Clinical trial results:
A Phase1/2, Randomized, Blinded, Placebo controlled, Multiple-ascending-dose Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of MEDI0382 in Overweight and Obese Subjects with a History of Type 2 Diabetes Mellitus

Summary

EudraCT number	2014-003716-36
Trial protocol	DE
Global end of trial date	24 February 2017

Results information

Result version number	v2 (current)
This version publication date	25 January 2019
First version publication date	30 May 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	D5670C00002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02548585
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	Milstein Building, Granta Park, Cambridge, United Kingdom, CB21 6GH
Public contact	Philip Ambery, MedImmune, LLC, +44 1223 895997, information.center@astrazeneca.com
Scientific contact	Philip Ambery, MedImmune, LLC, +44 1223 895997, 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	24 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the effect of MEDI0382 on glucose control (as measured by the standardized mixed-meal test [MMT] glucose data) and body weight from baseline to the end of a 4-week period at a stable dose.

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and were consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements. Subjects signed an informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 December 2015
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	Germany: 113
Worldwide total number of subjects	113
EEA total number of subjects	113

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)	104

From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 09 Dec 2015 to 24 Feb 2017 in Germany.

Pre-assignment

Screening details:

A total of 422 subjects were screened, of which 113 subjects were randomized in the study. One subject was randomized but not treated with study drug.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received placebo (matched to either 100 micrograms [mcg], or 150 mcg or 200 mcg or 300 mcg of MEDI0382) subcutaneously (SC) once daily from Day 1 to Day 7 (Cohort 1); or Day 1 to Day 11 (Cohort 2); or Day 1 to Day 15 (Cohort 3); or Day 1 to Day 41 (Cohort 4); or Day 1 to Day 22 (Cohort 5); or Day 1 to Day 17 (Cohort 6).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Sterile solution
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo matched to either 100 mcg, or 150 mcg or 200 mcg or 300 mcg of MEDI0382 was administered subcutaneously (SC) once daily from Day 1 to Day 7 (Cohort 1); or Day 1 to Day 11 (Cohort 2); or Day 1 to Day 15 (Cohort 3); or Day 1 to Day 41 (Cohort 4); or Day 1 to Day 22 (Cohort 5); or Day 1 to Day 17 (Cohort 6).

Arm title	Cohort 1: MEDI0382 100 mcg

Arm description:

Subjects received MEDI0382 100 mcg SC once daily from Day 1 to Day 7.

Arm type	Experimental
Investigational medicinal product name	MEDI0382
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

MEDI0382 100 mcg was administered SC once daily from Day 1 to Day 7.

Arm title	Cohort 2: MEDI0382 150 mcg

Arm description:

Subjects received MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4) and thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 7 days (Day 5 to Day 11).

Arm type	Experimental

Investigational medicinal product name	MEDI0382
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4) and thereafter an uptitrated dose of MEDI0382 150 mcg SC once daily for 7 days (Day 5 to Day 11).

Arm title	Cohort 3: MEDI0382 200 mcg

Arm description:

Subjects received MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4); thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 4 days (Day 5 to Day 8); followed by second up titrated dose of MEDI0382 200 mcg SC once daily for 7 days (Day 9 to Day 15).

Arm type	Experimental
Investigational medicinal product name	MEDI0382
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4); thereafter an uptitrated dose of MEDI0382 150 mcg SC once daily for 4 days (Day 5 to Day 8); followed by a second uptitrated dose of MEDI0382 200 mcg SC once daily for 7 days (Day 9 to Day 15).

Arm title	Cohort 4: MEDI0382 200 mcg

Arm description:

Subjects received MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4); thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 4 days (Day 5 to Day 8); followed by second up titrated dose of MEDI0382 200 mcg SC once daily for 4 days (Day 9 to Day 12), then a further MEDI0382 200 mcg SC once daily for 28 days (Day 13 to Day 40) at home-dosing; followed by MEDI0382 200 mcg SC once daily for 1 day in hospital (Day 41).

Arm type	Experimental
Investigational medicinal product name	MEDI0382
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4); thereafter an uptitrated dose of MEDI0382 150 mcg SC once daily for 4 days (Day 5 to Day 8); followed by a second uptitrated dose of MEDI0382 200 mcg SC once daily for 4 days (Day 9 to Day 12); then a further MEDI0382 200 mcg SC once daily for 28 days (Day 13 to Day 40) at home dosing; followed by MEDI0382 200 mcg SC once daily for 1 day in hospital (Day 41).

Arm title	Cohort 5: MEDI0382 300 mcg

Arm description:

Subjects received MEDI0382 100 mcg SC once daily for at least 5 days (Day 1 to Day 5); thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 5 days (Day 6 to Day 10); then a second up titrated dose of MEDI0382 200 mcg SC once daily for 5 days (Day 11 to Day 15); followed by third up titrated dose of MEDI0382 300 mcg SC once daily for 7 days (Day 16 to Day 22).

Arm type	Experimental
Investigational medicinal product name	MEDI0382
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

MEDI0382 100 mcg SC once daily for at least 5 days (Day 1 to Day 5); thereafter an uptitrated dose of MEDI0382 150 mcg SC once daily for 5 days (Day 6 to Day 10); then a second uptitrated dose of MEDI0382 200 mcg SC once daily for 5 days (Day 11 to Day 15); followed by third uptitrated dose of MEDI0382 300 mcg SC once daily for 7 days (Day 16 to Day 22). for 4 days (Day 9 to Day 12); then a further MEDI0382 200 mcg SC once daily for 28 days (Day 13 to Day 40) at home dosing; followed by MEDI0382 200 mcg SC once daily for 1 day in hospital (Day 41).

Arm title	Cohort 6: MEDI0382 300 mcg

Arm description:

Subjects received MEDI0382 100 mcg SC once daily for at least 5 days (Day 1 to Day 5); thereafter, an up titrated dose of MEDI0382 200 mcg SC once daily for 5 days (Day 6 to Day 10); followed by a second up titrated dose of MEDI0382 300 mcg SC once daily for 7 days (Day 11 to Day 17).

Arm type	Experimental
Investigational medicinal product name	MEDI0382
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

MEDI0382 100 mcg SC once daily for at least 5 days (Day 1 to Day 5); thereafter an uptitrated dose of MEDI0382 200 mcg SC once daily for 5 days (Day 6 to Day 10); followed by a second uptitrated dose of MEDI0382 300 mcg SC once daily for 7 days (Day 11 to Day 17).

Number of subjects in period 1[1]	Placebo	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg
Started	45	6	6
Completed	43	6	6
Not completed	2	0	0
Consent withdrawn by subject	-	-	-
Not Specified	1	-	-
Lost to follow-up	1	-	-

Number of subjects in period 1[1]	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg	Cohort 5: MEDI0382 300 mcg
Started	7	25	11
Completed	5	22	10
Not completed			1

Lost to follow-up	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Total subjects enrolled worldwide were 113; of which 1 subject was randomized but not treated. This 1 subject was not included in As-treated population and data for the subject was not captured for baseline characteristics.

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received placebo (matched to either 100 micrograms [mcg], or 150 mcg or 200 mcg or 300 mcg of MEDI0382) subcutaneously (SC) once daily from Day 1 to Day 7 (Cohort 1); or Day 1 to Day 11 (Cohort 2); or Day 1 to Day 15 (Cohort 3); or Day 1 to Day 41 (Cohort 4); or Day 1 to Day 22 (Cohort 5); or Day 1 to Day 17 (Cohort 6).	
Reporting group title	Cohort 1: MEDI0382 100 mcg
Reporting group description:	
Subjects received MEDI0382 100 mcg SC once daily from Day 1 to Day 7.	
Reporting group title	Cohort 2: MEDI0382 150 mcg
Reporting group description:	
Subjects received MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4) and thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 7 days (Day 5 to Day 11).	
Reporting group title	Cohort 3: MEDI0382 200 mcg
Reporting group description:	
Subjects received MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4); thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 4 days (Day 5 to Day 8); followed by second up titrated dose of MEDI0382 200 mcg SC once daily for 7 days (Day 9 to Day 15).	
Reporting group title	Cohort 4: MEDI0382 200 mcg
Reporting group description:	
Subjects received MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4); thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 4 days (Day 5 to Day 8); followed by second up titrated dose of MEDI0382 200 mcg SC once daily for 4 days (Day 9 to Day 12), then a further MEDI0382 200 mcg SC once daily for 28 days (Day 13 to Day 40) at home-dosing; followed by MEDI0382 200 mcg SC once daily for 1 day in hospital (Day 41).	
Reporting group title	Cohort 5: MEDI0382 300 mcg
Reporting group description:	
Subjects received MEDI0382 100 mcg SC once daily for at least 5 days (Day 1 to Day 5); thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 5 days (Day 6 to Day 10); then a second up titrated dose of MEDI0382 200 mcg SC once daily for 5 days (Day 11 to Day 15); followed by third up titrated dose of MEDI0382 300 mcg SC once daily for 7 days (Day 16 to Day 22).	
Reporting group title	Cohort 6: MEDI0382 300 mcg
Reporting group description:	
Subjects received MEDI0382 100 mcg SC once daily for at least 5 days (Day 1 to Day 5); thereafter, an up titrated dose of MEDI0382 200 mcg SC once daily for 5 days (Day 6 to Day 10); followed by a second up titrated dose of MEDI0382 300 mcg SC once daily for 7 days (Day 11 to Day 17).	

