Clinical trial results:
A Phase 2b, Randomised, Parallel, Double-Blind Placebo-Controlled and Open-Label Active Comparator Study to Evaluate the Efficacy and Safety of Cotadutide in the Treatment of Overweight and Obese Subjects with Type 2 Diabetes Mellitus

Summary

EudraCT number	2017-000626-35
Trial protocol	HU CZ SK BG
Global end of trial date	16 July 2019

Results information

Result version number	v1 (current)
This version publication date	21 June 2020
First version publication date	21 June 2020

Trial information

Trial identification

Sponsor protocol code	D5670C00004

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	151 85, Södertälje, Sweden,
Public contact	AstraZenenca Information Center, AstraZeneca, +1 18772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 18772409479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 July 2019
Global end of trial reached?	Yes
Global end of trial date	16 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of 100 µg, 200 µg and 300 µg of cotadutide on HbA1c and body weight versus placebo

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council for Harmonisation/GCP, applicable regulatory requirements, and the AstraZeneca policy on Bioethics and Human Biological Smaples.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 August 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 71
Country: Number of subjects enrolled	Canada: 56
Country: Number of subjects enrolled	Mexico: 61
Country: Number of subjects enrolled	Bulgaria: 78
Country: Number of subjects enrolled	Czech Republic: 63
Country: Number of subjects enrolled	Slovakia: 104
Country: Number of subjects enrolled	Germany: 148
Country: Number of subjects enrolled	Russian Federation: 253
Worldwide total number of subjects	834
EEA total number of subjects	393

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	635
From 65 to 84 years	199
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Date first participant signed informed consent was 2 August 2017 and the date of last participant visit was 14 June 2019. This study was conducted at 20 sites in 8 countries.

Pre-assignment

Screening details:

A total of 1154 subjects consented to participate in the study; 834 participants were randomized and treated. Of the 320 participants not randomized to a treatment group: 307 No longer met study criteria, 9 withdrew consent, 1 was non-compliant with study drug, and 3 did not continue for other reasons.

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:

Placebo / Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)

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

Dosage and administration details:

once daily IV administration

Arm title	Liraglutide

Arm description:

Liraglutide + Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)

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

Dosage and administration details:

6.0 mg/mL once daily SC administration

Arm title	MEDI0382 100 mcg

Arm description:

MEDI0382 low dose / Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)

Arm type	Experimental

Investigational medicinal product name	MEDI0382
Investigational medicinal product code	
Other name	Cotadutide
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mcg once daily IV administration

Arm title	MEDI0382 200 mcg

Arm description:

MEDI0382 mid dose / Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)

Arm type	Experimental
Investigational medicinal product name	MEDI0382
Investigational medicinal product code	
Other name	Cotadutide
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

200 mcg once daily IV administration

Arm title	MEDI0382 300 mcg

Arm description:

MEDI0382 high dose / Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)

Arm type	Experimental
Investigational medicinal product name	MEDI0382
Investigational medicinal product code	
Other name	Cotadutide
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

300 mcg once daily IV administration

Number of subjects in period 1	Placebo	Liraglutide	MEDI0382 100 mcg
Started	112	110	100
Completed	108	105	96
Not completed	4	5	4
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	3	2	2
Adverse event, non-fatal	-	-	1
Other reasons	-	1	-
Lost to follow-up	1	2	1

Number of subjects in period 1	MEDI0382 200 mcg	MEDI0382 300 mcg
Started	256	256
Completed	242	245
Not completed	14	11

Adverse event, serious fatal	2	1
Consent withdrawn by subject	5	7
Adverse event, non-fatal	4	1
Other reasons	1	2
Lost to follow-up	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo / Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)	
Reporting group title	Liraglutide
Reporting group description:	
Liraglutide + Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)	
Reporting group title	MEDI0382 100 mcg
Reporting group description:	
MEDI0382 low dose / Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)	
Reporting group title	MEDI0382 200 mcg
Reporting group description:	
MEDI0382 mid dose / Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)	
Reporting group title	MEDI0382 300 mcg
Reporting group description:	
MEDI0382 high dose / Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)	

Reporting group values	Placebo	Liraglutide	MEDI0382 100 mcg
Number of subjects	112	110	100
Age categorical Units: Subjects			
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)	84	88	78
From 65-84 years	28	22	22
85 years and over	0	0	0
In Utero	0	0	0
Age Continuous Units: Years			
arithmetic mean	57.3	55.5	57.6
standard deviation	± 9.5	± 9.8	± 9.9
Sex: Female, Male Units:			
Female	55	60	57
Male	57	50	43
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	3	3	0
Asian	1	1	0
Black or African American	0	3	1

White	107	103	99
Other	1	0	0

Reporting group values	MEDI0382 200 mcg	MEDI0382 300 mcg	Total
Number of subjects	256	256	834
Age categorical Units: Subjects			
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)	195	190	635
From 65-84 years	61	66	199
85 years and over	0	0	0
In Utero	0	0	0
Age Continuous Units: Years			
arithmetic mean	57.3	56.3	
standard deviation	± 9.9	± 10.2	-
Sex: Female, Male Units:			
Female	147	129	448
Male	109	127	386
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	5	0	11
Asian	3	1	6
Black or African American	3	3	10
White	245	252	806
Other	0	0	1

