means were calculated using MMRM model with independent variables: Baseline, Baseline HbA1C Group, Baseline BMI Group, Baseline Metformin Flag, Treatment, Time, Treatment*Time.	
APD: All randomized participants who received at least one dose of study drug and had a baseline and postbaseline value.	
End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	46	53	48
Units: Millimoles Per Litre (mmol/L)				
least squares mean (standard error)	0.3 (± 0.16)	-0.0 (± 0.16)	-0.5 (± 0.15)	-0.7 (± 0.15)

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	51		
Units: Millimoles Per Litre (mmol/L)				
least squares mean (standard error)	-0.8 (± 0.16)	-0.3 (± 0.15)		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide
Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.164
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.1

Statistical analysis title	Placebo, 5 mg Tirzepatide
Comparison groups	Placebo v 5 mg Tirzepatide

Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.4

Statistical analysis title	Placebo, 10 mg Tirzepatide
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.6

Statistical analysis title	Placebo, 15 mg Tirzepatide
Comparison groups	Placebo v 15 mg Tirzepatide
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-0.7

Secondary: Change From Baseline in Low-Density Lipoprotein Cholesterol (LDL-C)

End point title	Change From Baseline in Low-Density Lipoprotein Cholesterol (LDL-C)
End point description:	
LS means were calculated using MMRM model with independent variables: Baseline, Baseline HbA1C Group, Baseline BMI Group, Baseline Metformin Flag, Treatment, Time, Treatment*Time.	
APD: All randomized participants who received at least one dose of study drug and had a baseline and postbaseline value.	
End point type	Secondary
End point timeframe:	
Baseline, Week 26	

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	45	52	48
Units: Millimoles Per Litre (mmol/L)				
least squares mean (standard error)	0.2 (± 0.12)	0.2 (± 0.11)	0.0 (± 0.11)	-0.0 (± 0.11)

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	50		
Units: Millimoles Per Litre (mmol/L)				
least squares mean (standard error)	-0.1 (± 0.12)	-0.1 (± 0.11)		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide
Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.919
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.3

Statistical analysis title	Placebo, 5 mg Tirzepatide
Comparison groups	Placebo v 5 mg Tirzepatide
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.194
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.1

Statistical analysis title	Placebo, 10 mg Tirzepatide
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.145
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.1

Statistical analysis title	Placebo, 15 mg Tirzepatide
Comparison groups	Placebo v 15 mg Tirzepatide
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.067
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0

Secondary: Change From Baseline in Waist Circumference

End point title	Change From Baseline in Waist Circumference
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End point description:

LS means were calculated using MMRM model with independent variables: Baseline, Baseline HbA1C Group, Baseline BMI Group, Baseline Metformin Flag, Treatment, Time, Treatment*Time.

APD: All randomized participants who received at least one dose of study drug and had a baseline and postbaseline value excluding data after treatment discontinuation or rescue drug initiation.

End point type	Secondary
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End point timeframe:

Baseline, Week 26

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	44	47	44
Units: centimeters (cm)				
least squares mean (standard error)	-1.3 (± 0.91)	-2.1 (± 0.89)	-5.1 (± 0.86)	-7.4 (± 0.88)

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	47		
Units: centimeters (cm)				
least squares mean (standard error)	-10.2 (± 1.00)	-2.5 (± 0.87)		

Statistical analyses

Statistical analysis title	Placebo, 1 mg Tirzepatide
Comparison groups	Placebo v 1 mg Tirzepatide
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.539
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	1.6

Statistical analysis title	Placebo, 5 mg Tirzepatide
Comparison groups	Placebo v 5 mg Tirzepatide
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	-1.5

Statistical analysis title	Placebo, 10 mg Tirzepatide
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	-3.7

Statistical analysis title	Placebo, 15 mg Tirzepatide
Comparison groups	Placebo v 15 mg Tirzepatide
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-8.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.3
upper limit	-6.4

Secondary: Number of Participants With Anti-Drug Antibodies

End point title	Number of Participants With Anti-Drug Antibodies
End point description: Number of Participants With Anti-Drug Antibodies.	
APD: All randomized participants who received at least one dose of study drug.	
End point type	Secondary
End point timeframe: Baseline through Week 30	