Reporting group values	Placebo	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg
Number of subjects	45	6	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	42	4	6
From 65-84 years	3	2	0

85 years and over	0	0	0

Age Continuous Units: Years			
arithmetic mean	57.2	62.5	60.2
standard deviation	± 6.0	± 2.9	± 4.2
Sex: Female, Male Units: Subjects			
Male	27	5	2
Female	18	1	4
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	0
White	44	6	6
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	45	6	6
Unknown or Not Reported	0	0	0

Reporting group values	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg	Cohort 5: MEDI0382 300 mcg
Number of subjects	7	25	11
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	23	10
From 65-84 years	0	2	1
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	57.0	56.0	54.8
standard deviation	± 4.9	± 7.2	± 6.8
Sex: Female, Male Units: Subjects			
Male	5	13	7
Female	2	12	4

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	7	25	11
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	7	25	11
Unknown or Not Reported	0	0	0

Reporting group values	Cohort 6: MEDI0382 300 mcg	Total	
Number of subjects	12	112	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	11	103	
From 65-84 years	1	9	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	54.6		
standard deviation	± 6.5	-	
Sex: Female, Male Units: Subjects			
Male	9	68	
Female	3	44	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	1	
White	12	111	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	

Not Hispanic or Latino	12	112	
Unknown or Not Reported	0	0	

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received placebo (matched to either 100 micrograms [mcg], or 150 mcg or 200 mcg or 300 mcg of MEDI0382) subcutaneously (SC) once daily from Day 1 to Day 7 (Cohort 1); or Day 1 to Day 11 (Cohort 2); or Day 1 to Day 15 (Cohort 3); or Day 1 to Day 41 (Cohort 4); or Day 1 to Day 22 (Cohort 5); or Day 1 to Day 17 (Cohort 6).	
Reporting group title	Cohort 1: MEDI0382 100 mcg
Reporting group description:	
Subjects received MEDI0382 100 mcg SC once daily from Day 1 to Day 7.	
Reporting group title	Cohort 2: MEDI0382 150 mcg
Reporting group description:	
Subjects received MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4) and thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 7 days (Day 5 to Day 11).	
Reporting group title	Cohort 3: MEDI0382 200 mcg
Reporting group description:	
Subjects received MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4); thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 4 days (Day 5 to Day 8); followed by second up titrated dose of MEDI0382 200 mcg SC once daily for 7 days (Day 9 to Day 15).	
Reporting group title	Cohort 4: MEDI0382 200 mcg
Reporting group description:	
Subjects received MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4); thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 4 days (Day 5 to Day 8); followed by second up titrated dose of MEDI0382 200 mcg SC once daily for 4 days (Day 9 to Day 12), then a further MEDI0382 200 mcg SC once daily for 28 days (Day 13 to Day 40) at home-dosing; followed by MEDI0382 200 mcg SC once daily for 1 day in hospital (Day 41).	
Reporting group title	Cohort 5: MEDI0382 300 mcg
Reporting group description:	
Subjects received MEDI0382 100 mcg SC once daily for at least 5 days (Day 1 to Day 5); thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 5 days (Day 6 to Day 10); then a second up titrated dose of MEDI0382 200 mcg SC once daily for 5 days (Day 11 to Day 15); followed by third up titrated dose of MEDI0382 300 mcg SC once daily for 7 days (Day 16 to Day 22).	
Reporting group title	Cohort 6: MEDI0382 300 mcg
Reporting group description:	
Subjects received MEDI0382 100 mcg SC once daily for at least 5 days (Day 1 to Day 5); thereafter, an up titrated dose of MEDI0382 200 mcg SC once daily for 5 days (Day 6 to Day 10); followed by a second up titrated dose of MEDI0382 300 mcg SC once daily for 7 days (Day 11 to Day 17).	
Subject analysis set title	Cohort 4: Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received placebo (matched to MEDI0382 100 mcg) SC once daily for at least 4 days (Day 1 to Day 4); thereafter, an up titrated dose of placebo (matched to MEDI0382 150 mcg) SC once daily for 4 days (Day 5 to Day 8); followed by second up titrated dose of placebo (matched to MEDI0382 200 mcg) SC once daily for 4 days (Day 9 to Day 12), then a further placebo (matched to MEDI0382 200 mcg) SC once daily for 28 days (Day 13 to Day 40) at home-dosing; followed by placebo (matched to MEDI0382 200 mcg) SC once daily for 1 day in hospital (Day 41).	
Subject analysis set title	Cohort 1: Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received placebo matched to (MEDI0382 100 mcg) SC once daily from Day 1 to Day 7.	
Subject analysis set title	Cohort 2: Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received placebo (matched to MEDI0382 100 mcg) SC once daily for at least 4 days (Day 1 to	

Day 4) and thereafter, an up titrated dose of placebo (matched to MEDI0382 150 mcg) SC once daily for 7 days (Day 5 to Day 11).

Subject analysis set title	Cohort 3: Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received placebo (matched to MEDI0382 100 mcg) SC once daily for at least 4 days (Day 1 to Day 4); thereafter, an up titrated dose of placebo (matched to MEDI0382 150 mcg) SC once daily for 4 days (Day 5 to Day 8); followed by second up titrated dose of placebo (matched to MEDI0382 200 mcg) SC once daily for 7 days (Day 9 to Day 15).

Subject analysis set title	Cohort 5: Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received placebo (matched to MEDI0382 100 mcg) SC once daily for at least 5 days (Day 1 to Day 5); thereafter, an up titrated dose of placebo (matched to MEDI0382 150 mcg) SC once daily for 5 days (Day 6 to Day 10); then a second up titrated dose of placebo (matched to MEDI0382 200 mcg) SC once daily for 5 days (Day 11 to Day 15); followed by third up titrated dose of placebo (matched to MEDI0382 300 mcg) SC once daily for 7 days (Day 16 to Day 22).

Subject analysis set title	Cohort 6: Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received placebo (matched to MEDI0382 100 mcg) SC once daily for at least 5 days (Day 1 to Day 5); thereafter, an up titrated dose of placebo (matched to MEDI0382 200 mcg) SC once daily for 5 days (Day 6 to Day 10); followed by a second up titrated dose of placebo (matched to MEDI0382 300 mcg) SC once daily for 7 days (Day 11 to Day 17).

Primary: Percent Change From Baseline in Mixed-meal Test (MMT Under the Concentration-time Curve From Time 0 to 4 hours to t (EOT) (Cohort 4)

End point title	Percent Change From Baseline in Mixed-meal Test (MMT) Glucose Area Under the Concentration-time Curve From Time 0 to 4 hours to the End of Treatment (EOT) (Cohort 4)[1]

End point description:

Mixed-meal test involved consumption of a standardized meal (nutritional supplement containing the components of fat, carbohydrate and protein, which make up a standard MMT) within 5 minutes, and timed serial blood samples were obtained for measurement of glucose and parameters related to glucose metabolism just before and 4 hours (hrs) after consumption of the standardized meal (with no additional food intake during this time). Pharmacodynamic (PD) population was analysed for this end point, which included all subjects who received at least 1 dose of study drug and had at least 1 post-MMT PD blood sample.

End point type	Primary

End point timeframe:

0 minutes before; and 15, 30, 45, 60, 90, 120, 180, and 240 minutes post standardized meal intake (SMI) on Baseline (Day -1) and EOT (Day 41)

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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 4: MEDI0382 200 mcg	Cohort 4: Placebo		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	25	26		
Units: Percent change				
arithmetic mean (standard deviation)	-33.81 (± 18.62)	-9.24 (± 12.30)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Cohort 4: MEDI0382 200 mcg v Cohort 4: Placebo
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	ANCOVA

Notes:

[2] - p-value was based on pairwise comparison using analysis of covariance (ANCOVA) adjusted by baseline value.

Primary: Change From Baseline in Body Weight to the EOT (Coho

End point title	Change From Baseline in Body Weight to the EOT (Cohort 4)[3]

End point description:

Intent-to-treat (ITT) population was analysed for this end point, which included all subjects who were randomised and received any study drug and analysed according to the initial randomisation.

End point type	Primary

End point timeframe:

Baseline (Day 1) and EOT (Day 42)

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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 4: MEDI0382 200 mcg	Cohort 4: Placebo		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	25	26		
Units: Kilograms (Kg)				
arithmetic mean (standard deviation)	-3.83 (± 2.09)	-1.71 (± 2.10)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Cohort 4: MEDI0382 200 mcg v Cohort 4: Placebo

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0008 [4]
Method	ANCOVA

Notes:

[4] - p-value was based on pairwise comparison using ANCOVA adjusted by baseline value.

Secondary: Percent Change From Baseline in MMT Glucose AUC0- (Cohorts 1, 2, 3, 5, and 6)

End point title	Percent Change From Baseline in MMT Glucose AUC0-4h to the EOT (Cohorts 1, 2, 3, 5, and 6)[5]

End point description:

Mixed-meal test involved consumption of a standardized meal (nutritional supplement containing the components of fat, carbohydrate and protein, which make up a standard MMT) within 5 minutes, and timed serial blood samples were obtained for measurement of glucose and parameters related to glucose metabolism just before and 4 hrs after consumption of the standardized meal (with no additional food intake during this time). PD population was analysed for this end point.

End point type	Secondary

End point timeframe:

0 minutes before; and 15, 30, 45, 60, 90, 120, 180, and 240 minutes post SMI on Baseline (Day -1) and EOT (Day 7 for Cohort 1; Day 11 for Cohort 2; Day 15 for Cohort 3; Day 22 for Cohort 5; and Day 17 for Cohort 6)

Notes:

[5] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 5: MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	11
Units: Percent change				
arithmetic mean (standard deviation)	-41.80 (± 11.07)	-36.73 (± 10.09)	-39.58 (± 5.27)	-41.66 (± 9.97)

End point values	Cohort 6: MEDI0382 300 mcg	Cohort 1: Placebo	Cohort 2: Placebo	Cohort 3: Placebo
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	3	3	3
Units: Percent change				
arithmetic mean (standard deviation)	-38.19 (± 12.51)	-14.60 (± 5.56)	-15.07 (± 13.46)	-0.47 (± 15.16)

End point values	Cohort 5: Placebo	Cohort 6: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	5		

Units: Percent change				
arithmetic mean (standard deviation)	-14.52 (± 8.12)	-4.80 (± 3.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Weight to the EOT (Co 6)

End point title	Change From Baseline in Body Weight to the EOT (Cohorts 1, 2, 3, 5, and 6)[6]

End point description:

ITT population was analysed for this end point. Subjects who did not complete the treatment were not included in this analysis.

End point type	Secondary

End point timeframe:

Cohort 1: Baseline (Day 1) to EOT (Day 8); Cohort 2: Baseline (Day 1) to EOT (Day 12); Cohort 3: Baseline (Day 1) to EOT (Day 16); Cohort 5: Baseline (Day 1) to EOT (Day 22); Cohort 6: Baseline (Day 1) to EOT (Day 17)

Notes:

[6] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 5: MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	11
Units: Kg				
arithmetic mean (standard deviation)	-2.32 (± 1.29)	-1.52 (± 0.57)	-4.63 (± 1.98)	-3.26 (± 1.99)

End point values	Cohort 6: MEDI0382 300 mcg	Cohort 1: Placebo	Cohort 2: Placebo	Cohort 3: Placebo
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	3	3	3
Units: Kg				
arithmetic mean (standard deviation)	-2.04 (± 1.52)	-1.20 (± 0.44)	-1.00 (± 1.13)	-2.90 (± 1.05)

End point values	Cohort 5: Placebo	Cohort 6: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	5		
Units: Kg				
arithmetic mean (standard deviation)	-0.98 (± 2.12)	-0.94 (± 3.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Hemoglobin A1c (H (Cohorts 4,5,and 6)

End point title	Percent Change From Baseline in Hemoglobin A1c (HbA1c) to the EOT (Cohorts 4, 5, and 6)[7]

End point description:

ITT population was analysed for this end point. Subjects who did not complete the treatment were not included in this analysis.