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo / Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)	
Reporting group title	Liraglutide
Reporting group description:	
Liraglutide + Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)	
Reporting group title	MEDI0382 100 mcg
Reporting group description:	
MEDI0382 low dose / Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)	
Reporting group title	MEDI0382 200 mcg
Reporting group description:	
MEDI0382 mid dose / Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)	
Reporting group title	MEDI0382 300 mcg
Reporting group description:	
MEDI0382 high dose / Metformin tablets, total daily dose of ≥1500 mg (unless only tolerated at a lower dose)	

Primary: Change in HbA1c at Week 14

End point title	Change in HbA1c at Week 14[1]
End point description:	
To assess the effect of 100, 200, 300 µg of cotadutide on HbA1c versus placebo	
End point type	Primary
End point timeframe:	
From baseline to 14 weeks	

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: Analysis for this primary study objective is to assess the effect of 100 µg, 200 µg and 300 µg of cotadutide on HbA1c and
body weight versus placebo.

End point values	Placebo	MEDI0382 100 mcg	MEDI0382 200 mcg	MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	100	256	256
Units: percentage				
least squares mean (confidence interval 95%)	-0.18 (-0.34 to -0.02)	-1.01 (-1.18 to -0.84)	-1.22 (-1.33 to -1.11)	-1.09 (-1.20 to -0.98)

Statistical analyses

Statistical analysis title	Primary Endpoint Analysis
Comparison groups	Placebo v MEDI0382 100 mcg

Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	-0.59

Statistical analysis title	Primary Endpoint Analysis
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.23
upper limit	-0.85

Statistical analysis title	Primary Endpoint Analysis
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.11
upper limit	-0.72

Primary: Percent change in body weight at Week 14

End point title	Percent change in body weight at Week 14[2]

End point description:

To assess the effect of 100, 200, 300 µg of cotadutide on body weight versus placebo

End point type	Primary

End point timeframe:

From baseline to 14 weeks

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Analysis for this primary study objective is to assess the effect of 100 µg, 200 µg and 300 µg of cotadutide on HbA1c and
body weight versus placebo.

End point values	Placebo	MEDI0382 100 mcg	MEDI0382 200 mcg	MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	100	256	256
Units: percentage				
least squares mean (confidence interval 95%)	-0.70 (-1.44 to 0.04)	-2.70 (-3.49 to -1.91)	-3.47 (-3.95 to -2.98)	-4.33 (-4.82 to -3.84)

Statistical analyses

Statistical analysis title	Primary Endpoint Analysis
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.08
upper limit	-0.91

Statistical analysis title	Primary Endpoint Analysis
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.76

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.65
upper limit	-1.87

Statistical analysis title	Primary Endpoint Analysis
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.51
upper limit	-2.73

Secondary: Change in HbA1c at Weeks 26 and 54

End point title	Change in HbA1c at Weeks 26 and 54[3]

End point description:

To assess the effect of 100, 200, and 300 µg of cotadutide on HbA1c versus placebo

End point type	Secondary

End point timeframe:

from baseline to 26 weeks and 54 weeks

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: Analysis for this secondary study objective is to assess the effect of 100 µg, 200 µg and 300 µg of cotadutide on additional
measures of glycaemic control and body weight versus placebo.

End point values	Placebo	MEDI0382 100 mcg	MEDI0382 200 mcg	MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	100	256	256
Units: percentage				
least squares mean (confidence interval 95%)				
from baseline to 26 weeks	-0.40 (-0.58 to -0.22)	-1.06 (-1.25 to -0.87)	-1.22 (-1.34 to -1.10)	-1.12 (-1.24 to -1.00)
from baseline to 54 weeks	-0.44 (-0.63 to -0.24)	-0.96 (-1.16 to -0.75)	-1.06 (-1.19 to -0.93)	-1.01 (-1.14 to -0.88)

Statistical analyses

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 26	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	-0.4

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 26	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	-0.6

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 26	
Comparison groups	Placebo v MEDI0382 300 mcg

Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	-0.51

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 54	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.24

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 54	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	-0.39

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 54	
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.34

Secondary: Percentage of participants achieving an HbA1c target < 7.0%

End point title	Percentage of participants achieving an HbA1c target < 7.0%[4]
End point description: To assess the effect of 100, 200, and 300 µg of cotadutide on percentage of participants achieving an HbA1c target of <7% versus placebo	
End point type	Secondary
End point timeframe: after 14, 26, and 54 weeks	

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Analysis for this secondary study objective is to assess the effect of 100 µg, 200 µg and 300 µg of cotadutide on additional
measures of glycaemic control and body weight versus placebo.