End point values	Placebo	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	55	51
Units: Participants	0	16	19	24

End point values	15 mg Tirzepatide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	54		
Units: Participants	26	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Model Predicted Concentration at Steady State (Css) of Tirzepatide

End point title	Pharmacokinetics (PK): Model Predicted Concentration at Steady State (Css) of Tirzepatide ^[1]
End point description: Pharmacokinetics (PK): Model Predicted Concentration at Steady State (Css) of Tirzepatide.	
APD: All randomized participants who received at least one dose of Tirzepatide study drug excluding post rescue data.	
End point type	Secondary
End point timeframe: Predose: Week 1,8,12 and 26; Postdose: Week 1,2,4 and 12	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, PK data were only collected for Tirzepatide and Dulaglutide.

End point values	1 mg Tirzepatide	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	55	51	53
Units: Nanograms Per Millilitre (ng/mL)				
geometric mean (geometric coefficient of variation)	78.6 (± 29)	394 (± 29)	787 (± 29)	1180 (± 29)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up To 34 Weeks

Adverse event reporting additional description:

All randomized participants who received at least one dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	LY 1mg
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Reporting group description:

1 milligrams (mg) tirzepatide administered SC once weekly. Dulaglutide placebo administered SC once weekly.

Reporting group title	LY 5mg
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Reporting group description:

5 mg tirzepatide administered SC once weekly. Dulaglutide placebo administered SC once weekly.

Reporting group title	LY 10mg
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Reporting group description:

10 mg tirzepatide administered SC once weekly. Dulaglutide placebo administered SC once weekly.

Reporting group title	LY 15mg
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Reporting group description:

15 mg tirzepatide administered SC once weekly. Dulaglutide placebo administered SC once weekly.

Reporting group title	Placebo
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Reporting group description:

Tirzepatide placebo and dulaglutide placebo administered subcutaneously (SC) once weekly.

Reporting group title	Dula 1.5mg
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Reporting group description:

1.5 mg Dulaglutide administered SC once weekly. Tirzepatide placebo administered SC once weekly.

Serious adverse events	LY 1mg	LY 5mg	LY 10mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 52 (3.85%)	1 / 55 (1.82%)	3 / 51 (5.88%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
lung adenocarcinoma stage iv			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular disorders			
accelerated hypertension			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
coronary artery disease			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
coronary artery occlusion			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	1 / 52 (1.92%)	0 / 55 (0.00%)	0 / 51 (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
torsade de pointes			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	1 / 52 (1.92%)	0 / 55 (0.00%)	0 / 51 (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
ventricular fibrillation			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	1 / 52 (1.92%)	0 / 55 (0.00%)	0 / 51 (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
Nervous system disorders			
cluster headache			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
transient ischaemic attack			

alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vertebrobasilar insufficiency			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
enteritis			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
mesenteric vein thrombosis			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatitis acute			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	1 / 55 (1.82%)	0 / 51 (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
Hepatobiliary disorders			
cholecystitis			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholecystitis acute			
alternative dictionary used: MedDRA 21.0			

subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pathological fracture			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
perirectal abscess			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urosepsis			
alternative dictionary used: MedDRA 21.0			

subjects affected / exposed	1 / 52 (1.92%)	0 / 55 (0.00%)	0 / 51 (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
Metabolism and nutrition disorders			
lactic acidosis			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	1 / 52 (1.92%)	0 / 55 (0.00%)	0 / 51 (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

Serious adverse events	LY 15mg	Placebo	Dula 1.5mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 53 (3.77%)	2 / 51 (3.92%)	3 / 54 (5.56%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
lung adenocarcinoma stage iv			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	1 / 51 (1.96%)	0 / 54 (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
Vascular disorders			
accelerated hypertension			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 51 (0.00%)	0 / 54 (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			
coronary artery disease			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 51 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
coronary artery occlusion			
alternative dictionary used: MedDRA 21.0			

subjects affected / exposed	0 / 53 (0.00%)	0 / 51 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
torsade de pointes			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 51 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ventricular fibrillation			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 51 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
cluster headache			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 51 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
transient ischaemic attack			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 51 (0.00%)	0 / 54 (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
vertebrobasilar insufficiency			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 51 (0.00%)	0 / 54 (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
Gastrointestinal disorders			
enteritis			
alternative dictionary used: MedDRA 21.0			

subjects affected / exposed	1 / 53 (1.89%)	0 / 51 (0.00%)	0 / 54 (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
mesenteric vein thrombosis alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 51 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatitis acute alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 51 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
cholecystitis alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 51 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholecystitis acute alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 51 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
acute kidney injury alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 51 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
back pain alternative dictionary used: MedDRA 21.0			

subjects affected / exposed	0 / 53 (0.00%)	0 / 51 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pathological fracture			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	1 / 51 (1.96%)	0 / 54 (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
Infections and infestations			
perirectal abscess			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 51 (0.00%)	0 / 54 (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
pneumonia			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	2 / 51 (3.92%)	0 / 54 (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
urosepsis			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 51 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
lactic acidosis			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 51 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	LY 1mg	LY 5mg	LY 10mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 52 (32.69%)	29 / 55 (52.73%)	32 / 51 (62.75%)
Investigations			
amylase increased			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	2 / 55 (3.64%)	4 / 51 (7.84%)
occurrences (all)	0	3	7
lipase increased			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	1 / 52 (1.92%)	3 / 55 (5.45%)	4 / 51 (7.84%)
occurrences (all)	1	3	7
weight decreased			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	2 / 52 (3.85%)	2 / 55 (3.64%)	5 / 51 (9.80%)
occurrences (all)	2	2	5
Injury, poisoning and procedural complications			
contusion			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	3 / 55 (5.45%)	0 / 51 (0.00%)
occurrences (all)	0	3	0
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 52 (0.00%)	0 / 55 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	4 / 52 (7.69%)	2 / 55 (3.64%)	2 / 51 (3.92%)
occurrences (all)	4	2	2
headache			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	2 / 52 (3.85%)	2 / 55 (3.64%)	1 / 51 (1.96%)
occurrences (all)	2	2	1
Gastrointestinal disorders			

abdominal discomfort alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 55 (1.82%) 1	1 / 51 (1.96%) 2
abdominal distension alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	2 / 55 (3.64%) 2	5 / 51 (9.80%) 5
abdominal pain upper alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 55 (1.82%) 1	0 / 51 (0.00%) 0
constipation alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	2 / 55 (3.64%) 2	6 / 51 (11.76%) 6
diarrhoea alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	7 / 52 (13.46%) 13	13 / 55 (23.64%) 17	12 / 51 (23.53%) 13
dyspepsia alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 55 (1.82%) 2	6 / 51 (11.76%) 7
nausea alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 2	11 / 55 (20.00%) 17	11 / 51 (21.57%) 13
vomiting alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 2	4 / 55 (7.27%) 8	8 / 51 (15.69%) 9
Respiratory, thoracic and mediastinal disorders			

cough alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	1 / 55 (1.82%) 1	0 / 51 (0.00%) 0
Infections and infestations			
bronchitis alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	1 / 55 (1.82%) 1	3 / 51 (5.88%) 3
influenza alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 2	2 / 55 (3.64%) 2	4 / 51 (7.84%) 4
nasopharyngitis alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 2	3 / 55 (5.45%) 3	2 / 51 (3.92%) 5
upper respiratory tract infection alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	3 / 55 (5.45%) 3	2 / 51 (3.92%) 3
urinary tract infection alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 2	2 / 55 (3.64%) 2	1 / 51 (1.96%) 1
Metabolism and nutrition disorders			
decreased appetite alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 2	11 / 55 (20.00%) 12	13 / 51 (25.49%) 14

Non-serious adverse events	LY 15mg	Placebo	Dula 1.5mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 53 (73.58%)	17 / 51 (33.33%)	31 / 54 (57.41%)
Investigations			

<p>amylase increased</p> <p>alternative dictionary used: MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 53 (1.89%)</p> <p>3</p>	<p>1 / 51 (1.96%)</p> <p>1</p>	<p>0 / 54 (0.00%)</p> <p>0</p>
<p>lipase increased</p> <p>alternative dictionary used: MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 53 (3.77%)</p> <p>3</p>	<p>1 / 51 (1.96%)</p> <p>1</p>	<p>1 / 54 (1.85%)</p> <p>1</p>
<p>weight decreased</p> <p>alternative dictionary used: MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 53 (3.77%)</p> <p>2</p>	<p>0 / 51 (0.00%)</p> <p>0</p>	<p>0 / 54 (0.00%)</p> <p>0</p>
<p>Injury, poisoning and procedural complications</p> <p>contusion</p> <p>alternative dictionary used: MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 53 (0.00%)</p> <p>0</p>	<p>2 / 51 (3.92%)</p> <p>2</p>	<p>1 / 54 (1.85%)</p> <p>1</p>
<p>Vascular disorders</p> <p>hypertension</p> <p>alternative dictionary used: MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 53 (1.89%)</p> <p>1</p>	<p>1 / 51 (1.96%)</p> <p>1</p>	<p>3 / 54 (5.56%)</p> <p>3</p>
<p>Nervous system disorders</p> <p>dizziness</p> <p>alternative dictionary used: MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>headache</p> <p>alternative dictionary used: MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>5 / 53 (9.43%)</p> <p>5</p> <p>5 / 53 (9.43%)</p> <p>5</p>	<p>2 / 51 (3.92%)</p> <p>3</p> <p>2 / 51 (3.92%)</p> <p>2</p>	<p>1 / 54 (1.85%)</p> <p>1</p> <p>1 / 54 (1.85%)</p> <p>1</p>
<p>Gastrointestinal disorders</p> <p>abdominal discomfort</p> <p>alternative dictionary used: MedDRA 21.0</p>			

subjects affected / exposed	4 / 53 (7.55%)	2 / 51 (3.92%)	0 / 54 (0.00%)
occurrences (all)	7	2	0
abdominal distension			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	4 / 53 (7.55%)	1 / 51 (1.96%)	3 / 54 (5.56%)
occurrences (all)	4	1	3
abdominal pain upper			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	3 / 53 (5.66%)	1 / 51 (1.96%)	1 / 54 (1.85%)
occurrences (all)	3	1	1
constipation			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	2 / 53 (3.77%)	0 / 51 (0.00%)	3 / 54 (5.56%)
occurrences (all)	2	0	3
diarrhoea			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	17 / 53 (32.08%)	2 / 51 (3.92%)	9 / 54 (16.67%)
occurrences (all)	23	2	12
dyspepsia			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	2 / 53 (3.77%)	0 / 51 (0.00%)	2 / 54 (3.70%)
occurrences (all)	2	0	2
nausea			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	21 / 53 (39.62%)	3 / 51 (5.88%)	16 / 54 (29.63%)
occurrences (all)	29	3	22
vomiting			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	14 / 53 (26.42%)	1 / 51 (1.96%)	5 / 54 (9.26%)
occurrences (all)	20	1	6
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 21.0			

subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 3	1 / 51 (1.96%) 1	1 / 54 (1.85%) 1
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	0 / 53 (0.00%)	3 / 51 (5.88%)	2 / 54 (3.70%)
occurrences (all)	0	4	2
influenza			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	1 / 53 (1.89%)	1 / 51 (1.96%)	2 / 54 (3.70%)
occurrences (all)	1	1	2
nasopharyngitis			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	3 / 53 (5.66%)	2 / 51 (3.92%)	6 / 54 (11.11%)
occurrences (all)	6	3	6
upper respiratory tract infection			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	1 / 53 (1.89%)	3 / 51 (5.88%)	4 / 54 (7.41%)
occurrences (all)	1	3	5
urinary tract infection			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	4 / 53 (7.55%)	0 / 51 (0.00%)	0 / 54 (0.00%)
occurrences (all)	4	0	0
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	10 / 53 (18.87%)	1 / 51 (1.96%)	3 / 54 (5.56%)
occurrences (all)	13	1	3

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