Clinical trial results:
An Exploratory Phase 2, Randomised, Double-blind, Placebo-controlled, and Open-label Active Comparator Study to Evaluate the Effect of MEDI0382 on Hepatic Glycogen Metabolism in Overweight and Obese Subjects with Type 2 Diabetes Mellitus

Summary

EudraCT number	2017-005081-22
Trial protocol	SE GB
Global end of trial date	26 August 2021

Results information

Result version number	v1
This version publication date	27 April 2022
First version publication date	27 April 2022

Trial information

Trial identification

Sponsor protocol code	D5670C00022

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca Clinical Study Information Center
Sponsor organisation address	One Medimmune Way, Gaithersburg, United States, 20878
Public contact	Medical Monitor, AstraZeneca Clinical Study Information Center, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Medical Monitor, AstraZeneca Clinical Study Information Center, +1 877-240-9479, information.center@astrazeneca.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	16 September 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of MEDI0382 on hepatic glycogen levels versus placebo after 28 days (Part A) and 35 days (Part B) of treatment

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).

Background therapy:

MEDI0382 is a synthetic peptide with both glucagon-like peptide-1 (GLP-1) and glucagon receptor agonist activity which is under development for the treatment of T2DM and non-alcoholic steatohepatitis (NASH). GLP-1 receptor agonists are established treatments for T2DM that improve glycaemic control, delay gastric emptying, and depress appetite leading to modest, but often non-sustained weight loss (typically 3% versus baseline at one year). Glucagon has similar effects to GLP-1 on gastric emptying and appetite, and has also been shown to promote increased energy expenditure (Lynch et al, 2014; Habegger et al, 2013). Oxyntomodulin, a naturally occurring peptide with GLP-1 and glucagon receptor co-agonist activity, has been shown to promote weight loss through effects on appetite and energy expenditure (Wynne et al, 2006) and co-infusion of GLP-1 and glucagon has synergistic effects on reducing food intake and promoting weight loss in human subjects (Bagger et al, 2015).

Evidence for comparator:

Liraglutide is an analog with 97% homology to human glucagon-like peptide (GLP-1) and acts as a GLP-1 receptor agonist. Several large, randomized, multicenter phase 3 trials evaluated the efficacy and safety of liraglutide by comparing monotherapy and combination therapy with other antidiabetic medications in adult patients with type 2 diabetes. The Liraglutide Effect and Action in Diabetes (LEAD) program demonstrated that liraglutide, when used alone or in combination with other antidiabetic medications, effectively controls hyperglycemia (glycosylated hemoglobin [A1C] reductions up to 1.6%) and assists patients in meeting established glycemic targets. Compared with certain other classes of antidiabetic agents, liraglutide is associated with a lower risk of hypoglycemia. Liraglutide has also been associated with weight loss (1.8 to 3.4 kg) and improved patient satisfaction and health-related quality of life.

Actual start date of recruitment	31 May 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 16
Country: Number of subjects enrolled	Sweden: 35
Worldwide total number of subjects	51
EEA total number of subjects	51

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)	21
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 51 participants (total for Part A [21 participants] and B [30 participants]) participated in the study from 31 May 2018 (date first participant enrolled) to 14 April 2021 (date of last participant last visit) at one site in Sweden for Part A, and 2 sites (one in Sweden and one in the Netherlands) for Part B.

Pre-assignment

Screening details:

A total of 95 participants consented to participate in the study (36 from Part A and 59 from Part B) from one site in Sweden for Part A, and 2 sites (one in Sweden and one in the Netherlands) for Part B. Of these, 15 participants from Part A and 29 participants from Part B were considered screen failures.

Pre-assignment period milestones

Number of subjects started	51
Number of subjects completed	51

Period 1

Period 1 title	Baseline period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	MEDI0382 (Part A)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Cotadutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

MEDI0382 100 µg for 7 days, followed by 200 µg for 7 days, followed by 300 µg for 14 days once daily in the morning via SC injection as

Arm title	Placebo (Part A)

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo for 28 days

Arm title	Liraglutide (Part B)

Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Victoza
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Open label liraglutide 0.6 mg for 7 days, followed by 1.2 mg for 7 days, followed by 1.8 mg for 21 days

Arm title	MEDI0382 (Part B)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Cotadutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

MEDI0382 50 µg for 7 days, followed by 100 µg for 7 days, followed by 200 µg for 7 days, followed by 300 µg for 14 days

Arm title	Placebo (Part B)
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo for 35 days