End point values	Placebo	MEDI0382 100 mcg	MEDI0382 200 mcg	MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	100	256	256
Units: participants				
after 14 weeks	19	50	143	143
after 26 weeks	25	48	139	143
after 54 weeks	23	52	125	128

Statistical analyses

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 14	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	6.67
Confidence interval	
level	Other: 92 %
sides	2-sided
lower limit	3.34
upper limit	13.3

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 14	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	9.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.39
upper limit	18.36

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 14	
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	8.52

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.65
upper limit	15.61

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 26	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	3.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.98
upper limit	7.03

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 26	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.13
upper limit	9.34

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 26	
Comparison groups	Placebo v MEDI0382 300 mcg

Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	5.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.02
upper limit	8.97

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 54	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	4.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.61
upper limit	9.36

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 54	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	4.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.62
upper limit	7.89

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 54	
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	4.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.51
upper limit	7.51

Secondary: Percent change in body weight at Weeks 26 and 54

End point title	Percent change in body weight at Weeks 26 and 54[5]
End point description: To assess the effect of 100, 200, and 300 µg of cotadutide on body weight versus placebo	
End point type	Secondary
End point timeframe: from baseline to 26 weeks and 54 weeks	

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: Analysis for this secondary study objective is to assess the effect of 100 µg, 200 µg and 300 µg of cotadutide on additional
measures of glycaemic control and body weight versus placebo.

End point values	Placebo	MEDI0382 100 mcg	MEDI0382 200 mcg	MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	100	256	256
Units: percentage				
least squares mean (confidence interval 95%)				
from baseline to 26 weeks	-1.14 (-1.99 to -0.29)	-3.23 (-4.13 to -2.32)	-3.94 (-4.51 to -3.38)	-4.60 (-5.17 to -4.04)
from baseline to 54 weeks	-0.84 (-1.82 to 0.14)	-3.27 (-4.32 to -2.22)	-3.08 (-3.73 to -2.43)	-4.16 (-4.81 to -3.50)

Statistical analyses

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 26	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.32
upper limit	-0.85

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 26	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.82
upper limit	-1.79

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 26	
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.46

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.48
upper limit	-2.44

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 54	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.86
upper limit	-1

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 54	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.41
upper limit	-1.06

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 54	
Comparison groups	Placebo v MEDI0382 300 mcg

Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.49
upper limit	-2.14

Secondary: Absolute change in body weight

End point title	Absolute change in body weight[6]

End point description:

To assess the effect of 100, 200, and 300 µg of cotadutide on body weight versus placebo

End point type	Secondary

End point timeframe:

from baseline to 14 weeks, 26 weeks and 54 weeks

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: Analysis for this secondary study objective is to assess the effect of 100 µg, 200 µg and 300 µg of cotadutide on additional
measures of glycaemic control and body weight versus placebo.

End point values	Placebo	MEDI0382 100 mcg	MEDI0382 200 mcg	MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	100	256	256
Units: kg				
least squares mean (confidence interval 95%)				
from baseline to 14 weeks	-0.71 (-1.44 to 0.03)	-2.66 (-3.45 to -1.87)	-3.45 (-3.94 to -2.97)	-4.42 (-4.91 to -3.93)
from baseline to 26 weeks	-1.20 (-2.06 to -0.34)	-3.20 (-4.13 to -2.28)	-3.94 (-4.52 to -3.37)	-4.75 (-5.33 to -4.18)
from baseline to 54 weeks	-0.94 (-1.94 to 0.07)	-3.20 (-4.28 to -2.12)	-3.09 (-3.77 to -2.42)	-4.35 (-5.03 to -3.68)

Statistical analyses

Statistical analysis title	Secondary Endpoint Analysis

Statistical analysis description:

Week 14

Comparison groups	Placebo v MEDI0382 100 mcg

Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.03
upper limit	-0.87

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 14	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.63
upper limit	-1.86

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 14	
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	-2.82

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 26	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.27
upper limit	-0.74

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 26	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.78
upper limit	-1.71

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 26	
Comparison groups	Placebo v MEDI0382 300 mcg

Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.59
upper limit	-2.52

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 54	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.003
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.74
upper limit	-0.79

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
Week 54	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.37
upper limit	-0.95

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Week 54	
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.63
upper limit	-2.2

Secondary: Percent change in body weight versus active comparator

End point title	Percent change in body weight versus active comparator[7]
End point description: To assess the effect of 100, 200, and 300 µg of cotadutide on body weight versus liraglutide 1.8 mg once daily	
End point type	Secondary
End point timeframe: from baseline to 14 weeks, 26 weeks and 54 weeks	

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: Analysis for this secondary study objective is to assess the effect of 100 µg, 200 µg and 300 µg of cotadutide on weight
versus liraglutide 1.8 mg once daily.

End point values	Liraglutide	MEDI0382 100 mcg	MEDI0382 200 mcg	MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	100	256	256
Units: percentage				
least squares mean (confidence interval 95%)				
Percent change at 14 weeks	-3.40 (-4.14 to -2.65)	-2.70 (-3.49 to -1.91)	-3.47 (-3.95 to -2.98)	-4.33 (-4.82 to -3.84)
Percent change at 26 weeks	-4.12 (-4.98 to -3.27)	-3.23 (-4.13 to -2.32)	-3.94 (-4.51 to -3.38)	-4.60 (-5.17 to -4.04)
Percent change at 54 weeks	-3.20 (-4.19 to -2.21)	-3.27 (-4.32 to -2.22)	-3.08 (-3.73 to -2.43)	-4.16 (-4.81 to -3.50)

Statistical analyses

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Percent change at Week 14	
Comparison groups	Liraglutide v MEDI0382 100 mcg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.211
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.39
upper limit	1.79

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Percent change at Week 14	
Comparison groups	Liraglutide v MEDI0382 200 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.881
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	0.83

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Percent change at Week 14	
Comparison groups	Liraglutide v MEDI0382 300 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.042
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.93

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.82
upper limit	-0.04

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Percent change at Week 26	
Comparison groups	Liraglutide v MEDI0382 100 mcg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.158
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.35
upper limit	2.14

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Percent change at Week 26	
Comparison groups	Liraglutide v MEDI0382 200 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.734
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	1.2

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Percent change at Week 26	
Comparison groups	Liraglutide v MEDI0382 300 mcg

Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.357
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.51
upper limit	0.54

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Percent change at Week 54	
Comparison groups	Liraglutide v MEDI0382 100 mcg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.921
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.51
upper limit	1.37

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Percent change at Week 54	
Comparison groups	Liraglutide v MEDI0382 200 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.847
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	1.3

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Percent change at Week 54	
Comparison groups	Liraglutide v MEDI0382 300 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.112
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.15
upper limit	0.22

Secondary: Absolute change in body weight versus active comparator

End point title	Absolute change in body weight versus active comparator[8]
End point description: To assess the effect of 100, 200, and 300 µg of cotadutide on body weight versus liraglutide 1.8 mg once daily	
End point type	Secondary
End point timeframe: from baseline to 14 weeks, 26 weeks and 54 weeks	

Notes:

[8] - 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: Analysis for this secondary study objective is to assess the effect of 100 µg, 200 µg and 300 µg of cotadutide on weight
versus liraglutide 1.8 mg once daily.

End point values	Liraglutide	MEDI0382 100 mcg	MEDI0382 200 mcg	MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	100	256	256
Units: kg				
least squares mean (confidence interval 95%)				
Absolute change at 14 weeks	-3.25 (-4.00 to -2.51)	-2.66 (-3.45 to -1.87)	-3.45 (-3.94 to -2.97)	-4.42 (-4.91 to -3.93)
Absolute change at 26 weeks	-3.90 (-4.77 to -3.03)	-3.20 (-4.13 to -2.28)	-3.94 (-4.52 to -3.37)	-4.75 (-5.33 to -4.18)
Absolute change at 54 weeks	-2.94 (-3.96 to -1.92)	-3.20 (-4.28 to -2.12)	-3.09 (-3.77 to -2.42)	-4.35 (-5.03 to -3.68)

Statistical analyses

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Absolute change at Week 14	
Comparison groups	Liraglutide v MEDI0382 100 mcg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.284
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	1.68

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Absolute change at Week 14	
Comparison groups	Liraglutide v MEDI0382 200 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.658
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.09
upper limit	0.69

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Absolute change at Week 14	
Comparison groups	Liraglutide v MEDI0382 300 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.01
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.17

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.06
upper limit	-0.27

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Absolute change at Week 26	
Comparison groups	Liraglutide v MEDI0382 100 mcg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.279
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	1.97

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Absolute change at Week 26	
Comparison groups	Liraglutide v MEDI0382 200 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.94
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.08
upper limit	1

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Absolute change at Week 26	
Comparison groups	Liraglutide v MEDI0382 300 mcg

Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.11
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.89
upper limit	0.19

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Absolute change at Week 54	
Comparison groups	Liraglutide v MEDI0382 100 mcg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.73
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.74
upper limit	1.22

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Absolute change at Week 54	
Comparison groups	Liraglutide v MEDI0382 200 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.804
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.38
upper limit	1.07

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: Absolute change at Week 54	
Comparison groups	Liraglutide v MEDI0382 300 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.023
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.63
upper limit	-0.19

Secondary: Percentage of participants achieving weight loss of ≥5% and ≥10%

End point title	Percentage of participants achieving weight loss of ≥5% and ≥10%[9]
End point description: To assess the effect of 100, 200, and 300 µg of cotadutide on percentage of subjects achieving weight loss of ≥5% and ≥10% versus placebo	
End point type	Secondary
End point timeframe: after 14 weeks, 26 weeks and 54 weeks	

Notes:

[9] - 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: Analysis for this secondary study objective is to assess the effect of 100 µg, 200 µg and 300 µg of cotadutide on additional
measures of glycaemic control and body weight versus placebo