End point type	Secondary

End point timeframe:

Cohort 4: Baseline (Day -2) to EOT (Day 42); Cohort 5: Baseline (Day -2) to EOT (Day 22); Cohort 6: Baseline (Day -2) to EOT (Day 17)

Notes:

[7] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 4: MEDI0382 200 mcg	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg	Cohort 4: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	25	11	12	26
Units: Percent change				
arithmetic mean (standard deviation)	-0.92 (± 0.41)	-0.55 (± 0.35)	-0.42 (± 0.27)	-0.58 (± 0.30)

End point values	Cohort 5: Placebo	Cohort 6: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	5		
Units: Percent change				
arithmetic mean (standard deviation)	-0.10 (± 0.29)	-0.18 (± 0.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fructosamine to the EOT (C

End point title	Change From Baseline in Fructosamine to the EOT (Cohorts 4, 5, and 6)[8]

End point description:

ITT population was analysed for this end point. Subjects who did not complete the treatment were not included in this analysis.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: mg/dL				
arithmetic mean (standard deviation)	-74.48 (± 24.59)	-54.06 (± 19.51)	-63.67 (± 11.93)	-50.62 (± 33.61)

End point values	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg	Cohort 4: Placebo	Cohort 1: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	26	3
Units: mg/dL				
arithmetic mean (standard deviation)	-54.42 (± 19.75)	-55.21 (± 31.13)	-18.52 (± 18.88)	-32.44 (± 17.19)

End point values	Cohort 2: Placebo	Cohort 3: Placebo	Cohort 5: Placebo	Cohort 6: Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	5	5
Units: mg/dL				
arithmetic mean (standard deviation)	-49.86 (± 23.24)	-4.20 (± 33.73)	-32.08 (± 17.49)	-16.58 (± 12.45)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Glucose Area Under the Concentration-time Curve From Time 0 to 24 hours (AUC0-24h) after MMT to the EOT (Cohorts 1, 3, 4, 5, and 6)

End point title	Percent Change From Baseline in Glucose Area Under the Concentration-time Curve From Time 0 to 24 hours (AUC0-24h) after MMT to the EOT (Cohorts 1, 2, 3, 4, 5, and 6)[10]

End point description:

Mixed-meal test involved consumption of a standardized meal (nutritional supplement containing the components of fat, carbohydrate and protein, which make up a standard MMT) within 5 minutes, and timed serial blood samples were obtained for measurement of glucose and parameters related to glucose metabolism just before and 4 hrs after consumption of the standardized meal (with no additional food intake during this time). PD population was analysed for this end point.

End point type	Secondary

End point timeframe:

0 minutes before; and 15, 30, 45, 60, 90, 120, 180, 240 minutes, and 24 hrs post SMI on Baseline (Day -1) and EOT (Day 7 for Cohort 1; Day 11 for Cohort 2; Day 15 for Cohort 3; Day 41 for Cohort 4; Day 22 for Cohort 5; and Day 17 for Cohort 6)

Notes:

[10] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: Percent change				
arithmetic mean (standard deviation)	-28.34 (± 13.52)	-29.32 (± 17.24)	-27.07 (± 10.82)	-13.50 (± 18.19)

End point values	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg	Cohort 4: Placebo	Cohort 1: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	26	3
Units: Percent change				
arithmetic mean (standard deviation)	-34.51 (± 11.25)	-26.95 (± 9.45)	-1.06 (± 11.47)	-21.80 (± 1.41)

End point values	Cohort 2: Placebo	Cohort 3: Placebo	Cohort 5: Placebo	Cohort 6: Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	5	5
Units: Percent change				
arithmetic mean (standard deviation)	0.80 (± 39.55)	-13.80 (± 15.95)	-4.20 (± 28.58)	-10.10 (± 14.69)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adver and Treatment-Emergent Serious Adverse Events (TESAEs)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)[11]

End point description:

An Adverse Event (AE) is any unfavourable and unintended sign, symptoms, or diseases temporally associated with use of study drug, whether or not considered related to study drug. Serious adverse events (SAE) is any AE that resulted in death, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, life-threatening, a congenital anomaly/birth defect, or an important medical event. TEAEs and TESAEs are defined as AEs and SAEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug, up to 28 days after the last study dose of each

cohort (approximately 60 days). As-treated Population (ATP) was analysed for this end point, which included all subjects who received any study drug and analysed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

From Day 1 to follow-up period (28 days after the last study dose for each cohort [approximately 60 days])

Notes:

[11] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: Subjects				
TEAEs	6	5	7	22
TESAEs	0	0	1	0

End point values	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg	Cohort 4: Placebo	Cohort 1: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	26	3
Units: Subjects				
TEAEs	10	10	23	2
TESAEs	0	0	1	0

End point values	Cohort 2: Placebo	Cohort 3: Placebo	Cohort 5: Placebo	Cohort 6: Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	5	5
Units: Subjects				
TEAEs	3	3	4	2
TESAEs	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal Vital Signs and Reported as TEAEs

End point title	Number of Subjects With Abnormal Vital Signs and Physical Examination Reported as TEAEs[12]

End point description:

TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug, up to 28 days after the last study dose of each cohort (approximately 60 days). Number of subjects with TEAEs related to vital signs and physical examination abnormalities were reported. As-treated population was analysed for this end point.

End point type	Secondary

End point timeframe:

From Day 1 to follow-up period (28 days after the last study dose for each cohort [approximately 60 days])

Notes:

[12] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: Subjects				
Blood Pressure increased	0	0	0	1
Blood pressure systolic increased	0	0	0	0
Blood pressure diastolic increased	0	0	0	0
Physical Examinations	0	0	0	0

End point values	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg	Cohort 4: Placebo	Cohort 1: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	26	3
Units: Subjects				
Blood Pressure increased	0	0	2	0
Blood pressure systolic increased	1	0	0	0
Blood pressure diastolic increased	0	1	0	0
Physical Examinations	0	0	0	0

End point values	Cohort 2: Placebo	Cohort 3: Placebo	Cohort 5: Placebo	Cohort 6: Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	5	5
Units: Subjects				
Blood Pressure increased	0	0	0	0
Blood pressure systolic increased	0	0	0	1
Blood pressure diastolic increased	0	0	0	0
Physical Examinations	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal 12 Lead Electroc Reported as TEAEs

End point title	Number of Subjects With Abnormal 12 Lead Electrocardiogram (ECG) Reported as TEAEs[13]

End point description:

TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug, up to 28 days after the last study dose of each cohort (approximately 60 days). Number of subjects with TEAEs related to ECG abnormalities were reported. As-treated population was analysed for this end point.

End point type	Secondary

End point timeframe:

From Day 1 to follow-up period (28 days after the last study dose for each cohort [approximately 60 days])

Notes:

[13] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: Subjects				
Arrhythmia	1	0	0	0
Atrial fibrillation	0	0	0	1
Atrioventricular block first degree	1	0	0	0
Atrioventricular block second degree	1	0	0	0
Electrocardiogram ST segment depression	0	0	1	0
Extrasystoles	0	0	0	0
Sinus tachycardia	0	0	0	1
Supraventricular extrasystoles	0	0	0	0
Supraventricular tachycardia	1	0	1	0
Tachycardia	1	1	1	0
Ventricular extrasystoles	1	1	0	1
Ventricular tachycardia	0	0	1	0

End point values	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg	Cohort 4: Placebo	Cohort 1: Placebo

Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	26	3
Units: Subjects				
Arrhythmia	0	0	0	0
Atrial fibrillation	0	0	0	0
Atrioventricular block first degree	0	0	0	0
Atrioventricular block second degree	0	0	0	0
Electrocardiogram ST segment depression	0	0	0	0
Extrasystoles	0	0	0	0
Sinus tachycardia	0	0	0	0
Supraventricular extrasystoles	0	0	1	0
Supraventricular tachycardia	0	0	0	1
Tachycardia	0	0	0	0
Ventricular extrasystoles	0	0	1	0
Ventricular tachycardia	0	0	0	0

End point values	Cohort 2: Placebo	Cohort 3: Placebo	Cohort 5: Placebo	Cohort 6: Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	5	5
Units: Subjects				
Arrhythmia	0	0	0	0
Atrial fibrillation	0	0	0	0
Atrioventricular block first degree	0	0	0	0
Atrioventricular block second degree	0	0	0	0
Electrocardiogram ST segment depression	0	0	0	0
Extrasystoles	1	1	0	0
Sinus tachycardia	0	0	0	0
Supraventricular extrasystoles	0	0	0	0
Supraventricular tachycardia	1	1	0	0
Tachycardia	0	0	0	0
Ventricular extrasystoles	1	0	0	0
Ventricular tachycardia	0	1	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal Clinical Labora TEAEs

End point title	Number of Subjects With Abnormal Clinical Laboratory Reported as TEAEs[14]

End point description:

TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug, up to 28 days after the last study dose of each cohort (approximately 60 days). Number of subjects with TEAEs related to laboratory abnormalities were reported. As-treated population was analysed for this end point.

End point type	Secondary

End point timeframe:

From Day 1 to follow-up period (28 days after the last study dose for each cohort [approximately 60 days])

Notes:

[14] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: Subjects				
Lipase increased	0	1	0	1
Hypokalemia	0	0	0	1
C-reactive protein increased	0	0	1	0
Hypoglycemia	0	0	0	1
Chromaturia	0	0	0	1

End point values	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg	Cohort 4: Placebo	Cohort 1: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	26	3
Units: Subjects				
Lipase increased	2	1	0	0
Hypokalemia	0	1	1	0
C-reactive protein increased	0	0	0	0
Hypoglycemia	0	0	0	0
Chromaturia	1	0	0	0

End point values	Cohort 2: Placebo	Cohort 3: Placebo	Cohort 5: Placebo	Cohort 6: Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	5	5
Units: Subjects				
Lipase increased	0	0	0	0
Hypokalemia	0	0	0	0
C-reactive protein increased	0	0	0	0
Hypoglycemia	0	0	0	0
Chromaturia	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Any Suicidal Ideation as Columbia-Suicide Severity Rating Scale (C-SSRS) Score (Cohort

End point title	Number of Subjects With Any Suicidal Ideation as Assessed by Columbia-Suicide Severity Rating Scale (C-SSRS) Score (Cohorts 4, 5, and 6)[15]

End point description:

The C-SSRS is an interview-based rating scale to systematically assess suicidal ideation and suicidal behaviour of subjects. Yes/No responses are mapped to C-SSRS to assess whether subject experienced suicidal behaviour and suicidal ideation. Suicidal behaviour questions includes preparatory acts or behaviour, aborted attempt, interrupted attempt, actual attempt, and completed suicide. Suicidal ideation questions includes wish to be dead, non-specific active suicidal thoughts, active suicidal ideation with any methods (not plan) without intent to act, active suicidal ideation with some intent to act (without specific plan), and active suicidal ideation with specific plan and intent. Subjects with yes response to any category for suicidal ideation were reported. As-treated population was used for analysis. Here, 'n' denotes number of subjects analysed for specified time points. Arbitrary value '99999' signifies data not applicable as no subject was evaluable for specified time point.