Number of subjects in period 1	MEDI0382 (Part A)	Placebo (Part A)	Liraglutide (Part B)
Started	12	9	10
Completed	12	9	10

Number of subjects in period 1	MEDI0382 (Part B)	Placebo (Part B)
Started	9	11
Completed	9	11

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	MEDI0382 (Part A)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Cotadutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

MEDI0382 100 µg for 7 days, followed by 200 µg for 7 days, followed by 300 µg for 14 days once daily in the morning via SC injection as

Arm title	Placebo (Part A)

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo for 28 days

Arm title	Liraglutide (Part B)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Victoza
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Open label liraglutide 0.6 mg for 7 days, followed by 1.2 mg for 7 days, followed by 1.8 mg for 21 days

Arm title	MEDI0382 (Part B)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Cotadutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

MEDI0382 50 µg for 7 days, followed by 100 µg for 7 days, followed by 200 µg for 7 days, followed by 300 µg for 14 days

Arm title	Placebo (Part B)
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo for 35 days

Number of subjects in period 2	MEDI0382 (Part A)	Placebo (Part A)	Liraglutide (Part B)
Started	12	9	10
Completed	12	9	10

Number of subjects in period 2	MEDI0382 (Part B)	Placebo (Part B)
Started	9	11
Completed	9	11

Baseline characteristics

Reporting groups	
Reporting group title	MEDI0382 (Part A)
Reporting group description: -	
Reporting group title	Placebo (Part A)
Reporting group description: -	
Reporting group title	Liraglutide (Part B)
Reporting group description: -	
Reporting group title	MEDI0382 (Part B)
Reporting group description: -	
Reporting group title	Placebo (Part B)
Reporting group description: -	

Reporting group values	MEDI0382 (Part A)	Placebo (Part A)	Liraglutide (Part B)
Number of subjects	12	9	10
Age Categorical Units: Subjects			
aged ≥ 18 years	12	9	10
Gender Categorical Units: Subjects			
Female	5	3	4
Male	7	6	6

Reporting group values	MEDI0382 (Part B)	Placebo (Part B)	Total
Number of subjects	9	11	51
Age Categorical Units: Subjects			
aged ≥ 18 years	9	11	51
Gender Categorical Units: Subjects			
Female	3	2	17
Male	6	9	34

Subject analysis sets	
Subject analysis set title	As-treated population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who received any study IP were included in the as-treated population and participants were analysed according to the treatment they actually received.	
Subject analysis set title	Intent-to-treat population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants who received any study IP were included in the ITT population and participants were analysed according to their randomised treatment group.	

Reporting group values	As-treated population	Intent-to-treat population	
Number of subjects	51	51	
Age Categorical Units: Subjects			
aged ≥ 18 years	51	51	
Gender Categorical Units: Subjects			
Female	17	17	
Male	34	34	

End points

End points reporting groups

Reporting group title	MEDI0382 (Part A)
Reporting group description: -	
Reporting group title	Placebo (Part A)
Reporting group description: -	
Reporting group title	Liraglutide (Part B)
Reporting group description: -	
Reporting group title	MEDI0382 (Part B)
Reporting group description: -	
Reporting group title	Placebo (Part B)
Reporting group description: -	
Reporting group title	MEDI0382 (Part A)
Reporting group description: -	
Reporting group title	Placebo (Part A)
Reporting group description: -	
Reporting group title	Liraglutide (Part B)
Reporting group description: -	
Reporting group title	MEDI0382 (Part B)
Reporting group description: -	
Reporting group title	Placebo (Part B)
Reporting group description: -	
Subject analysis set title	As-treated population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who received any study IP were included in the as-treated population and participants were analysed according to the treatment they actually received.	
Subject analysis set title	Intent-to-treat population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants who received any study IP were included in the ITT population and participants were analysed according to their randomised treatment group.	

Primary: Change in hepatic glycogen concentration adjusted for liver volume as measured by MRS at T = 4 hours post standardised morning meal from baseline (Day -1) to the end of 28 days of treatment (Part A only)

End point title	Change in hepatic glycogen concentration adjusted for liver volume as measured by MRS at T = 4 hours post standardised morning meal from baseline (Day -1) to the end of 28 days of treatment (Part A only)
End point description:	
To assess the effect of cotadutide on hepatic glycogen levels versus placebo after 28 days (Part A)	
End point type	Primary
End point timeframe:	
from baseline (Day -1) to the end of 28 days of treatment (Part A only)	

End point values	MEDI0382 (Part A)	Placebo (Part A)	Intent-to-treat population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	9	21[1]	
Units: mmol/L				
least squares mean (confidence interval 90%)				
Change from baseline	-100.2 (-150.2 to -50.1)	5.5 (-47.2 to 58.3)	-105.7 (-178.8 to -32.6)	

Notes:

[1] - Part A Only MEDI0382 (Part A) vs. Placebo (Part A)

Statistical analyses

Statistical analysis title	Primary Analysis (Part A)

Statistical analysis description:

To assess the effect of cotadutide on hepatic glycogen levels versus placebo after 28 days (Part A)

Comparison groups	MEDI0382 (Part A) v Placebo (Part A)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-105.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-178.8
upper limit	-32.6

Primary: Percentage change in fasting hepatic glycogen concentration adjusted for liver volume as measured by MRS at T = 24 hours post standardised morning meal from baseline (Day 1) to the end of 35 days of treatment (Day 36) (Part B)

End point title	Percentage change in fasting hepatic glycogen concentration adjusted for liver volume as measured by MRS at T = 24 hours post standardised morning meal from baseline (Day 1) to the end of 35 days of treatment (Day 36) (Part B)

End point description:

End point type	Primary

End point timeframe:

from baseline (Day 1) to the end of 35 days of treatment (Day 36) (Part B)

End point values	MEDI0382 (Part B)	Placebo (Part B)	Intent-to-treat population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	9	11	20[2]	
Units: percent change from baseline				
least squares mean (confidence interval 100%)	-27.02 (-38.04 to -16.01)	-1.15 (-11.09 to 8.79)	-25.87 (-40.88 to -10.86)	

Notes:

[2] - Part B Only MEDI0382 (Part B) vs. Placebo (Part B)

Statistical analyses

Statistical analysis title	Primary Analysis (Part B)

Statistical analysis description:

To assess the effect of cotadutide on hepatic glycogen levels versus placebo after 35 days (Part B) of treatment

Comparison groups	MEDI0382 (Part B) v Placebo (Part B)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-25.87
Confidence interval	
level	90 %
sides	2-sided
lower limit	-40.88
upper limit	-10.86

Secondary: Percentage change in fasting hepatic glycogen concentration adjusted for liver volume as measured by MRS at T = 24 hours post standardised morning meal from baseline (Day -1) to the end of 35 days of treatment (Day 36) (Part B)

End point title	Percentage change in fasting hepatic glycogen concentration adjusted for liver volume as measured by MRS at T = 24 hours post standardised morning meal from baseline (Day -1) to the end of 35 days of treatment (Day 36) (Part B)

End point description:

End point type	Secondary

End point timeframe:

Day -1 to Day 36

End point values	Liraglutide (Part B)	Placebo (Part B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: percentage				
least squares mean (confidence interval 100%)				
percent change from baseline	-5.33 (-13.97 to 3.32)	-27.31 (-36.42 to -18.20)		

Statistical analyses

Statistical analysis title	Secondary Analysis (Part B)
Comparison groups	Liraglutide (Part B) v Placebo (Part B)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-21.99
Confidence interval	
level	90 %
sides	2-sided
lower limit	-34.55
upper limit	-9.43

Secondary: Development of ADA and titre (if confirmed positive)

End point title	Development of ADA and titre (if confirmed positive)

End point description:

End point type	Secondary

End point timeframe:

Baseline to (Follow-up Period) 28 days post last dose + (3-month poststudy)

End point values	MEDI0382 (Part A)	Placebo (Part A)	MEDI0382 (Part B)	Placebo (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	9	11
Units: participants				
Baseline ADA result	0	0	0	0
End of Treatment ADA	1	0	3	0
Follow-up ADA result	0	0	3	0
Post Study ADA result	0	1	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and tolerability of daily SC doses of MEDI0382 by assessment of the following using CTCAE V4.0: The number of Treatment Emergent Adverse events (TEAEs)

End point title	Safety and tolerability of daily SC doses of MEDI0382 by assessment of the following using CTCAE V4.0: The number of Treatment Emergent Adverse events (TEAEs)

End point description:

End point type	Secondary

End point timeframe:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

End point values	MEDI0382 (Part A)	Placebo (Part A)	Liraglutide (Part B)	MEDI0382 (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	10	9
Units: participants				
At least one event	11	7	8	7
At least one IP related event	11	5	7	7

End point values	Placebo (Part B)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: participants				
At least one event	6			
At least one IP related event	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and tolerability of daily SC doses of MEDI0382 by assessment of the following using CTCAE V4.0: The number of Treatment-Emergent Serious Adverse Events (TESAEs)

End point title	Safety and tolerability of daily SC doses of MEDI0382 by assessment of the following using CTCAE V4.0: The number of Treatment-Emergent Serious Adverse Events (TESAEs)

End point description:

End point type	Secondary

End point timeframe:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

End point values	MEDI0382 (Part A)	Placebo (Part A)	Liraglutide (Part B)	MEDI0382 (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	10	9
Units: participants				
Treatment Emergent Serious Adverse Events (TESAEs)	0	0	0	0

End point values	Placebo (Part B)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: participants				
Treatment Emergent Serious Adverse Events (TESAEs)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with clinically significant changes in heart rate (BPM) or systolic and diastolic blood pressure (mmHg)

End point title	Number of subjects with clinically significant changes in heart rate (BPM) or systolic and diastolic blood pressure (mmHg)

End point description:

End point type	Secondary

End point timeframe:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

End point values	MEDI0382 (Part A)	Placebo (Part A)	Liraglutide (Part B)	MEDI0382 (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	10	9
Units: participants				
clinically significant changes	0	0	0	0

End point values	Placebo (Part B)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: participants				
clinically significant changes	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with an ECG determined to be abnormal and clinically significant

End point title	Number of subjects with an ECG determined to be abnormal and clinically significant

End point description:

End point type	Secondary

End point timeframe:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

End point values	MEDI0382 (Part A)	Placebo (Part A)	Liraglutide (Part B)	MEDI0382 (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	10	9
Units: participants				
abnormal and clinically significant	0	0	0	0

End point values	Placebo (Part B)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: participants				
abnormal and clinically significant	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with clinically significant changes in in haematology and or clinical chemistry parameters

End point title	Number of subjects with clinically significant changes in in haematology and or clinical chemistry parameters

End point description:

End point type	Secondary

End point timeframe:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

End point values	MEDI0382 (Part A)	Placebo (Part A)	Liraglutide (Part B)	MEDI0382 (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	10	9
Units: participants				
clinically significant changes	0	0	0	0

End point values	Placebo (Part B)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: participants				
clinically significant changes	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with clinically significant changes in heart rate (BPM) or systolic and diastolic blood pressure (mmHg)

End point title	Percentage of subjects with clinically significant changes in heart rate (BPM) or systolic and diastolic blood pressure (mmHg)

End point description:

End point type	Secondary

End point timeframe:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

End point values	MEDI0382 (Part A)	Placebo (Part A)	Liraglutide (Part B)	MEDI0382 (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	10	9
Units: participants				
clinically significant changes	0	0	0	0

End point values	Placebo (Part B)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: participants				
clinically significant changes	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with an ECG determined to be abnormal and clinically significant

End point title	Percentage of subjects with an ECG determined to be abnormal and clinically significant

End point description:

End point type	Secondary

End point timeframe:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

End point values	MEDI0382 (Part A)	Placebo (Part A)	Liraglutide (Part B)	MEDI0382 (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	10	9
Units: participants				
abnormal and clinically significant	0	0	0	0

End point values	Placebo (Part B)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: participants				
abnormal and clinically significant	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with clinically significant changes in in haematology and or clinical chemistry parameters

End point title	Percentage of subjects with clinically significant changes in in haematology and or clinical chemistry parameters

End point description:

End point type	Secondary

End point timeframe:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

End point values	MEDI0382 (Part A)	Placebo (Part A)	Liraglutide (Part B)	MEDI0382 (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	10	9
Units: participants				
clinically significant changes	0	0	0	0

End point values	Placebo (Part B)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: participants				
clinically significant changes	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in hepatic fat fraction from baseline as measured by magnetic resonance imaging (Day -1) to the end of 35 days of treatment (Part B only)

End point title	Change in hepatic fat fraction from baseline as measured by magnetic resonance imaging (Day -1) to the end of 35 days of

	treatment (Part B only)

End point description:

End point type	Secondary

End point timeframe:

Day -1 to Day 36

End point values	Liraglutide (Part B)	MEDI0382 (Part B)	Placebo (Part B)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	11	
Units: percent				
least squares mean (confidence interval 100%)	-15.40 (-21.09 to -9.72)	-26.26 (-51.13 to -1.39)	8.79 (-10.46 to 28.05)	

Statistical analyses

Statistical analysis title	Secondary Analysis
Comparison groups	Liraglutide (Part B) v Placebo (Part B)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-11.72
Confidence interval	
level	90 %
sides	2-sided
lower limit	-20.13
upper limit	-3.3

Statistical analysis title	Secondary Analysis
Comparison groups	MEDI0382 (Part B) v Placebo (Part B)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.07
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-35.06

Confidence interval	
level	90 %
sides	2-sided
lower limit	-66.54
upper limit	-3.58

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug until last study visit	
Adverse event reporting additional description:	
Adverse events were coded with MedDRA version 21.0 or higher. Analysis of AEs included the type, incidence, severity and relationship to study IP summarised by MedDRA SOC and PT by study part treatment group as well as for combined study parts.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21

Reporting groups	
Reporting group title	MEDI0382 (Part A)
Reporting group description: -	
Reporting group title	Placebo (Part A)
Reporting group description: -	
Reporting group title	Liraglutide (Part B)
Reporting group description: -	
Reporting group title	MEDI0382 (Part B)
Reporting group description: -	
Reporting group title	Placebo (Part B)
Reporting group description: -	

Serious adverse events	MEDI0382 (Part A)	Placebo (Part A)	Liraglutide (Part B)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	MEDI0382 (Part B)	Placebo (Part B)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	MEDI0382 (Part A)	Placebo (Part A)	Liraglutide (Part B)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)	7 / 9 (77.78%)	8 / 10 (80.00%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Chills			
subjects affected / exposed	2 / 12 (16.67%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	4	0	1
Early satiety			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	6 / 12 (50.00%)	2 / 9 (22.22%)	1 / 10 (10.00%)
occurrences (all)	7	2	1
Feeling cold			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injection site erythema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injection site haematoma			
subjects affected / exposed	1 / 12 (8.33%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Injection site rash			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	2 / 12 (16.67%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	2	3	0
Pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pyrexia			

subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dry throat			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Productive cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhinalgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Apathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Daydreaming			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Irritability			

subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Investigations			
Heart rate increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Head injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Tachycardia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 12 (25.00%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	3	0	2
Headache			
subjects affected / exposed	5 / 12 (41.67%)	3 / 9 (33.33%)	1 / 10 (10.00%)
occurrences (all)	11	3	3
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Visual impairment			

subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 12 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Abdominal distension			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	2 / 12 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	5	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Breath odour			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	3 / 12 (25.00%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	3	0	2
Diarrhoea			
subjects affected / exposed	0 / 12 (0.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	0	4	0
Dry mouth			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	6 / 12 (50.00%)	2 / 9 (22.22%)	1 / 10 (10.00%)
occurrences (all)	10	3	2
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	3

Nausea			
subjects affected / exposed	8 / 12 (66.67%)	2 / 9 (22.22%)	1 / 10 (10.00%)
occurrences (all)	11	4	3
Vomiting			
subjects affected / exposed	5 / 12 (41.67%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	8	1	1
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Torticollis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Otitis media acute			
subjects affected / exposed	1 / 12 (8.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			

subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 12 (25.00%)	1 / 9 (11.11%)	2 / 10 (20.00%)
occurrences (all)	3	1	2
Food craving			
subjects affected / exposed	0 / 12 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	MEDI0382 (Part B)	Placebo (Part B)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 9 (77.78%)	6 / 11 (54.55%)	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Early satiety			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	3 / 9 (33.33%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Feeling cold			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Injection site erythema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Injection site haematoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Injection site rash			

subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 9 (11.11%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Dry throat			
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Productive cough			
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Rhinalgia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			

Apathy			
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Daydreaming			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Irritability			
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Investigations			
Heart rate increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Head injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Procedural pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Tachycardia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			

subjects affected / exposed	1 / 9 (11.11%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	1 / 9 (11.11%)	1 / 11 (9.09%)	
occurrences (all)	1	2	
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Visual impairment			
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Abdominal distension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Abdominal pain lower			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Breath odour			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	2 / 9 (22.22%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			

subjects affected / exposed	1 / 9 (11.11%)	1 / 11 (9.09%)	
occurrences (all)	2	1	
Dry mouth			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	5 / 9 (55.56%)	0 / 11 (0.00%)	
occurrences (all)	7	0	
Vomiting			
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 9 (0.00%)	2 / 11 (18.18%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Torticollis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Otitis media acute			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Pneumonia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Food craving			
subjects affected / exposed	0 / 9 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	

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