End point values	Placebo	MEDI0382 100 mcg	MEDI0382 200 mcg	MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	100	256	256
Units: participants				
Participants with weight loss ≥5% at Wk 14 (LOCF)	3	18	65	92
Participants with weight loss ≥5% at Wk 26 (LOCF)	11	28	76	110
Participants with weight loss ≥5% at Wk 54 (LOCF)	14	34	71	98
Participants with weight loss ≥10% at Wk 14 (LOCF)	0	6	15	20
Participants with weight loss ≥10% at Wk 26 (LOCF)	1	7	28	27

Participants with weight loss ≥10% at Wk 54 (LOCF)	2	11	21	32

Statistical analyses

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=5% at Week 14	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	8.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.38
upper limit	29.43

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=5% at Week 14	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	12.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.82
upper limit	40.64

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=5% at Week 14	
Comparison groups	Placebo v MEDI0382 300 mcg

Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	21.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.55
upper limit	68.97

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=5% at Week 26	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	3.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.72
upper limit	7.89

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=5% at Week 26	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	3.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	7.78

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=5% at Week 26	
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	7.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.72
upper limit	14.24

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=5% at Week 54	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	3.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.84
upper limit	7.45

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=5% at Week 54	
Comparison groups	Placebo v MEDI0382 200 mcg

Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.002
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	2.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.46
upper limit	5.09

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=5% at Week 54	
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Log odds ratio
Point estimate	4.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.42
upper limit	8.3

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=10% at Week 26	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.048
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	8.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	70.17

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=10% at Week 26	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.01
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	13.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.85
upper limit	102.91

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=10% at Week 26	
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.012
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	13.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.75
upper limit	97.68

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=10% at Week 54	
Comparison groups	Placebo v MEDI0382 100 mcg

Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.013
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	6.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.49
upper limit	32.07

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=10% at Week 54	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.032
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	4.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.15
upper limit	21.6

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: weight loss >=10% at Week 54	
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.005
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	7.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.86
upper limit	33.64

Secondary: Proportion of subjects rescued or discontinued for lack of glycaemic control

End point title	Proportion of subjects rescued or discontinued for lack of glycaemic control[10]

End point description:

To assess the effect of 100, 200, and 300 µg of cotadutide on the requirement for additional blood glucose-lowering therapies versus placebo

End point type	Secondary

End point timeframe:

at 14 weeks, 26 weeks and 54 weeks

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: Analysis for this secondary study objective is to assess the effect of 100 µg, 200 µg and 300 µg of cotadutide on the
requirement for additional blood glucose-lowering therapies versus placebo.

End point values	Placebo	MEDI0382 100 mcg	MEDI0382 200 mcg	MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	100	256	256
Units: participants				
received rescue medication at 14 wks	11	1	3	2
received rescue medication at 26 wks	20	3	8	6
received rescue medication at 54 wks	34	10	26	24
discontinued study IP at 14 wks	2	0	1	0
discontinued study IP at 26 wks	4	1	2	0
discontinued study IP at 54 wks	4	1	3	0

Statistical analyses

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description:	
received rescue medication at 14 wks	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.024
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.73

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: received rescue medication at 14 wks	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.4

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: received rescue medication at 14 wks	
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.33

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: received rescue medication at 26 wks	
Comparison groups	Placebo v MEDI0382 100 mcg

Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.002
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.48

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: received rescue medication at 26 wks	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.34

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: received rescue medication at 26 wks	
Comparison groups	Placebo v MEDI0382 300 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.28

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: received rescue medication at 54 wks	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	0.53

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: received rescue medication at 54 wks	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	0.44

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: received rescue medication at 54 wks	
Comparison groups	Placebo v MEDI0382 300 mcg

Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	0.41

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: discontinued IP at 14 wks	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.216
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	2.43

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: discontinued IP at 26 wks	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.253
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	2.52

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: discontinued IP at 26 wks	
Comparison groups	Placebo v MEDI0382 200 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.079
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	1.19

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: discontinued IP at 54 wks	
Comparison groups	Placebo v MEDI0382 100 mcg
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.252
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	2.5

Statistical analysis title	Secondary Endpoint Analysis
Statistical analysis description: discontinued IP at 54 wks	
Comparison groups	Placebo v MEDI0382 200 mcg

Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.143
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	1.47

Secondary: Pharmacokinetic (PK) endpoint: Trough plasma concentration (Cmin)

End point title	Pharmacokinetic (PK) endpoint: Trough plasma concentration (Cmin)[11]

End point description:

To characterise the PK profile of 100, 200, and 300 µg of cotadutide

End point type	Secondary

End point timeframe:

during dosing and follow-up (minimum 54 weeks)

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: Analysis for this secondary study objective is to characterise the PK profile and immunogenicity of 100 µg, 200 µg and 300
µg of cotadutide.

End point values	Placebo	MEDI0382 100 mcg	MEDI0382 200 mcg	MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[12]	100	256	256
Units: ng/mL				
arithmetic mean (standard deviation)				
Week 1	()	2.68 (± 1.27)	2.76 (± 1.88)	2.77 (± 1.84)
Week 2	()	2.66 (± 1.61)	5.13 (± 3.23)	5.18 (± 3.05)
Week 6	()	2.75 (± 1.44)	5.20 (± 3.57)	7.77 (± 4.88)
Week 10	()	3.18 (± 2.26)	5.74 (± 4.23)	8.23 (± 4.31)
Week 14	()	3.79 (± 4.05)	6.50 (± 5.26)	9.71 (± 7.64)
Week 18	()	4.58 (± 5.04)	7.43 (± 6.43)	10.8 (± 7.95)
Week 22	()	4.63 (± 4.28)	8.07 (± 7.01)	11.5 (± 9.77)
Week 26	()	4.39 (± 3.33)	8.12 (± 7.31)	12.9 (± 12.1)
Week 54	()	4.58 (± 3.89)	8.99 (± 9.22)	13.2 (± 14.3)

Notes:

[12] - study objective was to characterise the trough plasma concentration of 100, 200, 300 µg MEDI0382

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity endpoint: Overall ADA incidence (if positive)

End point title	Immunogenicity endpoint: Overall ADA incidence (if

End point description:

To characterise the immunogenicity of 100, 200, and 300 µg of cotadutide

End point type	Secondary

End point timeframe:

during dosing and follow-up (minimum 54 weeks)

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: Analysis for this secondary study objective is to characterise the PK profile and immunogenicity of 100 µg, 200 µg and 300
µg of cotadutide.

End point values	Placebo	MEDI0382 100 mcg	MEDI0382 200 mcg	MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	100	256	256
Units: participants				
ADA positive at baseline	1	1	0	0
ADA incidence	3	55	152	155
ADA positive post-baseline	3	54	152	155

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity endpoint: ADA response to MEDI0382 (if positive)

End point title	Immunogenicity endpoint: ADA response to MEDI0382 (if positive)[14]

End point description:

To characterise the immunogenicity of 100, 200, and 300 µg of cotadutide

End point type	Secondary

End point timeframe:

during dosing and follow-up (minimum 54 weeks)

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: Analysis for this secondary study objective is to characterise the PK profile and immunogenicity of 100 µg, 200 µg and 300
µg of cotadutide.

End point values	Placebo	MEDI0382 100 mcg	MEDI0382 200 mcg	MEDI0382 300 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	100	256	256
Units: titer				
median (full range (min-max))				
ADA positive at baseline, median titer	5.0 (5 to 5)	5.0 (5 to 5)	0 (0 to 0)	0 (0 to 0)

ADA incidence, median of maximum titer	5.0 (5 to 20)	20.0 (5 to 2560)	20.0 (5 to 640)	20.0 (5 to 5120)
ADA positive post-baseline, median of max. titer	5.0 (5 to 20)	20.0 (5 to 2560)	20.0 (5 to 640)	20.0 (5 to 5120)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From first dose of study drug until last study visit	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0
Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Liraglutide 1.8 mg
Reporting group description: -	
Reporting group title	MEDI0382 100 mcg
Reporting group description: -	
Reporting group title	MEDI0382 200 mcg
Reporting group description: -	
Reporting group title	MEDI0382 300 mcg
Reporting group description: -	

Serious adverse events	Placebo	Liraglutide 1.8 mg	MEDI0382 100 mcg
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 112 (10.71%)	8 / 110 (7.27%)	12 / 100 (12.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal stromal tumour			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoma			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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

Pancreatic carcinoma			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Prostate cancer metastatic			
subjects affected / exposed	0 / 112 (0.00%)	1 / 110 (0.91%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tongue neoplasm malignant stage unspecified			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Triple negative breast cancer			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Hypertensive crisis			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Impaired healing			

subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Acquired phimosis			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (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
Uterine prolapse			
subjects affected / exposed	0 / 112 (0.00%)	1 / 110 (0.91%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Asthma			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Dysphonia			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Pulmonary oedema			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Vocal cord dysfunction			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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

Injury, poisoning and procedural complications			
Anastomotic leak			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (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
Arterial bypass occlusion			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Craniocerebral injury			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (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
Limb injury			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural fistula			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Spinal column injury			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Subcutaneous haematoma			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Upper limb fracture			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (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
Angina pectoris			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Angina unstable			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve stenosis			
subjects affected / exposed	0 / 112 (0.00%)	1 / 110 (0.91%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Atrial fibrillation			

subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (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
Atrioventricular block complete			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (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
Bradycardia			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Myocardial ischaemia			

subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Silent myocardial infarction			
subjects affected / exposed	0 / 112 (0.00%)	1 / 110 (0.91%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular disorder			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic neuropathy			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Haemorrhagic stroke			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Ischaemic stroke			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (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
Vertigo CNS origin			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Eye disorders			

Retinal detachment			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (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
Retinal tear			
subjects affected / exposed	0 / 112 (0.00%)	1 / 110 (0.91%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Colitis ulcerative			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (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
Enterocutaneous fistula			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (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
Gastric polyps			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Hiatus hernia			

subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Inguinal hernia			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Irritable bowel syndrome			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Megacolon			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (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
Pancreatitis acute			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Retroperitoneal haematoma			
subjects affected / exposed	0 / 112 (0.00%)	1 / 110 (0.91%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Cholelithiasis			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder polyp			

subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Hepatic cirrhosis			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Nephrolithiasis			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (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
Perinephritis			
subjects affected / exposed	0 / 112 (0.00%)	1 / 110 (0.91%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prerenal failure			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Urinary tract disorder			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthrofibrosis			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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

Haematoma muscle			
subjects affected / exposed	0 / 112 (0.00%)	1 / 110 (0.91%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Meniscal degeneration			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Osteoarthritis			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Appendicitis			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (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
Cellulitis			

subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Chronic sinusitis			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Erysipelas			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Gastroenteritis			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Otitis media acute			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 112 (0.00%)	1 / 110 (0.91%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Pyelonephritis			
subjects affected / exposed	0 / 112 (0.00%)	1 / 110 (0.91%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis chronic			

subjects affected / exposed	0 / 112 (0.00%)	1 / 110 (0.91%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	0 / 100 (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
Urinary tract infection			
subjects affected / exposed	0 / 112 (0.00%)	1 / 110 (0.91%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 112 (0.89%)	0 / 110 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MEDI0382 200 mcg	MEDI0382 300 mcg	
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 256 (12.89%)	20 / 256 (7.81%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events	2	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stromal tumour			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			

subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer metastatic			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue neoplasm malignant stage unspecified			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Triple negative breast cancer			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 256 (0.39%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	2 / 256 (0.78%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Impaired healing			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Acquired phimosis			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphonia			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vocal cord dysfunction			

subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Anastomotic leak			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial bypass occlusion			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural fistula			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column injury			

subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous haematoma			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	2 / 256 (0.78%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	2 / 256 (0.78%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			

subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	1 / 256 (0.39%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Silent myocardial infarction			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular disorder			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ischaemic stroke			
subjects affected / exposed	2 / 256 (0.78%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo CNS origin			

subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal tear			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocutaneous fistula			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric polyps			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 256 (0.39%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Megacolon			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 256 (0.39%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			

subjects affected / exposed	2 / 256 (0.78%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder polyp			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perinephritis			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract disorder			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Arthrofibrosis			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma muscle			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 256 (0.39%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscal degeneration			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	3 / 256 (1.17%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			

subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 256 (0.39%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	0 / 256 (0.00%)	1 / 256 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 256 (0.00%)	0 / 256 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Liraglutide 1.8 mg	MEDI0382 100 mcg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 112 (60.71%)	67 / 110 (60.91%)	72 / 100 (72.00%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 112 (2.68%)	0 / 110 (0.00%)	4 / 100 (4.00%)
occurrences (all)	3	0	5
Headache			
subjects affected / exposed	1 / 112 (0.89%)	5 / 110 (4.55%)	3 / 100 (3.00%)
occurrences (all)	1	5	4
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	2 / 112 (1.79%)	2 / 110 (1.82%)	1 / 100 (1.00%)
occurrences (all)	2	3	1
Diarrhoea			
subjects affected / exposed	10 / 112 (8.93%)	4 / 110 (3.64%)	13 / 100 (13.00%)
occurrences (all)	10	7	15
Dyspepsia			
subjects affected / exposed	2 / 112 (1.79%)	3 / 110 (2.73%)	7 / 100 (7.00%)
occurrences (all)	2	3	13
Eructation			
subjects affected / exposed	0 / 112 (0.00%)	0 / 110 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2
Nausea			
subjects affected / exposed	12 / 112 (10.71%)	17 / 110 (15.45%)	23 / 100 (23.00%)
occurrences (all)	13	21	28
Vomiting			
subjects affected / exposed	5 / 112 (4.46%)	3 / 110 (2.73%)	10 / 100 (10.00%)
occurrences (all)	6	3	12
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 112 (5.36%)	2 / 110 (1.82%)	8 / 100 (8.00%)
occurrences (all)	6	2	8
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	15 / 112 (13.39%)	11 / 110 (10.00%)	11 / 100 (11.00%)
occurrences (all)	19	13	13
Respiratory tract infection viral			
subjects affected / exposed	3 / 112 (2.68%)	1 / 110 (0.91%)	1 / 100 (1.00%)
occurrences (all)	3	1	1
Urinary tract infection			
subjects affected / exposed	6 / 112 (5.36%)	2 / 110 (1.82%)	3 / 100 (3.00%)
occurrences (all)	6	2	4
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 112 (0.89%)	1 / 110 (0.91%)	3 / 100 (3.00%)
occurrences (all)	1	1	3

Non-serious adverse events	MEDI0382 200 mcg	MEDI0382 300 mcg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	198 / 256 (77.34%)	203 / 256 (79.30%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	11 / 256 (4.30%)	15 / 256 (5.86%)	
occurrences (all)	12	19	
Headache			
subjects affected / exposed	15 / 256 (5.86%)	19 / 256 (7.42%)	
occurrences (all)	18	23	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	10 / 256 (3.91%)	13 / 256 (5.08%)	
occurrences (all)	10	14	
Diarrhoea			
subjects affected / exposed	49 / 256 (19.14%)	28 / 256 (10.94%)	
occurrences (all)	68	40	
Dyspepsia			
subjects affected / exposed	19 / 256 (7.42%)	28 / 256 (10.94%)	
occurrences (all)	26	38	
Eructation			
subjects affected / exposed	14 / 256 (5.47%)	12 / 256 (4.69%)	
occurrences (all)	17	15	
Nausea			
subjects affected / exposed	85 / 256 (33.20%)	105 / 256 (41.02%)	
occurrences (all)	115	143	
Vomiting			
subjects affected / exposed	51 / 256 (19.92%)	43 / 256 (16.80%)	
occurrences (all)	66	58	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	9 / 256 (3.52%)	9 / 256 (3.52%)	
occurrences (all)	12	9	
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	22 / 256 (8.59%)	28 / 256 (10.94%)	
occurrences (all)	28	44	
Respiratory tract infection viral			
subjects affected / exposed	13 / 256 (5.08%)	7 / 256 (2.73%)	
occurrences (all)	15	8	
Urinary tract infection			
subjects affected / exposed	13 / 256 (5.08%)	7 / 256 (2.73%)	
occurrences (all)	17	9	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	12 / 256 (4.69%)	14 / 256 (5.47%)	
occurrences (all)	12	14	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 October 2017	Modified inclusion criteria to remove the upper BMI limit for the study. MET monotherapy, inclusion criterion 5, was modified to allow use of another glucose-lowering medication for up to 2 weeks in the 2 months prior to screening. Exclusion criterion 5 was modified to allow daily SC insulin treatment for up to 2 weeks within 90 days prior to screening. Exclusion criterion 13 was updated to present basal calcitonin values in pg/mL. Exclusion criterion 18 was clarified to restrict enrolment of subjects with any history of psychosis or bipolar disorder; subjects with a history of major depressive disorder within the past year with the subject being clinically unstable. The protocol was modified to include collection of subjects' vital status at the end of study. Updated schedule of screening procedures to refer to a 2-week period. Restrictions for tobacco and caffeine use for 24 hours prior to the visit were removed and additional options for retesting laboratory results were added. Updated schedule of procedures to include immunogenicity laboratory sampling at Visits 4 & 6. Modified the schedule of procedures for the 92-week extension period to remove the requirement of AE collection, concomitant medication review, vital signs collection, and brief PE during the IP resupply visits. Clarification on urine collection for urinalysis was added. Term pancreatitis as 1 of the adjudicated events was updated to pancreatic disease. Updated protocol to allow for MET withhold during persistent symptoms of nausea and vomiting. Updated permitted concomitant medications for consistency with inclusion criterion 5. Additional clarifications added on use of antiemetic therapy. 5HT-3 antagonist treatment recommendation removed from the text. Clarified PK population to refer to cotadutide-treated subjects only. A clarification was added to the protocol synopsis on the use of liraglutide in patients with CHF NYHA class III and label updates with the data from the LEADER trial.
05 February 2018	Protocol modified to exclude the interim analysis and the analysis associated with the 26-week data. Due to fast enrolment to the study, timing for the primary analysis advanced, so there was no longer a need for the interim analysis. Similarly, the separate analysis associated with the 26-week data was removed because fast enrolment lead to an insufficient number of subjects reaching 26 weeks at the time of the primary analysis to provide satisfactory statistical power.
20 April 2018	The methods for unblinding and statistical considerations were modified to include an analysis when all subject reached 26 weeks of treatment. To inform about efficacy at 6 months and guide the selection process for the optimal dose regimen because the impact of weight loss on improved insulin sensitivity and glucose control might not be adequately captured at 14 weeks. Information was added to include collection of specific information for events of pancreatic carcinoma. Description of clinical event adjudication updated to add pancreatic carcinoma and thyroid neoplasm to the list of adjudicated events. Given the controversy of whether GLP-1–based therapy increases the risk for specific malignant disease like pancreatic carcinoma and thyroid cancer, AstraZeneca decided to adjudicate pancreatic carcinoma and thyroid cancer in the Phase 2b study.
04 December 2018	Protocol updated to reduce the length of the treatment extension period from 92 to 40 weeks. The rationale for this change is to allow participants adequate time to transition to other therapies and allow continued collection of safety and efficacy data to inform further decisions regarding cotadutide doses.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported