Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study With an Open-Label Extension Assessing the Efficacy, Safety, and Pharmacokinetics/Pharmacodynamics of Tirzepatide in Pediatric and Adolescent Participants With Type 2 Diabetes Mellitus Inadequately Controlled With Metformin, or Basal Insulin, or Both.

Summary

EudraCT number	2021-003612-31
Trial protocol	IT FR
Global end of trial date	28 January 2025

Results information

Result version number	v1 (current)
This version publication date	21 August 2025
First version publication date	21 August 2025

Trial information

Trial identification

Sponsor protocol code	I8F-MC-GPGV

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05260021
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17121

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	illy Corporate Center, Indianapolis, IN, United States, 46285-0001
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly, EU_Lilly_Clinical_Trials@lilly.com
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559, EU_Lilly_Clinical_Trials@lilly.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 January 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 July 2024
Global end of trial reached?	Yes
Global end of trial date	28 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to learn more about the safety and efficacy of tirzepatide compared to placebo in children or teenagers with type 2 diabetes taking metformin, or basal insulin, or both. The overall study will last about 60 weeks with up to 14 clinic visits and 6 phone visits. Clinic visits will include blood sample collection, physical exam and questionnaire.

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	13 April 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Brazil: 16
Country: Number of subjects enrolled	India: 6
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Mexico: 31
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 32
Worldwide total number of subjects	99
EEA total number of subjects	3

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)	5
Adolescents (12-17 years)	94
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Not applicable

Period 1

Period 1 title	Double-blind 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	5 Milligram (mg) Tirzepatide

Arm description:

Participants received 5 mg Tirzepatide once weekly (QW) administered as subcutaneous (SC) injection via single-dose pen (SDP) for 30 weeks in double-blind period.

Arm type	Experimental
Investigational medicinal product name	Tirzepatide
Investigational medicinal product code	LY3298176
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 5 mg Tirzepatide QW administered as SC injection via SDP for 30 weeks in double-blind period.

Arm title	10 mg Tirzepatide

Arm description:

Participants received 10 mg Tirzepatide QW administered as SC injection via SDP for 30 weeks in double-blind period.

Arm type	Experimental
Investigational medicinal product name	Tirzepatide
Investigational medicinal product code	LY3298176
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 10 mg Tirzepatide QW administered as SC injection via SDP for 30 weeks in double-blind period.

Arm title	Placebo

Arm description:

Participants received placebo QW administered as SC injection via SDP for 30 weeks in double-blind period.

Arm type	Experimental

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

Dosage and administration details:

Participants received placebo QW administered as SC injection via SDP for 30 weeks in double-blind period.

Number of subjects in period 1	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Placebo
Started	32	33	34
Received at Least 1 Dose of Study Drug	32	33	34
Completed	29	29	32
Not completed	3	4	2
Consent withdrawn by subject	1	2	1
Adverse event, non-fatal	2	-	-
Withdrawal due to Caregiver Circumstances	-	1	-
Sponsor-Terminated Enrollment Error	-	1	-
Lost to follow-up	-	-	1

Period 2

Period 2 title	Open-label Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	5 mg Tirzepatide

Arm description:

Participants received 5 mg Tirzepatide QW administered as SC injection via SDP for 22 weeks in open-label period

Arm type	Experimental
Investigational medicinal product name	Tirzepatide
Investigational medicinal product code	LY3298176
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 5 mg Tirzepatide QW administered as SC injection via SDP for 22 weeks in open-label period.

Arm title	10 mg Tirzepatide

Arm description:

Participants received 10 mg Tirzepatide QW administered as SC injection via SDP for 22 weeks in open-label period

Arm type	Experimental
Investigational medicinal product name	Tirzepatide
Investigational medicinal product code	LY3298176
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 10 mg Tirzepatide QW administered as SC injection via SDP for 22 weeks in open-label period

Arm title	5 mg Tirzepatide

Arm description:

Participants received placebo QW administered as SC injection via SDP for 30 weeks in double-blind period and 5 mg Tirzepatide QW administered as SC injection via SDP for 22 weeks in open-label period.

Arm type	Experimental
Investigational medicinal product name	Tirzepatide
Investigational medicinal product code	LY3298176
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

articipants received placebo QW administered as SC injection via SDP for 30 weeks in double-blind period and 5 mg Tirzepatide QW administered as SC injection via SDP for 22 weeks in open-label period.

Number of subjects in period 2	5 mg Tirzepatide	10 mg Tirzepatide	5 mg Tirzepatide
Started	29	29	32
Completed	29	29	32

Baseline characteristics

Reporting groups	
Reporting group title	5 Milligram (mg) Tirzepatide
Reporting group description:	
Participants received 5 mg Tirzepatide once weekly (QW) administered as subcutaneous (SC) injection via single-dose pen (SDP) for 30 weeks in double-blind period.	
Reporting group title	10 mg Tirzepatide
Reporting group description:	
Participants received 10 mg Tirzepatide QW administered as SC injection via SDP for 30 weeks in double-blind period.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo QW administered as SC injection via SDP for 30 weeks in double-blind period.	

Reporting group values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Placebo
Number of subjects	32	33	34
Age categorical			
Units: Subjects			
Age continuous			
All randomized participants.			
Units: years			
arithmetic mean	15.00	14.60	14.60
standard deviation	± 1.93	± 1.83	± 1.79
Gender categorical			
All randomized participants.			
Units: Subjects			
Female	21	18	21
Male	11	15	13
Ethnicity (NIH/OMB)			
All randomized participants.			
Units: Subjects			
Hispanic or Latino	24	17	24
Not Hispanic or Latino	8	16	9
Unknown or Not Reported	0	0	1
Race (NIH/OMB)			
All randomized participants.			
Units: Subjects			
American Indian or Alaska Native	7	5	8
Asian	1	2	3
Native Hawaiian or Other Pacific Islander	1	2	0
Black or African American	5	4	2
White	17	19	21
More than one race	1	1	0
Unknown or Not Reported	0	0	0
Region of Enrollment			
All randomized participants.			

Units: Subjects			
Australia	1	1	0
Brazil	8	5	3
India	1	2	3
Israel	1	4	3
Italy	0	2	1
Mexico	10	8	13
United Kingdom	0	0	1
United States	11	11	10
Percentage of Hemoglobin A1c (HbA1c) at Baseline			
HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time.			
Units: Percentage of HbA1c			
arithmetic mean	8.22	7.89	8.02
standard deviation	± 1.17	± 1.22	± 1.30

Reporting group values	Total		
Number of subjects	99		
Age categorical			
Units: Subjects			
Age continuous			
All randomized participants.			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
All randomized participants.			
Units: Subjects			
Female	60		
Male	39		
Ethnicity (NIH/OMB)			
All randomized participants.			
Units: Subjects			
Hispanic or Latino	65		
Not Hispanic or Latino	33		
Unknown or Not Reported	1		
Race (NIH/OMB)			
All randomized participants.			
Units: Subjects			
American Indian or Alaska Native	20		
Asian	6		
Native Hawaiian or Other Pacific Islander	3		
Black or African American	11		
White	57		
More than one race	2		
Unknown or Not Reported	0		
Region of Enrollment			
All randomized participants.			
Units: Subjects			

Australia	2		
Brazil	16		
India	6		
Israel	8		
Italy	3		
Mexico	31		
United Kingdom	1		
United States	32		
Percentage of Hemoglobin A1c (HbA1c) at Baseline			
HbA1c is the glycosylated fraction of hemoglobin A. 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	5 Milligram (mg) Tirzepatide
Reporting group description:	
Participants received 5 mg Tirzepatide once weekly (QW) administered as subcutaneous (SC) injection via single-dose pen (SDP) for 30 weeks in double-blind period.	
Reporting group title	10 mg Tirzepatide
Reporting group description:	
Participants received 10 mg Tirzepatide QW administered as SC injection via SDP for 30 weeks in double-blind period.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo QW administered as SC injection via SDP for 30 weeks in double-blind period.	
Reporting group title	5 mg Tirzepatide
Reporting group description:	
Participants received 5 mg Tirzepatide QW administered as SC injection via SDP for 22 weeks in open-label period	
Reporting group title	10 mg Tirzepatide
Reporting group description:	
Participants received 10 mg Tirzepatide QW administered as SC injection via SDP for 22 weeks in open-label period	
Reporting group title	5 mg Tirzepatide
Reporting group description:	
Participants received placebo QW administered as SC injection via SDP for 30 weeks in double-blind period and 5 mg Tirzepatide QW administered as SC injection via SDP for 22 weeks in open-label period.	
Subject analysis set title	Pooled doses of Tirzepatide (5mg/10mg)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants received either 5 mg or 10 mg Tirzepatide QW administered as SC injection via SDP for 30 weeks in double-blind period.	
Subject analysis set title	Placebo/5 mg Tirzepatide
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received placebo QW administered as SC injection via SDP for 30 weeks in double-blind period were administered with 5 mg Tirzepatide QW administered as SC injection via SDP for 22 weeks in open-label period.	
Subject analysis set title	5 mg Tirzepatide
Subject analysis set type	Full analysis
Subject analysis set description:	
5 mg Tirzepatide/5 mg Tirzepatide: Participants received 5 mg Tirzepatide QW administered as SC injection via SDP for 30 weeks in double-blind period and 22 weeks in open-label period with an additional 4 weeks of safety follow-up. Placebo/5 mg Tirzepatide: Participants received placebo QW administered as SC injection via SDP for 30 weeks in double-blind period and 5 mg Tirzepatide QW administered as SC injection via SDP for 22 weeks in open-label period.	

Primary: Change From Baseline in Hemoglobin A1c (HbA1c) (Pooled Doses of Tirzepatide 5 mg and 10 mg)

End point title	Change From Baseline in Hemoglobin A1c (HbA1c) (Pooled Doses of Tirzepatide 5 mg and 10 mg)[1]
End point description:	
HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time. Least Squares (LS) mean was determined by ANCOVA model for endpoint measures: Variable = Baseline + Baseline Antihyperglycemic medication	

+ Baseline Age group + Treatment (Type III sum of squares)
(APD): All randomized participants who received at least one dose of study drug and had evaluable data for this outcome obtained during the double-blind period regardless of adherence to study intervention or initiation of rescue antihyperglycemic medication. This analysis was planned to measure the outcome by combining the 5 mg tirzepatide treatment arm and 10 mg tirzepatide treatment arm as pooled doses of tirzepatide (5 mg/10 mg).

End point type	Primary

End point timeframe:

Baseline, Week 30

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: No inferential statistics was performed for this event.

End point values	Placebo	Pooled doses of Tirzepatide (5mg/10mg)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	32	56		
Units: percentage of HbA1c				
least squares mean (standard error)	-0.23 (± 0.229)	-2.03 (± 0.165)		

Statistical analyses

Statistical analysis title	Statistical Analysis

Statistical analysis description:

Pooled doses of Tirzepatide (5mg/10mg), Placebo

Comparison groups	Placebo v Pooled doses of Tirzepatide (5mg/10mg)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.35
upper limit	-1.25

Secondary: Change From Baseline in HbA1c (Individual Doses)

End point title	Change From Baseline in HbA1c (Individual Doses)

End point description:

HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time. LS mean was determined by ANCOVA model for endpoint measures: Variable = Baseline + Baseline Antihyperglycemic medication + Baseline Age group + Treatment (Type III sum of squares).
APD: All randomized participants who received at least one dose of study drug and had evaluable data

for this outcome obtained during the double-blind period regardless of adherence to study intervention or initiation of rescue antihyperglycemic medication.

End point type	Secondary

End point timeframe:

Baseline, Week 30

End point values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	27	32	
Units: percentage of HbA1c				
least squares mean (standard error)	-1.90 (± 0.236)	-2.16 (± 0.232)	-0.23 (± 0.229)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: 5 mg Tirzepatide, Placebo	
Comparison groups	Placebo v 5 Milligram (mg) Tirzepatide
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.31
upper limit	-1.02

Statistical analysis title	Statistical analysis 2
Statistical analysis description: 10 mg Tirzepatide, Placebo	
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-1.93

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.57
upper limit	-1.29

Secondary: Percentage of Participants Who Achieve ≤6.5% of HbA1c

End point title	Percentage of Participants Who Achieve ≤6.5% of HbA1c

End point description:

HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time. Imputed data includes observed value and imputed value if the endpoint measure is missing.
Imputed data includes observed value and imputed value if the endpoint measure is missing.
APD: All randomized participants who received at least one dose of study drug and had evaluable data for this outcome obtained during the double-blind period regardless of adherence to study intervention or initiation of rescue antihyperglycemic medication.

End point type	Secondary

End point timeframe:

Week 30

End point values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Placebo	Pooled doses of Tirzepatide (5mg/10mg)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	32	33	34	65
Units: percentage of participants				
number (not applicable)	66.4	80.6	28.2	73.6

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

5 mg Tirzepatide, Placebo

Comparison groups	Placebo v 5 Milligram (mg) Tirzepatide
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	40.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.6
upper limit	61.7

Statistical analysis title	Statistical analysis 2
Statistical analysis description: 10 mg Tirzepatide, Placebo	
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	51.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.1
upper limit	72.2

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Pooled doses of Tirzepatide (5 mg/10 mg), Placebo	
Comparison groups	Placebo v Pooled doses of Tirzepatide (5mg/10mg)
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	45.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	27.5
upper limit	64.1

Secondary: Change From Baseline in Body Mass Index (BMI) Standard Deviation Score (Age and Sex-matched)

End point title	Change From Baseline in Body Mass Index (BMI) Standard Deviation Score (Age and Sex-matched)

End point description:

BMI SDS (age and sex matched), calculated using the World Health Organization (WHO) growth reference standards. BMI is calculated as weight in kilograms divided by height in meters squared (kg/m^2) and converted to a Z-score (SDS) based on WHO reference data. A Z-score of 0 represents the population mean for a given age and sex. A BMI SDS between -1 and +1 is considered normal. Obesity is defined as BMI SDS > +2. Reductions in BMI SDS indicate improvement in weight status for individuals with obesity.

LS mean was determined by ANCOVA model for endpoint measures: Variable = Baseline + Baseline Antihyperglycemic medication + Baseline Age group + Treatment (Type III sum of squares)
APD: All randomized participants who received at least one dose of study drug and had evaluable data for this outcome obtained during the double-blind period regardless of adherence to the study intervention or initiation of rescue antihyperglycemic medication.

End point type	Secondary

End point timeframe:

Baseline, Week 30

End point values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Placebo	Pooled doses of Tirzepatide (5mg/10mg)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	29	29	34	58
Units: Z-score				
least squares mean (standard error)	-0.45 (± 0.072)	-0.76 (± 0.072)	-0.09 (± 0.069)	-0.60 (± 0.050)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

5 mg Tirzepatide, Placebo

Comparison groups	5 Milligram (mg) Tirzepatide v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	-0.16

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

10 mg Tirzepatide, Placebo

Comparison groups	Placebo v 10 mg Tirzepatide

Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	-0.47

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Pooled doses of Tirzepatide (5 mg/10 mg), Placebo	
Comparison groups	Placebo v Pooled doses of Tirzepatide (5mg/10mg)
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	-0.34

Secondary: Percentage of Participants Who Achieve <7.0% of HbA1c

End point title	Percentage of Participants Who Achieve <7.0% of HbA1c

End point description:

HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time. Imputed data includes observed value and imputed value if the endpoint measure is missing. Imputed data includes observed value and imputed value if the endpoint measure is missing.
APD: All randomized participants who received at least one dose of study drug and had evaluable data for this outcome obtained during the double-blind period regardless of adherence to the study intervention or initiation of rescue antihyperglycemic medication.

End point type	Secondary

End point timeframe:

Week 30

End point values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Placebo	Pooled doses of Tirzepatide (5mg/10mg)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	32	33	34	65
Units: percentage of participants				
number (not applicable)	79.6	84.5	37.4	82.1

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: 5mg Tirzepatide, Placebo	
Comparison groups	5 Milligram (mg) Tirzepatide v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	43.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.3
upper limit	64.4

Statistical analysis title	Statistical analysis 2
Statistical analysis description: 10 mg Tirzepatide, Placebo	
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	47.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	26.4
upper limit	67.7

Statistical analysis title	Statistical analysis 3

Statistical analysis description: Pooled doses of Tirzepatide (5 mg/10 mg), Placebo	
Comparison groups	Placebo v Pooled doses of Tirzepatide (5mg/10mg)
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	45.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	26.3
upper limit	64.1

Secondary: Change From Baseline in Fasting Serum Glucose (FSG)

End point title	Change From Baseline in Fasting Serum Glucose (FSG)
End point description: LS mean was determined by ANCOVA model for endpoint measures: Variable = Baseline + Baseline Antihyperglycemic medication + Baseline Age group + Treatment (Type III sum of squares). APD: All randomized participants who received at least one dose of study drug and had evaluable data for this outcome obtained during the double-blind period regardless of adherence to study intervention or initiation of rescue antihyperglycemic medication.	
End point type	Secondary
End point timeframe: Baseline, Week 30	

End point values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Placebo	Pooled doses of Tirzepatide (5mg/10mg)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	28	28	33	56
Units: milligram per deciliter (mg/dL)				
least squares mean (standard error)	-35.5 (± 7.76)	-50.6 (± 7.40)	-6.6 (± 7.36)	-43.0 (± 5.42)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: 5 mg Tirzepatide, Placebo	
Comparison groups	5 Milligram (mg) Tirzepatide v Placebo

Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-28.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.7
upper limit	-8

Statistical analysis title	Statistical analysis 2
Statistical analysis description: 10 mg Tirzepatide, Placebo	
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-64.3
upper limit	-23.6

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Pooled doses of Tirzepatide (5 mg/10 mg), Placebo	
Comparison groups	Placebo v Pooled doses of Tirzepatide (5mg/10mg)
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-36.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.2
upper limit	-18.6

Secondary: Percent Change from Baseline in BMI

End point title	Percent Change from Baseline in BMI

End point description:

LS mean was determined by ANCOVA model for endpoint measures: Variable = Baseline + Baseline Antihyperglycemic medication + Baseline Age group + Treatment (Type III sum of squares).
APD: All randomized participants who received at least one dose of study drug and had evaluable data for this outcome obtained during the double-blind period regardless of adherence to study intervention or initiation of rescue antihyperglycemic medication.

End point type	Secondary

End point timeframe:

Baseline, Week 30

End point values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Placebo	Pooled doses of Tirzepatide (5mg/10mg)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	29	29	34	58
Units: Percent Change of BMI				
least squares mean (standard error)	-6.73 (± 1.155)	-11.07 (± 1.154)	-0.55 (± 1.107)	-8.90 (± 0.808)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

5 mg Tirzepatide, Placebo

Comparison groups	5 Milligram (mg) Tirzepatide v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-6.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.31
upper limit	-3.05

Statistical analysis title	Statistical analysis 2

Statistical analysis description:	
10 mg Tirzepatide, Placebo	
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-10.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.67
upper limit	-7.38

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Pooled doses of Tirzepatide (5 mg/10 mg), Placebo	
Comparison groups	Placebo v Pooled doses of Tirzepatide (5mg/10mg)
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-8.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.05
upper limit	-5.66

Secondary: Percent Change From Baseline for Serum Lipid Levels

End point title	Percent Change From Baseline for Serum Lipid Levels

End point description:

Geometric LS mean was determined by the MMRM model for post-baseline measures: log(Actual Measurement/Baseline) = log(Baseline) + Baseline Antihyperglycemic medication + Baseline Age group + Treatment + Time + Treatment*Time (Type III sum of squares). Variance-Covariance structure (Change from Baseline) = Unstructured. APD:All randomized participants who received at least one dose of study drug and had evaluable data for this outcome obtained during the double-blind period regardless of adherence to study intervention or initiation of rescue antihyperglycemic medication.

End point type	Secondary

End point timeframe:

Baseline, Week 30

End point values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Placebo	Pooled doses of Tirzepatide (5mg/10mg)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	27	28	32	55
Units: Percent change				
least squares mean (standard error)				
Serum Cholesterol	-8.07 (± 2.319)	-13.82 (± 2.115)	5.07 (± 2.456)	-10.99 (± 1.564)
Serum HDL Cholesterol 3RD generation, enzymatic	5.56 (± 3.269)	1.72 (± 3.087)	0.92 (± 2.887)	3.62 (± 2.247)
Serum Triglycerides	-27.6 (± 4.816)	-35.8 (± 4.165)	-1.74 (± 6.022)	-31.8 (± 3.165)
Serum LDL Cholesterol Combined	-6.08 (± 3.870)	-11.97 (± 3.540)	9.84 (± 4.185)	-9.07 (± 2.618)
Serum VLDL Cholesterol Combined	-25.9 (± 5.005)	-34.8 (± 4.293)	-0.26 (± 6.211)	-30.5 (± 3.276)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieve <5.7% of HbA1c

End point title	Percentage of Participants Who Achieve <5.7% of HbA1c

End point description:

HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time. Imputed data includes observed value and imputed value if endpoint measure is missing. Imputed data includes observed value and imputed value if endpoint measure is missing.
APD: All randomized participants who received at least one dose of study drug and had evaluable data for this outcome obtained during the double-blind period regardless of adherence to study intervention or initiation of rescue antihyperglycemic medication.

End point type	Secondary

End point timeframe:

Baseline, Week 30

End point values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Placebo	Pooled doses of Tirzepatide (5mg/10mg)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	32	33	34	65
Units: percentage of participants				
number (not applicable)	44.1	56.2	15.9	50.2

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: 5 mg Tirzepatide, Placebo	
Comparison groups	5 Milligram (mg) Tirzepatide v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	29.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.6
upper limit	50.3

Statistical analysis title	Statistical analysis 2
Statistical analysis description: 10 mg Tirzepatide, Placebo	
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	39.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.8
upper limit	60.2

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Pooled doses of Tirzepatide (5 mg/10 mg), Placebo	
Comparison groups	Placebo v Pooled doses of Tirzepatide (5mg/10mg)
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	34.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	17
upper limit	52.1

Secondary: Change From Baseline in Height Standard Deviation Score (SDS)

End point title	Change From Baseline in Height Standard Deviation Score (SDS)

End point description:

Height SDS (age and sex-matched), calculated using the World Health Organization (WHO) growth reference standards. Height SDS is derived by comparing a child's height to the median height for their age and sex in the WHO reference population, then expressing the difference in standard deviation units (Z-scores). A Z-score of 0 represents the population mean. A Height SDS below -2 indicates short stature. Positive changes in Height SDS from baseline reflect improvement in growth velocity or catch-up growth.
LS mean was determined by MMRM model for post-baseline measures: Variable = Baseline + Baseline Age group + Baseline Antihyperglycemic medication + Treatment + Time + Treatment*Time(Type III sum of squares). Variance-Covariance structure (Actual Value) = Unstructured. Variance-Covariance structure (Change from Baseline) = Unstructured
APD: randomized participants who received atleast one dose of study drug and had evaluable PK data.

End point type	Secondary

End point timeframe:

Baseline, Week 30

End point values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Placebo	Pooled doses of Tirzepatide (5mg/10mg)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	29	29	34	58
Units: SDS				
least squares mean (standard error)	-0.092 (± 0.0275)	-0.11 (± 0.0274)	-0.11 (± 0.0259)	-0.100 (± 0.0194)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

5 mg Tirzepatide, Placebo

Comparison groups	5 Milligram (mg) Tirzepatide v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.708
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	0.014

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.061
upper limit	0.089

Statistical analysis title	Statistical analysis 2
Statistical analysis description: 10 mg Tirzepatide, Placebo	
Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.976
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.001
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.076
upper limit	0.074

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Pooled doses of Tirzepatide (5 mg/10 mg), Placebo	
Comparison groups	Placebo v Pooled doses of Tirzepatide (5mg/10mg)
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.841
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	0.007
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.058
upper limit	0.071

Secondary: Change From Baseline in Weight SDS

End point title	Change From Baseline in Weight SDS

End point description:

Weight SDS, calculated using Centers for Disease Control and Prevention (CDC) growth reference

standards. Weight SDS is derived by comparing a child's weight to median weight for their age and sex in the CDC reference population, then expressing the difference in standard deviation units (Z-scores). A Z-score of 0 represents the population mean for a given age and sex. A Weight SDS below -2 may indicate underweight status, while a Weight SDS above +2 may indicate overweight or obesity. Change from baseline Weight SDS reflects shifts in growth trajectory, with positive changes indicating weight gain and negative changes indicating weight reduction.
LS mean was determined by MMRM model for post-baseline measures: Variable = Baseline + Baseline Age group + Baseline Antihyperglycemic medication + Treatment + Time + Treatment*Time(Type III sum of squares). Variance-Covariance structure (Actual Value) = Unstructured. Variance-Covariance structure (Change from Baseline) = Unstructured

End point type	Secondary

End point timeframe:

Baseline, Week 30
APD: All randomized participants who received at least one dose of study drug and had data for this outcome obtained during the double-blind period regardless of adherence to study drug or initiation of rescue antihyperglycemic drug.

End point values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Placebo	Pooled doses of Tirzepatide (5mg/10mg)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	29	29	34	58
Units: Z-score				
least squares mean (standard error)	-0.38 (± 0.0600)	-0.50 (± 0.0594)	-0.099 (± 0.0570)	-0.44 (± 0.0422)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

5 mg Tirzepatide, Placebo

Comparison groups	5 Milligram (mg) Tirzepatide v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	-0.12

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

10 mg Tirzepatide, Placebo

Comparison groups	Placebo v 10 mg Tirzepatide
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	-0.24

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Pooled doses of Tirzepatide (5mg/10 mg), Placebo	
Comparison groups	Placebo v Pooled doses of Tirzepatide (5mg/10mg)
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	-0.2

Secondary: Change From Baseline in PedsQL Generic Core Scale

End point title	Change From Baseline in PedsQL Generic Core Scale[2]

End point description:

The PedsQL Measurement Model measures health-related quality of life (HRQOL) in children (ages 8 to 12) and teenagers (ages 13 to 18). The 23-item PedsQL Generic Core Scale includes physical, emotional, social, and school functioning dimensions. The PedsQL Generic Core yields two summary scores: Physical Summary and Psychosocial Summary. Scores are transformed on a 0-100 scale, with higher scores indicating better functioning. Each item is scored from 0 (never) to 4 (almost always). Items are reverse scored and linearly transformed to a 0-100 scale so that higher scores indicate better HRQOL; the total score therefore ranges from 0 (worst) to 100 (best). Higher scores indicate better health-related quality of life. LS mean was determined by the MMRM model for post-baseline measures: Variable = Baseline + Baseline Antihyperglycemic Medication + Baseline Age Group + Treatment + Time + Treatment*Time (Type III sum of squares). Variance-Covariance structure (Actual Value) = Unstructured.

End point type	Secondary

End point timeframe:

Baseline, Week 52

Notes:

[2] - 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: No inferential statistics was performed for this event.

End point values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Pooled doses of Tirzepatide (5mg/10mg)	Placebo/5 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	29	27	56	26
Units: score on a scale				
least squares mean (standard error)				
Physical Functioning Score	4.26 (± 2.034)	3.06 (± 2.092)	3.66 (± 1.456)	5.03 (± 2.142)
Emotional Functioning Score	4.35 (± 3.506)	4.11 (± 3.601)	4.23 (± 2.514)	6.78 (± 3.705)
Social Functioning Score	4.16 (± 2.628)	3.00 (± 2.696)	3.58 (± 1.878)	4.54 (± 2.764)
School Functioning Score	13.30 (± 3.095)	0.18 (± 3.152)	6.74 (± 2.197)	12.03 (± 3.239)
Psychosocial Health Summary Score	7.82 (± 2.482)	2.20 (± 2.533)	5.01 (± 1.767)	7.47 (± 2.605)
Physical Health Summary Score	4.26 (± 2.034)	3.06 (± 2.092)	3.66 (± 1.456)	5.03 (± 2.142)
Total Score	6.65 (± 2.114)	2.45 (± 2.163)	4.55 (± 1.507)	6.61 (± 2.220)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline PedsQL (3.2) Diabetic Module

End point title	Change From Baseline PedsQL (3.2) Diabetic Module[3]

End point description:

The PedsQL 3.2 Diabetes Module has 33 items for ages 13 to 45 years and 32 items (1 less item for the Worry Scale) for ages 2 to 12 years. The 5 dimensions consist of diabetes symptoms, treatment barriers, treatment adherence, worry and communication. Scores range from 0 to 100. Higher scores indicate fewer problems. LS mean was determined by MMRM model for post-baseline measures: Variable = Baseline + Baseline Antihyperglycemic medication + Baseline Age group + Treatment + Time + Treatment*Time(Type III sum of squares). Variance-Covariance structure (Actual Value) = Unstructured. Variance- Covariance structure (Change from Baseline) = Unstructured.
APD:All randomized participants who received at least one dose of study drug and had evaluable data for this outcome obtained during the double-blind, open-label, and safety follow-up periods regardless of adherence to study intervention or initiation of rescue antihyperglycemic medication.

End point type	Secondary

End point timeframe:

Baseline, Week 52

Notes:

[3] - 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: No inferential statistics was performed for this event.

End point values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide	Pooled doses of Tirzepatide (5mg/10mg)	Placebo/5 mg Tirzepatide
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	29	27	56	25
Units: score on a scale				
least squares mean (standard error)				
Diabetes Management Summary Score	7.21 (± 2.669)	8.60 (± 2.733)	7.90 (± 1.907)	5.25 (± 2.872)
Total Score	8.79 (± 2.310)	8.74 (± 2.374)	8.76 (± 1.657)	6.03 (± 2.489)

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Area Under the Concentration Curve (AUC), Steady State (ss) of Tirzepatide

End point title	Pharmacokinetics (PK): Area Under the Concentration Curve (AUC), Steady State (ss) of Tirzepatide[4]

End point description:

PK: AUCss of Tirzepatide
APD:All randomized participants who received at least one dose of study drug and had evaluable PK data obtained during the double-blind period regardless of adherence to study intervention or initiation of rescue antihyperglycemic medication.

End point type	Secondary

End point timeframe:

Week 0: after the first dose anytime on the same day. Weeks 7, 16, and 29: 1 to 24 hours, 24 to 96 hours, or 120 to 168 hours post-dose, as assigned by IWRS.

Notes:

[4] - 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: No inferential statistics was performed for this event.

End point values	5 Milligram (mg) Tirzepatide	10 mg Tirzepatide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: nanogram*hour per milliliter (ng*hr/mL)				
geometric mean (confidence interval 95%)	92100 (85700 to 98600)	184000 (171000 to 197000)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline Up to Week 56

Adverse event reporting additional description:

All randomized participants who received at least one dose of study drug regardless of adherence to study intervention or initiation of rescue antihyperglycemic medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	TZP 5mg / Double-Blind Period

Reporting group description:

Participants received 5 mg of tirzepatide QW administered as SC injection via SDP for 30 weeks in a double-blind period.

Reporting group title	TZP 10mg / Double-Blind Period

Reporting group description:

Participants received 10 mg of tirzepatide QW administered as SC injection via SDP for 30 weeks in a double-blind period.

Reporting group title	Placebo / Double-Blind Period

Reporting group description:

Participants received placebo QW administered as SC injection via SDP for 30 weeks in a double-blind period.

Reporting group title	Placebo/TZP 5mg/ Open-Label and Safety Follow-Up Period

Reporting group description:

Participants who received placebo QW during the double-blind period were switched to 5 mg tirzepatide QW administered as SC injection via SDP for 22 weeks in the open-label period and 4 weeks in the safety follow-up period.

Reporting group title	TZP 5mg /5 mg Open-Label and Safety Follow-Up Period

Reporting group description:

Participants who received 5 mg tirzepatide during the double-blind period continued to receive 5 mg of tirzepatide QW administered as SC injection via SDP for 22 weeks in the open-label period and 4 weeks in the safety follow-up period.

Reporting group title	TZP 10mg /10 mg Open-Label and Safety Follow-Up Period

Reporting group description:

Participants who received 10 mg of tirzepatide during the double-blind period continued to receive 10 mg of tirzepatide QW administered as SC injection via SDP for 22 weeks in the open-label period and 4 weeks in the safety follow-up period.

Serious adverse events	TZP 5mg / Double-Blind Period	TZP 10mg / Double-Blind Period	Placebo / Double-Blind Period
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 32 (3.13%)	1 / 33 (3.03%)	1 / 34 (2.94%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Hepatobiliary disorders			
Cholecystitis			

alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 33 (0.00%)	0 / 34 (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
Psychiatric disorders			
borderline personality disorder			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 33 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
suicidal ideation			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 33 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
suicide attempt			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 33 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 33 (0.00%)	0 / 34 (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			
appendicitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 32 (3.13%)	0 / 33 (0.00%)	0 / 34 (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
mastoiditis			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	0 / 32 (0.00%)	1 / 33 (3.03%)	0 / 34 (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

Serious adverse events	Placebo/TZP 5mg/ Open-Label and Safety Follow-Up Period	TZP 5mg /5 mg Open-Label and Safety Follow-Up Period	TZP 10mg /10 mg Open-Label and Safety Follow-Up Period
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	1 / 33 (3.03%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Hepatobiliary disorders			
Cholecystitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 33 (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
Psychiatric disorders			
borderline personality disorder			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 33 (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
suicidal ideation			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 33 (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
suicide attempt			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 33 (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
mastoiditis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 33 (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	TZP 5mg / Double-Blind Period	TZP 10mg / Double-Blind Period	Placebo / Double-Blind Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 32 (53.13%)	19 / 33 (57.58%)	11 / 34 (32.35%)
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 32 (6.25%)	3 / 33 (9.09%)	1 / 34 (2.94%)
occurrences (all)	7	5	1
General disorders and administration site conditions			
injection site reaction			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	2 / 33 (6.06%)	0 / 34 (0.00%)
occurrences (all)	0	6	0
Pyrexia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 33 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	5 / 32 (15.63%)	1 / 33 (3.03%)	1 / 34 (2.94%)
occurrences (all)	5	1	1
abdominal pain upper			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 32 (6.25%)	4 / 33 (12.12%)	3 / 34 (8.82%)
occurrences (all)	18	4	4
nausea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	7 / 32 (21.88%)	6 / 33 (18.18%)	3 / 34 (8.82%)
occurrences (all)	27	7	3
diarrhoea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	8 / 32 (25.00%)	8 / 33 (24.24%)	2 / 34 (5.88%)
occurrences (all)	23	11	7
dyspepsia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 32 (6.25%)	4 / 33 (12.12%)	0 / 34 (0.00%)
occurrences (all)	2	5	0
vomiting			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	5 / 32 (15.63%)	4 / 33 (12.12%)	1 / 34 (2.94%)
occurrences (all)	7	24	1
Abdominal discomfort			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 33 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed[1]	0 / 21 (0.00%)	0 / 18 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal			

disorders			
oropharyngeal pain			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 32 (9.38%)	1 / 33 (3.03%)	2 / 34 (5.88%)
occurrences (all)	4	1	3
cough			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 32 (9.38%)	1 / 33 (3.03%)	1 / 34 (2.94%)
occurrences (all)	4	1	2
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 32 (3.13%)	2 / 33 (6.06%)	0 / 34 (0.00%)
occurrences (all)	2	2	0
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 32 (3.13%)	2 / 33 (6.06%)	2 / 34 (5.88%)
occurrences (all)	1	2	3
gastroenteritis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 33 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
tonsillitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 32 (6.25%)	0 / 33 (0.00%)	0 / 34 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 33 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
hyperglycaemia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 33 (0.00%)	5 / 34 (14.71%)
occurrences (all)	0	0	5

decreased appetite			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	4 / 33 (12.12%)	0 / 34 (0.00%)
occurrences (all)	0	5	0

Non-serious adverse events	Placebo/TZP 5mg/ Open-Label and Safety Follow-Up Period	TZP 5mg /5 mg Open-Label and Safety Follow-Up Period	TZP 10mg /10 mg Open-Label and Safety Follow-Up Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 32 (25.00%)	10 / 32 (31.25%)	7 / 33 (21.21%)
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 32 (3.13%)	3 / 32 (9.38%)	0 / 33 (0.00%)
occurrences (all)	1	4	0
General disorders and administration site conditions			
injection site reaction			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	1 / 33 (3.03%)
occurrences (all)	0	2	1
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
abdominal pain upper			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
nausea			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
diarrhoea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	6 / 32 (18.75%)	5 / 32 (15.63%)	1 / 33 (3.03%)
occurrences (all)	13	6	1
dyspepsia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
vomiting			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	2 / 33 (6.06%)
occurrences (all)	3	1	2
Abdominal discomfort			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed[1]	0 / 20 (0.00%)	2 / 21 (9.52%)	0 / 18 (0.00%)
occurrences (all)	0	8	0
Respiratory, thoracic and mediastinal disorders			
oropharyngeal pain			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	1 / 33 (3.03%)
occurrences (all)	0	2	3
cough			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			

anxiety			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	3 / 33 (9.09%)
occurrences (all)	1	3	3
gastroenteritis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
tonsillitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 32 (6.25%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	2	1	0
Metabolism and nutrition disorders			
hyperglycaemia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
decreased appetite			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender-specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

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