End point type	Secondary

End point timeframe:

Cohort 4: Day -1, and Days 13, 20, 27, 34, and 40; Cohort 5: Day -1 and Day 7-14 post last dose of MEDI0382 (approximately 36 days); Cohort 6: Day -1 and Day 7-14 post last dose of MEDI0382 (approximately 31 days)

Notes:

[15] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 4: MEDI0382 200 mcg	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg	Cohort 4: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	25	11	12	26
Units: Subjects				
Day -1 (n = 25, 11, 12, 26, 5, 5)	4	2	2	1
Day 13 (n = 25, 0, 0, 26, 0, 0)	0	99999	99999	1
Day 20 (n = 25, 0, 0, 26, 0, 0)	0	99999	99999	0
Day 27 (n = 25, 0, 0, 26, 0, 0)	0	99999	99999	0
Day 34 (n = 25, 0, 0, 26, 0, 0)	0	99999	99999	0
Day 40 (n = 25, 0, 0, 26, 0, 0)	0	99999	99999	0
Days 7-14 post last dose (n = 0, 11, 12, 0, 5, 5)	99999	1	0	99999

End point values	Cohort 5: Placebo	Cohort 6: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	5		
Units: Subjects				
Day -1 (n = 25, 11, 12, 26, 5, 5)	0	0		
Day 13 (n = 25, 0, 0, 26, 0, 0)	99999	99999		
Day 20 (n = 25, 0, 0, 26, 0, 0)	99999	99999		

End point values	Cohort 5: Placebo	Cohort 6: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	5		
Units: Subjects				
Day -1 (n = 25, 11, 12, 26, 5, 5)	0	0		
Day 13 (n = 25, 0, 0, 26, 0, 0)	99999	99999		
Day 20 (n = 25, 0, 0, 26, 0, 0)	99999	99999		
Day 27 (n = 25, 0, 0, 26, 0, 0)	99999	99999		
Day 34 (n = 25, 0, 0, 26, 0, 0)	99999	99999		
Day 40 (n = 25, 0, 0, 26, 0, 0)	99999	99999		
Days 7-14 post last dose (n = 0, 11, 12, 0, 5, 5)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Half Life (t 1/2) of MEDI0382

End point title	Terminal Elimination Half Life (t1/2) of MEDI0382 (Cohorts 1, 2, and 3)[17]

End point description:

Terminal elimination half Life is the time measured for the plasma concentration of MEDI0382 to decrease by one half. Pharmacokinetic (PK) population was analysed for this end point, which included all subjects who received at least 1 dose of study drug and had at least one PK sample taken that was above the lower limit of quantitation. Here, 'n' denotes number of subjects analysed for specified time points. Arbitrary value '99999' signifies data not applicable as no subject was analysed for the specified time points. 95% confidence interval (CI) data was not applicable as only one subject was evaluable; therefore, lower and upper CI values are presented with arbitrary values of '0.999999' and '99.9999', respectively for the specified time points.

End point type	Secondary

End point timeframe:

Cohort (C) 1 (Day [D] 1 and [&] D7), C2 (D5 & D11), and C3 (D9 & D15): pre-dose & 0.5, 1, 2, 4, 6, 8, 12, 24 hr post dose; and additional 48 hr post C1D7, C2D11, C3D15 dose

Notes:

[17] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: hr				
geometric mean (confidence interval 95%)				
Day 1 (n = 1, 0, 0)	8.5 (0.999999 to 99.9999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Day 5 (n = 0, 2, 0)	99999 (99999 to 99999)	10.3 (7.8 to 13.5)	99999 (99999 to 99999)	
Day 7 (n = 3, 0, 0)	11.7 (5.5 to 25.1)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Day 9 (n = 0, 0, 1)	99999 (99999 to 99999)	99999 (99999 to 99999)	8.3 (0.999999 to 99.9999)	
Day 11 (n = 0, 6, 0)	99999 (99999 to 99999)	11.3 (5.9 to 21.7)	99999 (99999 to 99999)	
Day 15 (n = 0, 0, 5)	99999 (99999 to 99999)	99999 (99999 to 99999)	11.3 (8.2 to 15.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Accumulation Ratio (Rac) of MEDI0382 (Cohorts 1, 2,

End point title	Accumulation Ratio (Rac) of MEDI0382 (Cohorts 1, 2, and 3)[18]

End point description:

Accumulation ratio was calculated as, Rac obtained from area under the curve from time zero to end of dosing interval (AUC[0-tau]) of Nth day divided by AUC(0-tau) of Day 1. PK population was analysed for this end point. Here, 'n' denotes number of subjects analysed for specified time points. Arbitrary value '99999' signifies data not applicable as no subject was evaluable for the specified time points and arbitrary value '999999' signifies data not reported, since accumulation ratio as described by the formula could not be derived for Cohort 1 Day 1, Cohort 2 Day 5, and for Cohort 3 Day 9.

End point type	Secondary

End point timeframe:

C1 (D1 & D7), C2 (D5 & D11), and C3 (D9 & D15): pre-dose & 0.5, 1, 2, 4, 6, 8, 12, 24 hr post dose; and additional 48 hr post C1D7, C2D11, C3D15 dose

Notes:

[18] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Ratio				
geometric mean (confidence interval 95%)				
Day 1 (n = 6, 0, 0)	999999 (999999 to 999999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Day 5 (n = 0, 6, 0)	99999 (99999 to 99999)	999999 (999999 to 999999)	99999 (99999 to 99999)	
Day 7 (n = 6, 0, 0)	1.3 (1.1 to 1.5)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Day 9 (n = 0, 0, 6)	99999 (99999 to 99999)	99999 (99999 to 99999)	999999 (999999 to 999999)	
Day 11 (n = 0, 6, 0)	99999 (99999 to 99999)	1.1 (0.9 to 1.8)	99999 (99999 to 99999)	
Day 15 (n = 0, 0, 5)	99999 (99999 to 99999)	99999 (99999 to 99999)	1.3 (1.1 to 1.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Time Curve From Time Zero to End of Dosing Interval (AUC[0-tau]) of MEDI0382 (Cohorts 1, 2, 3, 4, 5, and

End point title	Area Under the Concentration Time Curve From Time Zero to End of Dosing Interval (AUC[0-tau]) of MEDI0382 (Cohorts 1, 2, 3, 4, 5, and 6)[19]

End point description:

PK population was analysed for this end point. Here, 'n' denotes number of subjects analysed for specified time points. Arbitrary value '99999' signifies data not applicable as no subject was analysed for the specified time points.

End point type	Secondary

End point timeframe:

C1 (D1 & D7), C2 (D5 & D11), and C3 (D9 & D15): pre-dose & 0.5, 1, 2, 4, 6, 8, 12, 24 hr post dose and 48 hr post dose for C1D7, C2D11, C3D15; C4 (D9 & D41), C5 (D16 & D22), and C6 (D11 & D17): pre-dose & 0.5, 1, 2, 4, 6, 8, 12, 24 hr post dose

Notes:

[19] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: ng*hr/mL				
geometric mean (confidence interval 95%)				
Day 1 (n = 6, 0, 0, 0, 0, 0)	82.21 (44.56 to 151.69)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 5 (n = 0, 6, 0, 0, 0, 0)	99999 (99999 to 99999)	174.58 (87.41 to 348.67)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 7 (n = 6, 0, 0, 0, 0, 0)	107.01 (54.10 to 211.64)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 9 (n = 0, 0, 4, 23, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	194.78 (146.17 to 259.56)	164.05 (42.67 to 630.76)
Day 11 (n = 0, 6, 0, 0, 0, 11)	99999 (99999 to 99999)	157.31 (82.45 to 421.12)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 15 (n = 0, 0, 5, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	195.40 (89.8 to 425.17)	99999 (99999 to 99999)
Day 16 (n = 0, 0, 0, 0, 11, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 17 (n = 0, 0, 0, 0, 0, 11)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 22 (n = 0, 0, 0, 0, 10, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)

Day 41 (n = 0, 0, 0, 22, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	199.10 (84.57 to 468.75)

End point values	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: ng*hr/mL				
geometric mean (confidence interval 95%)				
Day 1 (n = 6, 0, 0, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 5 (n = 0, 6, 0, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 7 (n = 6, 0, 0, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 9 (n = 0, 0, 4, 23, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 11 (n = 0, 6, 0, 0, 0, 11)	99999 (99999 to 99999)	275.29 (169.33 to 447.48)		
Day 15 (n = 0, 0, 5, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 16 (n = 0, 0, 0, 0, 11, 0)	261.90 (166.58 to 411.74)	99999 (99999 to 99999)		
Day 17 (n = 0, 0, 0, 0, 0, 11)	99999 (99999 to 99999)	246.06 (130.34 to 464.51)		
Day 22 (n = 0, 0, 0, 0, 10, 0)	254.35 (196.10 to 329.9)	99999 (99999 to 99999)		
Day 41 (n = 0, 0, 0, 22, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve FromTime Zero to Extrapolat [AUC (0-inf)] of MEDI0382 (Cohorts 1,2,3,4,5,and 6)

End point title	Area Under the Curve From Time Zero to Extrapolated Infinite Time [AUC (0 - inf)] of MEDI0382 (Cohorts 1, 2, 3, 4, 5, and 6)[20]

End point description:

PK population was analysed for this end point. Here, 'n' denotes number of subjects analysed for specified time points. Arbitrary value '99999' signifies data not applicable as no subject was analysed for the specified time points. 95% CI data was not applicable as only one subject was evaluable; therefore, lower and upper CI values are presented with arbitrary values of '9.99999' and '999.999', respectively for the specified time points.

End point type	Secondary

End point timeframe:

C1 (D1 & D7), C2 (D5 & D11), and C3 (D9 & D15): pre-dose & 0.5, 1, 2, 4, 6, 8, 12, 24 hr post dose and additional 48 hr post dose for C1D7, C2D11, C3D15; C4 (D9 & D41), C5 (D16 & D22), and C6 (D11

& D17): pre-dose & 0.5, 1, 2, 4, 6, 8, 12, 24 hr post dose

Notes:

[20] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: ng*hr/mL				
geometric mean (confidence interval 95%)				
Day 1 (n = 1, 0, 0, 0, 0, 0)	103.46 (9.99999 to 999.999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 5 (n = 0, 2, 0, 0, 0, 0)	99999 (99999 to 99999)	207.15 (11.98 to 3580.41)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 7 (n = 3, 0, 0, 0, 0, 0)	184.68 (107.76 to 316.51)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 9 (n = 0, 0, 1, 13, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	242.60 (9.99999 to 999.999)	238.22 (80.99 to 700.67)
Day 11 (0, 6, 0, 0, 0, 0)	99999 (99999 to 99999)	215.80 (112.90 to 412.47)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 15 (n = 0, 0, 5, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	271.84 (119.33 to 619.24)	99999 (99999 to 99999)
Day 16 (n = 0, 0, 0, 0, 6, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 17 (n = 0, 0, 0, 0, 0, 4)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 22 (n = 0,0, 0, 0, 4, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 41 (n = 0, 0, 0, 11, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	262.17 (99.79 to 688.77)

End point values	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: ng*hr/mL				
geometric mean (confidence interval 95%)				
Day 1 (n = 1, 0, 0, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 5 (n = 0, 2, 0, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 7 (n = 3, 0, 0, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 9 (n = 0, 0, 1, 13, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Day 11 (0, 6, 0, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 15 (n = 0, 0, 5, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 16 (n = 0, 0, 0, 0, 6, 0)	317.93 (182.24 to 554.64)	99999 (99999 to 99999)		
Day 17 (n = 0, 0, 0, 0, 0, 4)	99999 (99999 to 99999)	327.28 (249.98 to 428.49)		
Day 22 (n = 0,0, 0, 0, 4, 0)	294.60 (172.52 to 503.05)	99999 (99999 to 99999)		
Day 41 (n = 0, 0, 0, 11, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of M (Cohorts 1, 2, 3, 4, 5, and 6)

End point title	Maximum Observed Plasma Concentration (Cmax) of MEDI0382 (Cohorts 1, 2, 3, 4, 5, and 6)[21]

End point description:

PK population was analysed for this end point. Here, 'n' denotes number of subjects analysed for specified time points. Arbitrary value '99999' signifies data not applicable as no subject was analysed for the specified time points.

End point type	Secondary

End point timeframe:

C1 (D1 & D7), C2 (D5 & D11), and C3 (D9 & D15): pre-dose & 0.5, 1, 2, 4, 6, 8, 12, 24 hr post dose and additional 48 hr post dose for C1D7, C2D11, C3D15; C4 (D9 & D41), C5 (D16 & D22), and C6 (D11 & D17): pre-dose & 0.5, 1, 2, 4, 6, 8, 12, 24 hr post dose

Notes:

[21] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: ng/mL				
geometric mean (confidence interval 95%)				
Day 1 (n = 6, 0, 0, 0, 0, 0)	4.97 (0.33 to 7.41)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 5 (n = 0, 6, 0, 0, 0,0)	99999 (99999 to 99999)	9.66 (4.68 to 19.95)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 7 (n = 6, 0, 0, 0, 0, 0)	6.26 (3.36 to 11.67)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 9 (n = 0, 0, 6, 23, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	10.57 (6.33 to 17.66)	11.64 (3.16 to 42.94)

Day 11 (n = 0, 6, 0, 0, 0, 11)	99999 (99999 to 99999)	9.57 (4.63 to 19.79)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 15 (n = 0, 0, 5, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	10.97 (4.62 to 26.06)	99999 (99999 to 99999)
Day 16 (n = 0, 0, 0, 0, 11, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 17 (n = 0, 0, 0, 0, 0, 11)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 22 (n = 0, 0, 0, 0, 10, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 41 (n = 0, 0, 0, 22, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	13.42 (4.77 to 37.75)

End point values	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: ng/mL				
geometric mean (confidence interval 95%)				
Day 1 (n = 6, 0, 0, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 5 (n = 0, 6, 0, 0, 0,0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 7 (n = 6, 0, 0, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 9 (n = 0, 0, 6, 23, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 11 (n = 0, 6, 0, 0, 0, 11)	99999 (99999 to 99999)	13.69 (5.73 to 32.71)		
Day 15 (n = 0, 0, 5, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 16 (n = 0, 0, 0, 0, 11, 0)	17.65 (8.82 to 35.29)	99999 (99999 to 99999)		
Day 17 (n = 0, 0, 0, 0, 0, 11)	99999 (99999 to 99999)	15.55 (7.55 to 32.01)		
Day 22 (n = 0, 0, 0, 0, 10, 0)	15.77 (10.02 to 24.8)	99999 (99999 to 99999)		
Day 41 (n = 0, 0, 0, 22, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Plasma Concentration (Cmin) of M 1, 2, 3, 4, 5, and 6)

End point title	Minimum Observed Plasma Concentration (Cmin) of MEDI0382 (Cohorts 1, 2, 3, 4, 5, and 6)[22]

End point description:

PK population was analysed for this end point. Here, 'n' denotes number of subjects analysed for specified time points. Arbitrary value '99999' signifies data not applicable as no subject was analysed for the specified time points.

End point type	Secondary

End point timeframe:

C1 (D1 & D7), C2 (D5 & D11), and C3 (D9 & D15): pre-dose & 0.5, 1, 2, 4, 6, 8, 12, 24 hr post dose and additional 48 hr post dose for C1D7, C2D11, C3D15; C4 (D9 & D41), C5 (D16 & D22), and C6 (D11 & D17): pre-dose & 0.5, 1, 2, 4, 6, 8, 12, 24 hr post dose

Notes:

[22] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: ng/mL				
geometric mean (confidence interval 95%)				
Day 1 (n = 6, 0, 0, 0, 0, 0)	0.705 (0.33 to 1.49)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 5 (n = 0, 6, 0, 0, 0, 0)	99999 (99999 to 99999)	2.685 (1.06 to 6.79)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 7 (n = 6, 0, 0, 0, 0, 0)	2.372 (1.18 to 4.78)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 9 (n = 0, 0, 6, 23, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	3.521 (2.16 to 5.75)	2.635 (0.79 to 8.83)
Day 11 (n = 0, 6, 0, 0, 0, 11)	99999 (99999 to 99999)	3.59 (1.62 to 7.94)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 15 (n = 0, 0, 5, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	4.973 (2.24 to 11.05)	99999 (99999 to 99999)
Day 16 (n = 0, 0, 0, 0, 11, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 17 (n = 0, 0, 0, 0, 0, 11)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 22 (n = 0, 0, 0, 0, 10, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 41 (n = 0, 0, 0, 22, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	3.378 (1.03 to 11.04)

End point values	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: ng/mL				
geometric mean (confidence interval 95%)				
Day 1 (n = 6, 0, 0, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 5 (n = 0, 6, 0, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 7 (n = 6, 0, 0, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 9 (n = 0, 0, 6, 23, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Day 11 (n = 0, 6, 0, 0, 0, 11)	99999 (99999 to 99999)	3.586 (1.45 to 8.88)		
Day 15 (n = 0, 0, 5, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		
Day 16 (n = 0, 0, 0, 0, 11, 0)	4.062 (1.68 to 9.84)	99999 (99999 to 99999)		
Day 17 (n = 0, 0, 0, 0, 0, 11)	99999 (99999 to 99999)	4.766 (2.74 to 8.3)		
Day 22 (n = 0, 0, 0, 0, 10, 0)	5.21 (1.97 to 13.81)	99999 (99999 to 99999)		
Day 41 (n = 0, 0, 0, 22, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Plasma Concentrat MEDI0382 (Cohorts 1, 2, 3, 4, 5, and 6)

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax) of MEDI0382 (Cohorts 1, 2, 3, 4, 5, and 6)[23]

End point description:

PK population was analysed for this end point. Here, 'n' denotes number of subjects analysed for specified time points. Arbitrary value '99999' signifies data not applicable as no subject was analysed for the specified time points.

End point type	Secondary

End point timeframe:

C1 (D1 & D7), C2 (D5 & D11), and C3 (D9 & D15): pre-dose & 0.5, 1, 2, 4, 6, 8, 12, 24 hr post dose and additional 48 hr post dose for C1D7, C2D11, C3D15; C4 (D9 & D41), C5 (D16 & D22), and C6 (D11 & D17): pre-dose & 0.5, 1, 2, 4, 6, 8, 12, 24 hr post dose

Notes:

[23] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: hr				
median (full range (min-max))				
Day 1 (n = 6, 0, 0, 0, 0, 0)	8 (6 to 8)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 5 (0, 6, 0, 0, 0, 0)	99999 (99999 to 99999)	6 (4 to 8)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 7 (n = 6, 0, 0, 0, 0, 0)	6 (4 to 6)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 9 (n = 0, 0, 6, 23, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	6 (6 to 8)	4 (1 to 6)
Day 11 (n = 0, 6, 0, 0, 0, 11)	99999 (99999 to 99999)	6 (4 to 6)	99999 (99999 to 99999)	99999 (99999 to 99999)
Day 15 (n = 0, 0, 5, 0, 0, 0)	99999 (99999 to 99999)	99999 (99999 to 99999)	6 (4 to 8)	99999 (99999 to 99999)

Notes:

[24] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: Subjects	0	0	0	0

End point values	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg	Cohort 4: Placebo	Cohort 1: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	26	3
Units: Subjects	0	0	0	0

End point values	Cohort 2: Placebo	Cohort 3: Placebo	Cohort 5: Placebo	Cohort 6: Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	5	5
Units: Subjects	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change FromBaseline in Insulin AUC0-4h a (Cohorts 1,2,3,4,5,and 6)

End point title	Percent Change From Baseline in Insulin AUC0-4h after MMT to EOT (Cohorts 1, 2, 3, 4, 5, and 6)[25]

End point description:

Mixed-meal test involved consumption of a standardized meal (nutritional supplement containing the components of fat, carbohydrate and protein, which make up a standard MMT) within 5 minutes, and timed serial blood samples were obtained for measurement of glucose and parameters related to glucose metabolism just before and 4 hrs after consumption of the standardized meal (with no additional food intake during this time). PD population was analysed for this end point.

End point type	Secondary

End point timeframe:

0 minutes before; and 15, 30, 45, 60, 90, 120, 180, and 240 minutes post SMI on Baseline (Day -1) and EOT (Day 7 for Cohort 1; Day 11 for Cohort 2; Day 15 for Cohort 3; Day 41 for Cohort 4; Day 22 for Cohort 5; and Day 17 for Cohort 6)

Notes:

[25] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: Percent change				
arithmetic mean (standard deviation)	-9.37 (± 29.17)	36.32 (± 35.21)	-17.47 (± 38.84)	-1.17 (± 44.20)

End point values	Cohort 5: MEDI0382 300 mcg	Cohort 6: MEDI0382 300 mcg	Cohort 4: Placebo	Cohort 1: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	26	3
Units: Percent change				
arithmetic mean (standard deviation)	1.01 (± 31.00)	-7.72 (± 37.03)	-8.63 (± 32.33)	10.83 (± 21.33)

End point values	Cohort 2: Placebo	Cohort 3: Placebo	Cohort 5: Placebo	Cohort 6: Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	5	5
Units: Percent change				
arithmetic mean (standard deviation)	-3.67 (± 13.76)	-20.43 (± 68.82)	-17.70 (± 16.47)	-8.18 (± 28.34)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change FromBaseline in Proinsulin AUC0-4 (Cohorts 1,2,3,and 4)

End point title	Percent Change From Baseline in Proinsulin AUC0-4h after MMT to EOT (Cohorts 1, 2, 3, and 4)[26]

End point description:

Mixed-meal test involved consumption of a standardized meal (nutritional supplement containing the components of fat, carbohydrate and protein, which make up a standard MMT) within 5 minutes, and timed serial blood samples were obtained for measurement of glucose and parameters related to glucose metabolism just before and 4 hrs after consumption of the standardized meal (with no additional food intake during this time). PD population was analysed for this end point.

End point type	Secondary

End point timeframe:

0 minutes before; and 15, 30, 45, 60, 90, 120, 180, and 240 minutes post SMI on Baseline (Day -1) and EOT (Day 7 for Cohort 1; Day 11 for Cohort 2; Day 15 for Cohort 3; Day 41 for Cohort 4)

Notes:

[26] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: Percent change				
arithmetic mean (standard deviation)	-52.10 (± 36.29)	-36.77 (± 19.62)	-54.13 (± 26.40)	-47.93 (± 22.12)

End point values	Cohort 4: Placebo	Cohort 1: Placebo	Cohort 2: Placebo	Cohort 3: Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	3	3	3
Units: Percent change				
arithmetic mean (standard deviation)	-29.72 (± 31.13)	-3.27 (± 38.92)	-33.13 (± 40.07)	81.27 (± 77.21)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in C-peptide AUC0-4h (Cohorts 1, 2, 3, and 4)

End point title	Percent Change From Baseline in C-peptide AUC0-4h after MMT to EOT (Cohorts 1, 2, 3, and 4)[27]

End point description:

Mixed-meal test involved consumption of a standardized meal (nutritional supplement containing the components of fat, carbohydrate and protein, which make up a standard MMT) within 5 minutes, and timed serial blood samples were obtained for measurement of glucose and parameters related to glucose metabolism just before and 4 hrs after consumption of the standardized meal (with no additional food intake during this time). PD population was analysed for this end point.

End point type	Secondary

End point timeframe:

0 minutes before; and 15, 30, 45, 60, 90, 120, 180, and 240 minutes post SMI on Baseline (Day -1) and EOT (Day 7 for Cohort 1; Day 11 for Cohort 2; Day 15 for Cohort 3; Day 41 for Cohort 4)

Notes:

[27] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: Percent change				
arithmetic mean (standard deviation)	-3.82 (± 21.29)	39.78 (± 32.88)	-9.07 (± 27.27)	15.66 (± 42.35)

End point values	Cohort 4: Placebo	Cohort 1: Placebo	Cohort 2: Placebo	Cohort 3: Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	3	3	3
Units: Percent change				
arithmetic mean (standard deviation)	8.08 (± 32.12)	10.17 (± 5.05)	-1.43 (± 6.02)	79.37 (± 91.56)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change FromBaseline in Incretin AUC0-4h (Cohorts 1,2,3,and 4)

End point title	Percent Change From Baseline in Incretin AUC0-4h after MMT to EOT (Cohorts 1, 2, 3, and 4)[28]

End point description:

Mixes-meal test involved consumption of a standardized meal (nutritional supplement containing the components of fat, carbohydrate and protein, which make up a standard MMT) within 5 minutes, and timed serial blood samples were obtained for measurement of glucose and parameters related to glucose metabolism just before and 4 hrs after consumption of the standardized meal (with no additional food intake during this time). Incretins included glucagon-like peptide-1 (GLP-1; active and inactive both), glucagon, and gastric inhibitory peptide (GIP). PD population was analysed for this end point. Here, 'n' denotes number of subjects analysed for specified parameters. Arbitrary value '999999' signifies standard deviation not applicable as only one subject was evaluable for the specified parameter.

End point type	Secondary

End point timeframe:

0 minutes before; and 15, 30, 45, 60, 90, 120, 180, and 240 minutes post SMI on Baseline (Day -1) and EOT (Day 7 for Cohort 1; Day 11 for Cohort 2; Day 15 for Cohort 3; Day 41 for Cohort 4)

Notes:

[28] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Cohort 1: MEDI0382 100 mcg	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg	Cohort 4: MEDI0382 200 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	7	25
Units: Percent change				
arithmetic mean (standard deviation)				

GLP-1, Active: Change at EOT (n=6,6,5,19,2,3,3,24)	-33.67 (± 16.84)	-50.45 (± 12.30)	-40.36 (± 26.90)	-49.73 (± 22.88)
GLP-1, Inactive:Change at EOT (n=1,3,3,8,1,1,2,14)	0.70 (± 99999)	-10.93 (± 22.36)	-8.07 (± 11.30)	-28.85 (± 16.73)
Glucagon: Change at EOT (n=4,5,2,12,2,3,3,18)	-20.25 (± 25.45)	-38.12 (± 16.33)	-3.05 (± 36.56)	-30.17 (± 25.56)
GIP: Change at EOT (n=2,5,5,12,2,2,2,17)	-46.50 (± 14.85)	-27.08 (± 25.03)	-21.34 (± 39.48)	-37.38 (± 23.14)

End point values	Cohort 4: Placebo	Cohort 1: Placebo	Cohort 2: Placebo	Cohort 3: Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	26	3	3	3
Units: Percent change				
arithmetic mean (standard deviation)				
GLP-1, Active: Change at EOT (n=6,6,5,19,2,3,3,24)	1.63 (± 26.43)	8.30 (± 13.15)	-10.40 (± 10.47)	-2.87 (± 20.32)
GLP-1, Inactive:Change at EOT (n=1,3,3,8,1,1,2,14)	3.99 (± 29.59)	-20.30 (± 99999)	-22.90 (± 99999)	1.75 (± 29.20)
Glucagon: Change at EOT (n=4,5,2,12,2,3,3,18)	-1.76 (± 21.47)	-13.85 (± 18.60)	-17.53 (± 19.46)	-18.73 (± 21.59)
GIP: Change at EOT (n=2,5,5,12,2,2,2,17)	-6.60 (± 19.43)	18.00 (± 2.83)	4.10 (± 24.61)	-6.30 (± 7.35)

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

From Day 1 to follow-up period (28 days after the last study dose for each cohort [approximately 60 days])

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Cohort 1: MEDI0382 100 mcg

Reporting group description:

Subjects received MEDI0382 100 mcg SC once daily from Day 1 to Day 7.

Reporting group title	Cohort 1: Placebo

Reporting group description:

Subjects received placebo matched to (MEDI0382 100 mcg) SC once daily from Day 1 to Day 7.

Reporting group title	Cohort 2: Placebo

Reporting group description:

Subjects received placebo (matched to MEDI0382 100 mcg) SC once daily for at least 4 days (Day 1 to Day 4) and thereafter, an up titrated dose of placebo (matched to MEDI0382 150 mcg) SC once daily for 7 days (Day 5 to Day 11).

Reporting group title	Cohort 3: Placebo

Reporting group description:

Participants received placebo (matched to MEDI0382 100 mcg) SC once daily for at least 4 days (Day 1 to Day 4); thereafter, an up titrated dose of placebo (matched to MEDI0382 150 mcg) SC once daily for 4 days (Day 5 to Day 8); followed by second up titrated dose of placebo (matched to MEDI0382 200 mcg) SC once daily for 7 days (Day 9 to Day 15).

Reporting group title	Cohort 2: MEDI0382 150 mcg

Reporting group description:

Subjects received MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4) and thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 7 days (Day 5 to Day 11).

Reporting group title	Cohort 3: MEDI0382 200 mcg

Reporting group description:

Subjects received MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4); thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 4 days (Day 5 to Day 8); followed by second up titrated dose of MEDI0382 200 mcg SC once daily for 7 days (Day 9 to Day 15).)

Reporting group title	Cohort 4: Placebo

Reporting group description:

Subjects received placebo (matched to MEDI0382 100 mcg) SC once daily for at least 4 days (Day 1 to Day 4); thereafter, an up titrated dose of placebo (matched to MEDI0382 150 mcg) SC once daily for 4 days (Day 5 to Day 8); followed by second up titrated dose of placebo (matched to MEDI0382 200 mcg) SC once daily for 4 days (Day 9 to Day 12), then a further placebo (matched to MEDI0382 200 mcg) SC once daily for 28 days (Day 13 to Day 40) at home-dosing; followed by placebo (matched to MEDI0382 200 mcg) SC once daily for 1 day in hospital (Day 41).

Reporting group title	Cohort 4: MEDI0382 200 mcg

Reporting group description:

Subjects received MEDI0382 100 mcg SC once daily for at least 4 days (Day 1 to Day 4); thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 4 days (Day 5 to Day 8); followed by second up titrated dose of MEDI0382 200 mcg SC once daily for 4 days (Day 9 to Day 12), then a further MEDI0382 200 mcg SC once daily for 28 days (Day 13 to Day 40) at home-dosing; followed by MEDI0382 200 mcg SC once daily for 1 day in hospital (Day 41).

Reporting group title	Cohort 5: Placebo

Reporting group description:

Subjects received placebo (matched to MEDI0382 100 mcg) SC once daily for at least 5 days (Day 1 to

Day 5); thereafter, an up titrated dose of placebo (matched to MEDI0382 150 mcg) SC once daily for 5 days (Day 6 to Day 10); then a second up titrated dose of placebo (matched to MEDI0382 200 mcg) SC once daily for 5 days (Day 11 to Day 15); followed by third up titrated dose of placebo (matched to MEDI0382 300 mcg) SC once daily for 7 days (Day 16 to Day 22).

Reporting group title	Cohort 5: MEDI0382 300 mcg

Reporting group description:

Subjects received MEDI0382 100 mcg SC once daily for at least 5 days (Day 1 to Day 5); thereafter, an up titrated dose of MEDI0382 150 mcg SC once daily for 5 days (Day 6 to Day 10); then a second up titrated dose of MEDI0382 200 mcg SC once daily for 5 days (Day 11 to Day 15); followed by third up titrated dose of MEDI0382 300 mcg SC once daily for 7 days (Day 16 to Day 22).

Reporting group title	Cohort 6: Placebo

Reporting group description:

Subjects received placebo (matched to MEDI0382 100 mcg) SC once daily for at least 5 days (Day 1 to Day 5); thereafter, an up titrated dose of placebo (matched to MEDI0382 200 mcg) SC once daily for 5 days (Day 6 to Day 10); followed by a second up titrated dose of placebo (matched to MEDI0382 300 mcg) SC once daily for 7 days (Day 11 to Day 17).

Reporting group title	Cohort 6: MEDI0382 300 mcg

Reporting group description:

Subjects received MEDI0382 100 mcg SC once daily for at least 5 days (Day 1 to Day 5); thereafter, an up titrated dose of MEDI0382 200 mcg SC once daily for 5 days (Day 6 to Day 10); followed by a second up titrated dose of MEDI0382 300 mcg SC once daily for 7 days (Day 11 to Day 17).

Serious adverse events	Cohort 1: MEDI0382 100 mcg	Cohort 1: Placebo	Cohort 2: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 3: Placebo	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Eye disorders			
Diplopia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (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			
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 4: Placebo	Cohort 4: MEDI0382 200 mcg	Cohort 5: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (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
Infections and infestations			
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 5: MEDI0382 300 mcg	Cohort 6: Placebo	Cohort 6: MEDI0382 300 mcg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (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			
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (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: 0 %

Non-serious adverse events	Cohort 1: MEDI0382 100 mcg	Cohort 1: Placebo	Cohort 2: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	2 / 3 (66.67%)	3 / 3 (100.00%)
Vascular disorders			
Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Early satiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Feeling hot			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site discolouration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Medical device site erosion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Medical device site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Medical device site pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Medical device site rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Medical device site reaction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergic oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal mucosal ulcer			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood pressure diastolic increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood pressure systolic increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram st segment depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Burns second degree			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Atrioventricular block second degree			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Extrasystoles			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia			

subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	7	1
Tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ventricular extrasystoles			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Ventricular tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Arrhythmia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness postural			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	3 / 6 (50.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			

subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Eructation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Faeces hard			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Faeces soft			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infrequent bowel movements			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Intra-abdominal haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pancreatolithiasis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Regurgitation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Ankle deformity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 3: Placebo	Cohort 2: MEDI0382 150 mcg	Cohort 3: MEDI0382 200 mcg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	5 / 6 (83.33%)	7 / 7 (100.00%)
Vascular disorders			
Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypotension			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Early satiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Feeling hot			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injection site discolouration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Injection site erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injection site haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	5	0	0
Injection site pain			

,QMHFWLRQ VLWH SUXULWXV
VXEMHFWV DIIHFWHG H[SRVHG
RFFXUUHQFHV DOO

,QMHFWLRQ VLWH UHDFWLRQ
VXEMHFWV DIIHFWHG H[SRVHG
RFFXUUHQFHV DOO

0DODLVH
VXEMHFWV DIIHFWHG H[SRVHG
RFFXUUHQFHV DOO

0HGLFDO GHYLFH VLWH HURVLRQ
VXEMHFWV DIIHFWHG H[SRVHG
RFFXUUHQFHV DOO

0HGLFDO GHYLFH VLWH HU\WKHPD
VXEMHFWV DIIHFWHG H[SRVHG
RFFXUUHQFHV DOO

0HGLFDO GHYLFH VLWH LQMXU\
VXEMHFWV DIIHFWHG H[SRVHG
RFFXUUHQFHV DOO

0HGLFDO GHYLFH VLWH LUULWDWLRQ
VXEMHFWV DIIHFWHG H[SRVHG
RFFXUUHQFHV DOO

0HGLFDO GHYLFH VLWH SDLQ
VXEMHFWV DIIHFWHG H[SRVHG
RFFXUUHQFHV DOO

0HGLFDO GHYLFH VLWH SUXULWXV
VXEMHFWV DIIHFWHG H[SRVHG
RFFXUUHQFHV DOO

0HGLFDO GHYLFH VLWH UDVK
VXEMHFWV DIIHFWHG H[SRVHG
RFFXUUHQFHV DOO

0HGLFDO GHYLFH VLWH UHDFWLRQ
VXEMHFWV DIIHFWHG H[SRVHG
RFFXUUHQFHV DOO

2HGHPD SHULSKHUDO

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Immune system disorders			
Allergic oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nasal mucosal ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood pressure diastolic increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Blood pressure systolic increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Electrocardiogram st segment depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Heart rate increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block second degree			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Extrasystoles			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Ventricular extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Ventricular tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Arrhythmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Dizziness postural			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	4 / 7 (57.14%)
occurrences (all)	6	3	6
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Visual acuity reduced			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 7 (14.29%)
occurrences (all)	0	2	1
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	8	0	2
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	3 / 7 (42.86%)
occurrences (all)	0	0	3
Eructation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Faeces discoloured			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Faeces hard			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Faeces soft			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Infrequent bowel movements			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Intra-abdominal haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	3 / 6 (50.00%)	3 / 7 (42.86%)
occurrences (all)	0	7	4
Pancreatolithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Regurgitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	3 / 7 (42.86%)
occurrences (all)	0	2	8
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Ankle deformity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	6 / 7 (85.71%)
occurrences (all)	1	2	6
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 4: Placebo	Cohort 4: MEDI0382 200 mcg	Cohort 5: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 26 (88.46%)	22 / 25 (88.00%)	4 / 5 (80.00%)
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Phlebitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Thrombophlebitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Early satiety			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Fatigue			

subjects affected / exposed	0 / 26 (0.00%)	5 / 25 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Feeling hot			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Injection site discolouration			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	0 / 26 (0.00%)	3 / 25 (12.00%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Injection site haematoma			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Injection site haemorrhage			
subjects affected / exposed	2 / 26 (7.69%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Injection site pain			
subjects affected / exposed	0 / 26 (0.00%)	2 / 25 (8.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Injection site pruritus			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injection site reaction			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	6	0
Malaise			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Medical device site erosion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Medical device site erythema			
subjects affected / exposed	2 / 26 (7.69%)	3 / 25 (12.00%)	0 / 5 (0.00%)
occurrences (all)	2	3	0
Medical device site injury			

subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nasal mucosal ulcer			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood pressure diastolic increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	2 / 26 (7.69%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	6	5	0
Blood pressure systolic increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram st segment depression			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lipase increased			

subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Atrial fibrillation			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block second degree			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Extrasystoles			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Sinus tachycardia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Supraventricular extrasystoles			

subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Supraventricular tachycardia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Ventricular tachycardia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Arrhythmia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 26 (19.23%)	4 / 25 (16.00%)	0 / 5 (0.00%)
occurrences (all)	6	6	0
Dizziness postural			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 26 (0.00%)	2 / 25 (8.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	2 / 26 (7.69%)	9 / 25 (36.00%)	1 / 5 (20.00%)
occurrences (all)	6	10	1
Paraesthesia			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Presyncope			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Sciatica			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 26 (0.00%)	3 / 25 (12.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Abdominal distension			
subjects affected / exposed	0 / 26 (0.00%)	6 / 25 (24.00%)	0 / 5 (0.00%)
occurrences (all)	0	9	0
Abdominal pain			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	1	4	0
Abdominal pain lower			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Constipation			

subjects affected / exposed	3 / 26 (11.54%)	6 / 25 (24.00%)	1 / 5 (20.00%)
occurrences (all)	5	7	1
Diarrhoea			
subjects affected / exposed	3 / 26 (11.54%)	4 / 25 (16.00%)	1 / 5 (20.00%)
occurrences (all)	4	6	1
Dry mouth			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	1 / 26 (3.85%)	7 / 25 (28.00%)	0 / 5 (0.00%)
occurrences (all)	1	7	0
Eructation			
subjects affected / exposed	1 / 26 (3.85%)	4 / 25 (16.00%)	0 / 5 (0.00%)
occurrences (all)	1	4	0
Faeces discoloured			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Faeces hard			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Faeces soft			
subjects affected / exposed	2 / 26 (7.69%)	2 / 25 (8.00%)	0 / 5 (0.00%)
occurrences (all)	3	2	0
Flatulence			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infrequent bowel movements			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Intra-abdominal haematoma			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Nausea			

subjects affected / exposed	5 / 26 (19.23%)	13 / 25 (52.00%)	1 / 5 (20.00%)
occurrences (all)	7	39	2
Pancreatolithiasis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Regurgitation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 26 (0.00%)	8 / 25 (32.00%)	0 / 5 (0.00%)
occurrences (all)	0	40	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 26 (3.85%)	2 / 25 (8.00%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Dermatitis contact			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Pruritus			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	1 / 26 (3.85%)	3 / 25 (12.00%)	0 / 5 (0.00%)
occurrences (all)	1	3	0
Skin reaction			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Chromaturia			

subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Micturition urgency			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Ankle deformity			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 26 (3.85%)	2 / 25 (8.00%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Flank pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Cellulitis			

subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gastrointestinal infection			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	6 / 26 (23.08%)	4 / 25 (16.00%)	1 / 5 (20.00%)
occurrences (all)	7	4	1
Tonsillitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 26 (0.00%)	5 / 25 (20.00%)	1 / 5 (20.00%)
occurrences (all)	0	5	1
Hypoglycaemia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Increased appetite			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Cohort 5: MEDI0382 300 mcg	Cohort 6: Placebo	Cohort 6: MEDI0382 300 mcg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 11 (90.91%)	2 / 5 (40.00%)	10 / 12 (83.33%)
Vascular disorders			

Haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Early satiety			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Feeling hot			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site discolouration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site haemorrhage			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Injection site pruritus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Medical device site erosion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Medical device site erythema			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Medical device site injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Medical device site irritation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Medical device site pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Medical device site pruritus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Medical device site rash			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Medical device site reaction			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergic oedema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Dysphonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasal mucosal ulcer			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood pressure diastolic increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Blood pressure increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood pressure systolic increased			
subjects affected / exposed	1 / 11 (9.09%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	1	4	0
Body temperature increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram st segment depression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	3	0	1
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block second degree			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Extrasystoles			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ventricular tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Arrhythmia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	2 / 12 (16.67%)
occurrences (all)	2	0	2
Dizziness postural			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	3 / 11 (27.27%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	3	1	1
Paraesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Visual acuity reduced			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	2 / 12 (16.67%)
occurrences (all)	2	0	2
Dry mouth			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	4 / 11 (36.36%)	0 / 5 (0.00%)	2 / 12 (16.67%)
occurrences (all)	7	0	2
Eructation			
subjects affected / exposed	3 / 11 (27.27%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Faeces discoloured			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0

Faeces hard			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Faeces soft			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Infrequent bowel movements			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Intra-abdominal haematoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	3 / 11 (27.27%)	0 / 5 (0.00%)	5 / 12 (41.67%)
occurrences (all)	6	0	7
Pancreatolithiasis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Regurgitation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Salivary hypersecretion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	3 / 11 (27.27%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	9	0	2
Skin and subcutaneous tissue disorders			
Alopecia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	3 / 12 (25.00%)
occurrences (all)	1	0	4
Pruritus			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	2 / 12 (16.67%)
occurrences (all)	1	0	2
Rash			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin reaction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Micturition urgency			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Ankle deformity			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Arthralgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Flank pain			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 11 (18.18%)	1 / 5 (20.00%)	3 / 12 (25.00%)
occurrences (all)	2	1	3
Tonsillitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 11 (36.36%)	0 / 5 (0.00%)	3 / 12 (25.00%)
occurrences (all)	4	0	3
Hypoglycaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Increased appetite			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 February 2015	Number of anticipated study sites was changed from approximately 3 to 5 to "up to 8" (Section 9.1) • Data for progression from single-ascending dose (SAD) study to Cohort 1 of this multiple-ascending dose (MAD) study were updated (Section 9.4.3.1) • Provision that relevant data for progression from SAD study to the MAD study will be summarized and provided to appropriate regulatory body and central ethics committee was added. Additionally, approval to proceed with MAD study will be obtained from the appropriate regulatory body prior to initiating enrollment was added (Section 9.4.3.1) • Text were added for subject safety (Section 9.4.3.1) • The following text was added for clarification: the decision for progression from Cohort 1 to Cohort 2, and from Cohort 2 to Cohort 3 will be made by Dose Escalation Committee (DEC); relevant data will be summarized and provided to appropriate regulatory body and central ethics committee. And, approval to proceed with Cohort 4 will be obtained from the appropriate regulatory body prior to initiating enrollment (Section 9.4.3.1) • DEC recommendations were updated (Section 9.4.3.1) • Significant vomiting was clarified as "3 or more episodes of vomiting on a single day or across 2 consecutive days, despite adjustment to diet having been made" (Section 9.4.5)• Starting dose reported for SAD study was updated from 30 µg/day to 5 µg/day. Dose rationale was updated. A new table was added (Section 9.2) • A note was added to clarify Inclusion Criterion 9 (about contraception) (Section 9.3.1) • The exclusion criterion "Concurrent participation in another study of any kind is prohibited" was added (Section 9.3.2) • Text was modified to add that an individual subject will not receive any further study drug if that subject has more than 2 symptomatic hypoglycemic events; or persistent hyperglycemia, Section 9.3.3).
14 August 2015	Updated and modified text to include a summary of the safety information and statement regarding the current status from the SAD study (D5670C00001) • Changed text to specify change from baseline in glucose and body weight was to be evaluated (Sections 8 and 9.5.1.1) • Objective 1/endpoint 1 were changed to specify change from baseline to be used to evaluate glucose control, blood sample collection parameters at Day 1 were rationalized (Sections 8 and 9.5.1.1) • Clarified that subjects should be treated with a daily dose of statin at baseline. Amended text to include measurement of metformin concentration (Sections 9.5.1.1 and 9.7.1.4) • Analysis of non-esterified fatty acids and beta-hydroxybutyrate were added to the lipid endpoints (Sections 9.5.1.1 and 9.7.1.5) • Number of anticipated clinical sites was increased from 8 to 10. In addition, the inclusion of overweight as well as obese subjects was reflected due to the increased range for body weight eligibility (Section 9.1) • Amended text to lengthen the screening period from 28 days to 42 days • Edited text to clarify that subjects were admitted to the clinic 2 evenings before the receipt of study drug • The Day 1 assessment of MMT and blood samples for glucose metabolism panel were removed from the protocol (Section 9.5.1.2) • Data form SAD study wad added (Section 9.2) • Amended the dose escalation stopping decision and cardiac stopping criteria (Section 9.4.3.1) • Inclusion, exclusion and removal of subjects from therapy or assessment sections were amended (Section 9.3.1, Section 9.3.2, Section 9.3.3) • Schedule of screening procedures (GFR, glucose) and a predose blood sample (Section 9.5.1.2) • Identity of study drug text was modified (Section 9.4.2) • Dose preparation steps were modified • Process of SAE reporting by the Sponsor and the implementation of electronic SAE reporting were modified • Appendix 6 was added • References were updated • Appendix 2 was revised.

10 October 2015	Text was amended to reflect a reduction in the maximum dose that was to administered in this study from 400 to 300 µg/day (Section 9.4.3.1) • Amended text to provide the predicted safety margins for the 300 µg/day dose (Section 9.2) • An exclusion criterion excluding subjects with a history of lactic acidosis or ketoacidosis was added (Section 9.3.2) • Text was amended to include collection of finger prick glucose samples 15 minutes prior to and 2 hours after breakfast and before going to bed in addition to the measures taken before and after the mid-day and evening meals to increase glucose monitoring (Section 9.5.1.2) • The footnotes describing the timing of ECG capture were corrected to be consistent with the measurements indicated in the tables (Section 9.5.1.2) • The volume of injection was reduced consistent with the reduction in dose from 400 to 300 µg • The needle gauge was amended from 27G to 29G.
18 March 2016	Texts were modified to be consistent with the updated results from SAD study (Section 9.2) • Inclusion criteria related to statin therapy was removed (Sections 9.3.1 and 9.4.7.1) • Exploratory objectives/endpoints and their assessment methods were added (Sections 8.3, 9.5.1.1, 9.5.1.2, 9.7.1.3, and 9.7.1.5) • Study design was changed related to telemetry and return home for subjects in Cohorts 3 and 4 (Sections 9.1 and 9.5.1.2) • Screening window was changed from 42 days to 60 days • Requirement that regulatory approval be obtained "prior to initiating enrollment" in order to proceed with Cohort 4 was changed to "prior to initiating dosing" • Age range for inclusion criteria, upper and lower range of screening HbA1c, and inclusion criterion for HbA1c were changed (Section 9.1 and 9.3.1) • Exclusion criteria for fasting blood glucose was removed; upper range of abnormal systolic and diastolic BP was increased and text was added to note for vital signs criteria and exclusion criteria concerning QRS duration; exclusion criteria regarding subject's use of weight loss diets/agents, and conditions where MRI is contraindicated were added for Cohort 4 only if site has access to an MRI (Section 9.3.2) • Exclusion criterion of "history of cancer, with exception of non-melanoma skin cancer" was changed to "history of cancer within the last 10 years, with the exception of non-melanoma skin cancer (Section 9.3.2).
27 April 2016	The text was changed from "up to 10 study sites" to "approximately 10 study sites" (Section 9.1) • The study design was reverted to state that subjects will be admitted to and remain in the unit for all doses and all dose levels during the up-titration period. Relevant text was modified to reflect the reversion in study design (Section 9.5.1.2) • The age range for inclusion in the study was changed from 18 through <= 69 years to 18 through <= 65 years and relevant text was modified to reflect this change (Sections 9.1 and 9.3.1) • The upper range of screening HbA1c was changed from 9.0% to 8.5% (Sections 9.1 and 9.3.1) • The exclusion criterion of "fasting blood glucose >= 200 mg/dL (11.11 mmol/L)" was reinstated (Section 9.3.2) • The upper range of abnormal systolic BP was decreased by 10 mm Hg for both age groups (< 60 years old, >= 60 years old), and the upper range of abnormal diastolic BP was decreased by 10 mm Hg (Section 9.3.2).
21 July 2016	Exploratory endpoint 7 was updated (Sections 9.5.1.1)• Text was changed from "approximately 10 study sites" to "approximately 12 study sites"; "48 subjects" to "approximately 48 subjects" (Section 9.1) • Text was revised to clarify maximum dose in the study (Section 9.1); widen window of pre-dose MRI scan (Table 9.5.1.2-4); criteria of MRI scan (Table 9.5.1.1-1 and Table 9.5.1.2-4); clarification for post dose MRI scan (Table 9.5.1.1-1 and Table 9.5.1.2-4); subjects may be rescreened more than once; subjects will wear the accelerometer on the nondominant wrist continuously for approximately 7 days (Section 9.5.1.3); diluent is not required for Cohort 4 and that a 0.3 mL insulin syringe will be utilized during the in clinic and at-home treatment periods • summary of SAD Study D5670C00001 was revised and Cohort 1-3 safety data from this MAD study was included • Exclusion criteria 35 was revised • Serum chemistries panel note, daily diary training, dose preparation steps were updated.
25 August 2016	Text was reverted to specify that subjects may be rescreened only once (Section 9.4.3) • Text was reverted to state that additional subjects may be screened and available to ensure that a sufficient number of subjects are randomized into each cohort (Section 9.4.3).

23 September 2016	Text was added/updated to: include Part C of the study and to describe the details of Cohorts 5 and 6 (Sections 9.1, 9.2, and 9.4.1, and Figure 9.1-1); provide rationale for using the 300 µg dose in Part C; add study endpoints related to the addition of Part C, including Cohorts 5 and 6, to the study (Section 9.5.1.1); describe the inpatient periods and clinic visits for Cohorts 5 and 6; concerning the timing of the MMT procedures for Cohorts 5 and 6; to make clear that, for Cohorts 4, 5, and 6, the last PK sample was collected 24 hours after the last dose; provide details of the sample size calculation resulting in 32 subjects in total in Cohorts 5 and 6 (Section 9.7.2); specify 24-hour ABPM was applicable to Cohorts 5 and 6, in addition to Cohort 4 (Section 9.3.2); add Cohorts 5 and 6 to the measuring of body weight during the outpatient periods, and at the 28-day End of Study Visit; describe the sentinel dosing approach for Cohorts 5 and 6 (Section 9.4.3.1); modify description of hypertension; clarify randomization ratio for Cohorts 5 and 6; include 5-day up-titration periods for Cohorts 5 and 6; • 300 µg results were added to the table, and human PK parameters were updated (Section 9.2 and Table 9.2-1) • Number of subjects was increased from 75 to 107 (Sections 9.1 and 9.2) • 'Cohort 4' was removed from description of analysis of efficacy endpoints • Updated the inclusion and exclusion criteria; and safety criteria related to the addition of Part C, including Cohorts 5 and 6, to the study • Modified the C SSRS assessment Cohort 4 table (Table 9.5.1.2-4) and 24-hour ABPM assessment • Procedures for Cohorts 5 and 6, were added (Table 9.5.1.2-6 and Table 9.5.1.2-7).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported