Clinical trial results:
An Exploratory Phase 2a Randomized, Placebo-controlled, Double-blind Study to Evaluate the Efficacy and Safety of MEDI0382 versus Placebo in Overweight/Obese Subjects with Type 2 Diabetes Mellitus Treated with Dapagliflozin and Metformin

Summary

EudraCT number	2017-002817-78
Trial protocol	HU DE
Global end of trial date	06 December 2018

Results information

Result version number	v1 (current)
This version publication date	21 December 2019
First version publication date	21 December 2019

Trial information

Trial identification

Sponsor protocol code	D5670C00007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03444584
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	Milstein Building, Granta Park, Cambridge, United Kingdom, CB21 6GH
Public contact	Armando Flor, MedImmune, LLC, +1 3013981955, information.center@astrazeneca.com
Scientific contact	Armando Flor, MedImmune, LLC, +1 3013981955, 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	20 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 December 2018
Global end of trial reached?	Yes
Global end of trial date	06 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to compare the change in glucose area under the concentration time-curve (AUC) as measured by a standardized mixed-meal tolerance test (MMTT) in participants treated with dapagliflozin and metformin receiving MEDI0382 or placebo for 28 days.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 May 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Hungary: 24
Worldwide total number of subjects	49
EEA total number of subjects	49

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	32
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in Germany and Hungary between 08May2018 and 06Dec2018.

Pre-assignment

Screening details:

A total of 128 participants consented to participate in the study, of which 79 were screen failures. A total of 49 participants were randomised to the study.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received subcutaneous dose of placebo matched to MEDI0382 daily for 28 days. Participants were on metformin and dapagliflozin background dual therapy during the treatment period.

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

Dosage and administration details:

Subcutaneous (SC) dose of placebo matched to MEDI0382 daily for 28 days.

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Oral metformin tablet (Maximum tolerated dose >1 g) throughout the study including screening period (up to 60 days), 4-week run-in period (for 28 days), and study treatment period for 28 days.

Investigational medicinal product name	Dapagliflozin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Oral dapagliflozin 10 mg per day was provided during the 4-week run-in period (for 28 days) for participants treated with metformin monotherapy during the screening period (up to 60 days). During the study treatment period, oral dapagliflozin 10 mg per day was provided for all participants for 28 days.

Arm title	MEDI0382

Arm description:

Participants received subcutaneous dose of MEDI0382 daily (titrated up from 100 µg for 7 days to 200

µg for 7 days and to 300 µg for 14 days) for 28 days. Participants were on metformin and dapagliflozin background dual therapy during the treatment period.

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

Dosage and administration details:

Subcutaneous (SC) dose of MEDI0382 daily (titrated up from 100 µg for 7 days to 200 µg for 7 days and to 300 µg for 14 days) for 28 days.

Investigational medicinal product name	Dapagliflozin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Oral dapagliflozin 10 mg per day was provided during the 4-week run-in period (for 28 days) for participants treated with metformin monotherapy during the screening period (up to 60 days). During the study treatment period, oral dapagliflozin 10 mg per day was provided for all participants for 28 days.

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Oral metformin tablet (Maximum tolerated dose >1 g) throughout the study including screening period (up to 60 days), 4-week run-in period (for 28 days), and study treatment period for 28 days.

Number of subjects in period 1	Placebo	MEDI0382
Started	24	25
Completed	24	23
Not completed	0	2
Consent withdrawn by subject	-	1
Not specified	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received subcutaneous dose of placebo matched to MEDI0382 daily for 28 days. Participants were on metformin and dapagliflozin background dual therapy during the treatment period.	
Reporting group title	MEDI0382
Reporting group description:	
Participants received subcutaneous dose of MEDI0382 daily (titrated up from 100 µg for 7 days to 200 µg for 7 days and to 300 µg for 14 days) for 28 days. Participants were on metformin and dapagliflozin background dual therapy during the treatment period.	

Reporting group values	Placebo	MEDI0382	Total
Number of subjects	24	25	49
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	16	16	32
From 65-84 years	8	9	17
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	58.4	61.0	
standard deviation	± 10.0	± 8.2	-
Sex: Female, Male			
Units: Subjects			
Female	12	10	22
Male	12	15	27
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	24	25	49
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	23	25	48
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received subcutaneous dose of placebo matched to MEDI0382 daily for 28 days. Participants were on metformin and dapagliflozin background dual therapy during the treatment period.	
Reporting group title	MEDI0382
Reporting group description:	
Participants received subcutaneous dose of MEDI0382 daily (titrated up from 100 µg for 7 days to 200 µg for 7 days and to 300 µg for 14 days) for 28 days. Participants were on metformin and dapagliflozin background dual therapy during the treatment period.	

Primary: Change From Baseline to Day 28 in Plasma Glucose Area Under the Concentration Time-curve From Time 0 to 4 Hours (AUC0-4hrs) as Measured by Mixed-meal Tolerance Test (MMTT)

End point title	Change From Baseline to Day 28 in Plasma Glucose Area Under the Concentration Time-curve From Time 0 to 4 Hours (AUC0-4hrs) as Measured by Mixed-meal Tolerance Test (MMTT)
End point description:	
The MMTT test involved the consumption of a standardised liquid meal (nutritional supplement of fat, carbohydrate, and protein) within 5 minutes. On Day -1 and on Day 28, following a minimum 10-hour fast, serial of blood samples were obtained prior and through 240 minutes after consumption of standardized meal for the measurement of glucose metabolism (with no additional food intake during this time). Intent-to-treat (ITT) population was analysed which included all participants who received any dose of study drugs analysed according to their randomized treatment group. Here, number of participants analysed "N" signifies participants who were analyzed for the specified end point.	
End point type	Primary
End point timeframe:	
Zero minutes before and 15, 30, 45, 60, 90, 120, 180, and 240 minutes after consumption of the standardised meal on Day -1 (Baseline) and Day 28	

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	24		
Units: hr·mg/dL				
least squares mean (confidence interval 95%)	-11.28 (-51.05 to 28.50)	-154.37 (-192.45 to -116.29)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v MEDI0382

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-143.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-198.2
upper limit	-87.98

Primary: Percent Change From Baseline to Day 28 in Plasma Glucose AUC0-4hrs as Measured by MMTT

End point title	Percent Change From Baseline to Day 28 in Plasma Glucose AUC0-4hrs as Measured by MMTT

End point description:

The MMTT test involved the consumption of a standardised liquid meal (nutritional supplement of fat, carbohydrate, and protein) within 5 minutes. On Day -1 and on Day 28, following a minimum 10-hour fast, serial of blood samples were obtained prior and through 240 minutes after consumption of standardized meal for the measurement of glucose metabolism (with no additional food intake during this time). An ITT population was analysed which included all participants who received any dose of study drugs analysed according to their randomised treatment group. Here, number of participants analysed "N" signifies participants who were analysed for the specified end point.

End point type	Primary

End point timeframe:

Zero minutes before and 15, 30, 45, 60, 90, 120, 180, and 240 minutes after consumption of the standardised meal on Day -1 (Baseline) and Day 28

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	24		
Units: Percent change in Glucose AUC0-4hrs				
least squares mean (confidence interval 95%)	-0.13 (-5.96 to 5.69)	-22.30 (-27.88 to -16.73)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v MEDI0382

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-22.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.24
upper limit	-14.1

Secondary: Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience(immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. The TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. As-treated population was analysed which included all participants who received any dose of study drug and analysed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Day 1 through 28 days after the last dose of MEDI0382 (approximately 8 weeks)

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Participants				
TEAEs	14	13		
TESAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal 12-lead Electrocardiogram (ECG) Reported as TEAEs

End point title	Number of Participants With Abnormal 12-lead Electrocardiogram (ECG) Reported as TEAEs

End point description:

Number of participants with abnormal 12-lead ECG reported as TEAEs are reported. As-treated population was analysed which included all participants who received any dose of study drug and analysed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Day 1 through 28 days after the last dose of MEDI0382 (approximately 8 weeks)

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Vital Signs Reported as TEAEs

End point title	Number of Participants With Abnormal Vital Signs Reported as TEAEs

End point description:

Number of participants with abnormal vital signs reported as TEAEs are reported. As-treated population was analysed which included all participants who received any dose of study drug and analysed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Day 1 through 28 days after the last dose of MEDI0382 (approximately 8 weeks)

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Participants				
Tachycardia	2	1		
Tachycardia paroxysmal	1	0		
Palpitations	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Physical Examinations Reported as TEAEs

End point title	Number of Participants With Abnormal Physical Examinations Reported as TEAEs

End point description:

Number of participants with abnormal physical examinations reported as TEAEs are reported. As-treated population was analysed which included all participants who received any dose of study drug and analysed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Day 1 through 28 days after the last dose of MEDI0382 (approximately 8 weeks)

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Clinical Laboratory Parameters Reported as TEAEs

End point title	Number of Participants With Abnormal Clinical Laboratory Parameters Reported as TEAEs

End point description:

Number of participants with abnormal clinical laboratory parameters reported as TEAEs are reported. As-treated population was analysed which included all participants who received any dose of study drug and analysed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Day 1 through 28 days after the last dose of MEDI0382 (approximately 8 weeks)

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Participants				
Hypoglycemia	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Time Curve From Time Zero to

Infinity (AUC [0-∞]) of MEDI0382

End point title	Area Under the Plasma Concentration Time Curve From Time Zero to Infinity (AUC [0-∞]) of MEDI0382[1]

End point description:

Area under the plasma concentration time curve from time zero to infinity (AUC [0-∞]) of MEDI0382 is reported. MEDI0382 pharmacokinetic (PK) population was analysed which included all participants who received at least 1 dose of MEDI0382 and had at least 1 MEDI0382 PK sample above the lower limit of quantitation. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Pre-dose and 0.5, 1, 2, 4, 6, 8, 12, and 24 hours post-dose on Days 7, 14, and 28

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: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	MEDI0382			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ng.hr/mL				
geometric mean (full range (min-max))				
Day 7 (MEDI0382 100 µg) (n=9)	106.4 (57.7 to 251.8)			
Day 14 (MEDI0382 200 µg) (n=9)	196.7 (99.4 to 472.0)			
Day 28 (MEDI0382 300 µg) (n=9)	314.6 (211.0 to 537.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Time Curve From Time Zero to Infinity (AUC [0-∞]) of Dapagliflozin

End point title	Area Under the Plasma Concentration Time Curve From Time Zero to Infinity (AUC [0-∞]) of Dapagliflozin

End point description:

Area under the plasma concentration time curve from time zero to infinity (AUC [0-∞]) of Dapagliflozin is reported. Dapagliflozin PK population was analysed which included all participants who received at least 1 dose of dapagliflozin and had at least 1 dapagliflozin PK sample above the lower limit of quantitation. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Pre-dose and 0.5, 1, 2, 4, 6, 8, 12, and 24 hours post-dose on Days -1, 7, 14, and 28

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: ng.hr/mL				
geometric mean (full range (min-max))				
Day -1 (n= 20, 24)	432.6 (271.5 to 918.6)	473.8 (288.8 to 1073.2)		
Day 7 (n=15, 12)	410.2 (209.9 to 1024.2)	438.0 (222.2 to 833.6)		
Day 14 (n=16, 8)	421.0 (219.0 to 1327.8)	448.6 (247.0 to 615.9)		
Day 28 (n=15, 16)	405.7 (261.1 to 799.5)	523.4 (319.5 to 946.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve During the Dosing Period (AUCtau) of MEDI0382

End point title	Area Under the Plasma Concentration-time Curve During the Dosing Period (AUCtau) of MEDI0382[2]

End point description:

Area under the plasma concentration-time curve during the dosing period (AUCtau) of MEDI0382 is reported. MEDI0382 pharmacokinetic (PK) population was analysed which included all participants who received at least 1 dose of MEDI0382 and had at least 1 MEDI0382 PK sample above the lower limit of quantitation. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Pre-dose and 0.5, 1, 2, 4, 6, 8, 12, and 24 hours post-dose on Days 7, 14, and 28

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: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	MEDI0382			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ng.hr/mL				
geometric mean (full range (min-max))				
Day 7 (MEDI0382 100 µg) (n=23)	89.6 (43.1 to 199.4)			
Day 14 (MEDI0382 200 µg) (n=23)	165.0 (86.9 to 365.5)			
Day 28 (MEDI0382 300 µg) (n=22)	265.9 (101.7 to 795.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve During the Dosing Period (AUCtau) of Dapagliflozin

End point title	Area Under the Plasma Concentration-time Curve During the Dosing Period (AUCtau) of Dapagliflozin

End point description:

Area under the plasma Concentration-time curve during the dosing period (AUCtau) of Dapagliflozin is reported. Dapagliflozin PK population was analysed which included all participants who received at least 1 dose of dapagliflozin and had at least 1 dapagliflozin PK sample above the lower limit of quantitation. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Pre-dose and 0.5, 1, 2, 4, 6, 8, 12, and 24 hours post-dose on Days -1, 7, 14, and 28

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: ng.hr/mL				
geometric mean (full range (min-max))				
Day -1 (n= 24, 24)	400.9 (182.4 to 1011.5)	430.3 (252.5 to 815.2)		
Day 7 (n=24, 25)	377.5 (76.4 to 910.7)	406.8 (211.5 to 1142.6)		
Day 14 (n= 23, 23)	417.1 (209.0 to 1107.7)	396.8 (215.4 to 669.7)		
Day 28 (n= 23, 24)	423.1 (180.6 to 977.3)	463.8 (284.3 to 1245.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax) of MEDI0382

End point title	Maximum Observed Serum Concentration (Cmax) of

End point description:

Maximum observed serum concentration (Cmax) of MEDI0382 is reported. MEDI0382 pharmacokinetic (PK) population was analysed which included all participants who received at least 1 dose of MEDI0382 and had at least 1 MEDI0382 PK sample above the lower limit of quantitation. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Pre-dose and 0.5, 1, 2, 4, 6, 8, 12, and 24 hours post-dose on Days 7, 14, and 28

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: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	MEDI0382			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ng/mL				
geometric mean (full range (min-max))				
Day 7 (MEDI0382 100 µg) (n = 25)	5.2 (2.7 to 11.9)			
Day 14 (MEDI0382 200 µg) (n= 24)	10.1 (4.4 to 21.7)			
Day 28 (MEDI0382 300 µg) (n= 22)	17.2 (6.1 to 45.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax) of Dapagliflozin

End point title	Maximum Observed Serum Concentration (Cmax) of Dapagliflozin

End point description:

Maximum observed serum concentration (Cmax) of Dapagliflozin is reported. Dapagliflozin PK population was analysed which included all participants who received at least 1 dose of dapagliflozin and had at least 1 dapagliflozin PK sample above the lower limit of quantitation. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Pre-dose and 0.5, 1, 2, 4, 6, 8, 12, and 24 hours post-dose on Days -1, 7, 14, and 28

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: ng/mL				
geometric mean (full range (min-max))				
Day -1 (n= 24,25)	110.1 (46.3 to 208.3)	116.7 (38.2 to 206.8)		
Day 7 (n= 24, 25)	92.0 (5.2 to 256.7)	84.4 (24.1 to 211.7)		
Day 14 (n= 23, 24)	95.6 (33.5 to 280.7)	61.1 (15.8 to 149.9)		
Day 28 (n= 23, 24)	112.2 (47.0 to 235.4)	94.2 (25.2 to 182.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Serum Concentration (Tmax) of

MEDI0382

End point title	Time to Reach Maximum Observed Serum Concentration (Tmax) of MEDI0382[4]

End point description:

Time to reach maximum observed serum concentration (Tmax) of MEDI0382 is reported. MEDI0382 pharmacokinetic (PK) population was analysed which included all participants who received at least 1 dose of MEDI0382 and had at least 1 MEDI0382 PK sample above the lower limit of quantitation. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Pre-dose and 0.5, 1, 2, 4, 6, 8, 12, and 24 hours post-dose on Days 7, 14, and 28

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: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	MEDI0382			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Hours				
median (full range (min-max))				
Day 7 (MEDI0382 100 µg) (n= 25)	5.5 (2 to 8)			
Day 14 (MEDI0382 200 µg) (n= 24)	5.1 (2 to 8)			
Day 28 (MEDI0382 300 µg) (n= 22)	4 (1.9 to 8.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Serum Concentration (Tmax) of Dapagliflozin

End point title	Time to Reach Maximum Observed Serum Concentration (Tmax) of Dapagliflozin

End point description:

Time to reach maximum observed serum concentration (Tmax) of Dapagliflozin is reported. Dapagliflozin PK population was analysed which included all participants who received at least 1 dose of dapagliflozin and had at least 1 dapagliflozin PK sample above the lower limit of quantitation. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Pre-dose and 0.5, 1, 2, 4, 6, 8, 12, and 24 hours post-dose on Days -1, 7, 14, and 28

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Hours				
median (full range (min-max))				
Day -1 (n= 24, 25)	1 (0.5 to 2)	1 (0.4 to 23.9)		
Day 7 (n= 24, 25)	1 (0.5 to 11.4)	1 (0.5 to 4)		
Day 14 (23, 24)	1.1 (0.5 to 6)	1 (0 to 8.1)		
Day 28 (23, 24)	1 (0.2 to 1.8)	1 (0.5 to 8.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Half-life (t½) of MEDI0382

End point title	Terminal Elimination Half-life (t½) of MEDI0382[5]

End point description:

Terminal half-life is the time required for the plasma concentration to fall by 50% during the terminal phase. The t½ of MEDI0382 is reported. MEDI0382 pharmacokinetic (PK) population was analysed which included all participants who received at least 1 dose of MEDI0382 and had at least 1 MEDI0382 PK sample above the lower limit of quantitation. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Pre-dose and 0.5, 1, 2, 4, 6, 8, 12, and 24 hours post-dose on Days 7, 14, and 28

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: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	MEDI0382			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Hours				
geometric mean (full range (min-max))				
Day 7 (MEDI0382 100 µg) (n= 9)	8.8 (6.1 to 11.9)			
Day 14 (MEDI0382 200 µg) (n= 9)	9 (5.6 to 11.8)			
Day 28 (MEDI0382 300 µg) (n= 9)	9.1 (5.1 to 11.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Half-life (t½) of Dapagliflozin

End point title	Terminal Elimination Half-life (t½) of Dapagliflozin

End point description:

Terminal half-life is the time required for the plasma concentration to fall by 50% during the terminal phase. The t½ of Dapagliflozin is reported. Dapagliflozin PK population was analysed which included all participants who received at least 1 dose of dapagliflozin and had at least 1 dapagliflozin PK sample above the lower limit of quantitation. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Pre-dose and 0.5, 1, 2, 4, 6, 8, 12, and 24 hours post-dose on Days -1, 7, 14, and 28

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Hours				
geometric mean (full range (min-max))				
Day -1 (n= 20, 24)	8.2 (5.3 to 11.2)	7.8 (5.4 to 11.3)		
Day 7 (n= 15, 12)	7.9 (4.1 to 10.4)	8.3 (5.8 to 11.1)		
Day 14 (n= 16, 8)	7.0 (5.1 to 11.4)	8.5 (7 to 10)		
Day 28 (15, 16)	7.6 (5.8 to 11.0)	9.1 (6.1 to 11.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent clearance (CL/F) of MEDI0382

End point title	Apparent clearance (CL/F) of MEDI0382[6]

End point description:

Clearance of a drug is a measure of the rate at which a drug is metabolized or eliminated by normal biological processes. The CL/F of MEDI0382 is reported. MEDI0382 pharmacokinetic (PK) population was analysed which included all participants who received at least 1 dose of MEDI0382 and had at least 1 MEDI0382 PK sample above the lower limit of quantitation. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Pre-dose and 0.5, 1, 2, 4, 6, 8, 12, and 24 hours post-dose on Days 7, 14, and 28

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: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	MEDI0382			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: L/hr				
geometric mean (full range (min-max))				
Day 7 (MEDI0382 100 µg) (n= 9)	1.1 (0.5 to 1.9)			
Day 14 (MEDI0382 200 µg) (n= 9)	1.3 (0.5 to 2.2)			
Day 28 (MEDI0382 300 µg) (n= 9)	1.2 (0.8 to 1.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent clearance (CL/F) of Dapagliflozin

End point title	Apparent clearance (CL/F) of Dapagliflozin

End point description:

Clearance of a drug is a measure of the rate at which a drug is metabolized or eliminated by normal biological processes. The CL/F of Dapagliflozin is reported. Dapagliflozin PK population was analysed which included all participants who received at least 1 dose of dapagliflozin and had at least 1 dapagliflozin PK sample above the lower limit of quantitation. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Pre-dose and 0.5, 1, 2, 4, 6, 8, 12, and 24 hours post-dose on Days -1, 7, 14, and 28

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: L/Hr				
geometric mean (full range (min-max))				
Day -1 (n= 20, 24)	25.5 (13.3 to 38.9)	23.3 (12.3 to 39.6)		
Day 7 (n= 15, 12)	26.7 (11.0 to 52.8)	25.7 (14.2 to 47.3)		
Day 14 (n= 16, 8)	25.9 (9.0 to 47.7)	25.5 (18.8 to 46.4)		
Day 28 (n= 15, 16)	26.8 (13.8 to 40.2)	22.2 (13.4 to 35.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Anti-drug Antibodies (ADA) Titer to MEDI0382

End point title	Number of Participants With Positive Anti-drug Antibodies

	(ADA) Titer to MEDI0382

End point description:

Number of participants with positive Anti-drug antibodies (ADA) titer to MEDI0382 are reported. Immunogenicity population included was analysed which included all participants who received any dose of study drug (MEDI0382 or placebo) and analysed according to the treatment they actually received and had at least one serum sample for immunogenicity testing. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Day 1 (pre-dose), on Day 29 , and 28 days post last dose (end of study visit; approximately 8 weeks)

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Participants				
Day 1 (n= 24, 25)	0	3		
Day 29 (n= 24, 24)	0	1		
End of Study (n= 24, 24)	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Plasma Glucose AUC24-hrs to the end of Each Dosing Level as Measured by Continuous Glucose Monitoring (CGM)

End point title	Change From Baseline in Plasma Glucose AUC24-hrs to the end of Each Dosing Level as Measured by Continuous Glucose Monitoring (CGM)

End point description:

Continuous glucose monitoring is a minimally invasive device applied to the skin in the upper arm that provides a measure of interstitial glucose levels every 15 minutes. Continuous glucose monitoring measures glucose excursions during different meals and at different times of the day. End of dosing: Day 7 for MEDI0382 100 µg; Day 14 for MEDI0382 200 µg; and Day 28 for MEDI0382 300 µg. An ITT population was analysed which included all participants who received any dose of study drug (MEDI0382 or placebo) and analysed according to their randomized treatment group. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Day -1 (Baseline) through Day 7 for MEDI0382 100 µg, Day 14 for MEDI0382 200 µg, and Day 28 for MEDI0382 300 µg

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: hr.mg/dL				
arithmetic mean (standard deviation)				
Day 7 (MEDI0382 100 µg) (n= 10, 12)	49.14 (± 667.30)	-832.66 (± 506.22)		
Day 14 (MEDI0382 200 µg) (n= 9, 13)	57.30 (± 379.95)	-666.05 (± 647.63)		
Day 28 (MEDI0382 300 µg) (n= 12, 18)	229.47 (± 589.19)	-726.85 (± 710.71)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean 24-hrs Plasma Glucose to the end of Each Dosing Level as Measured by CGM

End point title	Change From Baseline in Mean 24-hrs Plasma Glucose to the end of Each Dosing Level as Measured by CGM

End point description:

Continuous glucose monitoring is a minimally invasive device applied to the skin in the upper arm that provides a measure of interstitial glucose levels every 15 minutes. Continuous glucose monitoring measures glucose excursions during different meals and at different times of the day. End of dosing: Day 7 for MEDI0382 100 µg; Day 14 for MEDI0382 200 µg; and Day 28 for MEDI0382 300 µg. An ITT population was analysed which included all participants who received any dose of study drug (MEDI0382 or placebo) and analysed according to their randomized treatment group. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Day -1 (Baseline) through Day 7 for MEDI0382 100 µg, Day 14 for MEDI0382 200 µg, and Day 28 for MEDI0382 300 µg

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: mg/dL				
arithmetic mean (standard deviation)				
Day 7 (MEDI0382 100 µg) (n= 10, 12)	2.59 (± 28.96)	-34.74 (± 20.34)		
Day 14 (MEDI0382 200 µg) (n= 9, 13)	2.83 (± 17.01)	-28.34 (± 27.12)		
Day 28 (MEDI0382 300 µg) (n= 12, 18)	9.70 (± 24.73)	-30.55 (± 29.82)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Standard Deviation of 24-hrs Plasma Glucose Readings to the end of Each Dosing Level as Measured by CGM

End point title	Change From Baseline in Standard Deviation of 24-hrs Plasma Glucose Readings to the end of Each Dosing Level as Measured by CGM

End point description:

Continuous glucose monitoring is a minimally invasive device applied to the skin in the upper arm that provides a measure of interstitial glucose levels every 15 minutes. Continuous glucose monitoring measures glucose excursions during different meals and at different times of the day. End of dosing: Day 7 for MEDI0382 100 µg; Day 14 for MEDI0382 200 µg; and Day 28 for MEDI0382 300 µg. An ITT population was analysed which included all participants who received any dose of study drug (MEDI0382 or placebo) and analysed according to their randomized treatment group. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Day -1 (Baseline) through Day 7 for MEDI0382 100 µg, Day 14 for MEDI0382 200 µg, and Day 28 for MEDI0382 300 µg

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: mg/dL				
arithmetic mean (standard deviation)				
Day 7 (MEDI0382 100 µg) (n= 10, 12)	-3.01 (± 13.84)	-7.21 (± 11.05)		
Day 14 (MEDI0382 200 µg) (n= 9, 13)	1.38 (± 9.47)	-7.52 (± 9.73)		
Day 28 (MEDI0382 300 µg) (n= 12, 18)	-4.39 (± 10.67)	-9.76 (± 10.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Coefficient of Variation of 24-hrs Plasma Glucose Readings to the end of Each Dosing Level as Measured by CGM

End point title	Change From Baseline in Coefficient of Variation of 24-hrs Plasma Glucose Readings to the end of Each Dosing Level as Measured by CGM

End point description:

Continuous glucose monitoring is a minimally invasive device applied to the skin in the upper arm that provides a measure of interstitial glucose levels every 15 minutes. Continuous glucose monitoring measures glucose excursions during different meals and at different times of the day. End of dosing: Day 7 for MEDI0382 100 µg; Day 14 for MEDI0382 200 µg; and Day 28 for MEDI0382 300 µg. An ITT population was analysed which included all participants who received any dose of study drug (MEDI0382 or placebo) and analysed according to their randomized treatment group. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Day -1 (Baseline) through Day 7 for MEDI0382 100 µg, Day 14 for MEDI0382 200 µg, and Day 28 for MEDI0382 300 µg

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Percent of coefficient of variation				
arithmetic mean (standard deviation)				
Day 7 (MEDI0382 100 µg) (n= 10, 12)	-2.37 (± 9.06)	-0.45 (± 6.68)		
Day 14 (MEDI0382 200 µg) (n= 9, 13)	0.96 (± 8.74)	-2.06 (± 6.59)		
Day 28 (MEDI0382 300 µg) (n= 12, 18)	-4.26 (± 7.16)	-3.21 (± 7.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean Amplitude of Glucose Excursions (MAGE) of 24-hrs Plasma Glucose Readings to the end of Each Dosing Level as Measured by CGM

End point title	Change From Baseline in Mean Amplitude of Glucose Excursions (MAGE) of 24-hrs Plasma Glucose Readings to the end of Each Dosing Level as Measured by CGM

End point description:

Continuous glucose monitoring is a minimally invasive device applied to the skin in the upper arm that provides a measure of interstitial glucose levels every 15 minutes. Continuous glucose monitoring measures glucose excursions during different meals and at different times of the day. End of dosing: Day 7 for MEDI0382 100 µg; Day 14 for MEDI0382 200 µg; and Day 28 for MEDI0382 300 µg. An ITT population was analysed which included all participants who received any dose of study drug (MEDI0382 or placebo) and analysed according to their randomized treatment group. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Day -1 (Baseline) through Day 7 for MEDI0382 100 µg, Day 14 for MEDI0382 200 µg, and Day 28 for MEDI0382 300 µg

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: mg/dL				
arithmetic mean (standard deviation)				
Day 7 (MEDI0382 100 µg) (n= 10, 12)	-13.46 (± 32.07)	-25.74 (± 35.06)		
Day 14 (MEDI0382 200 µg) (n= 9, 13)	18.05 (± 47.60)	-26.59 (± 25.60)		
Day 28 (MEDI0382 300 µg) (n= 12, 18)	-8.09 (± 27.68)	-27.92 (± 23.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Percentage of 24-hrs Glucose Readings That Falls Within the Euglycemic Range to the end of Each Dosing as Measured by CGM

End point title	Change From Baseline in the Percentage of 24-hrs Glucose Readings That Falls Within the Euglycemic Range to the end of Each Dosing as Measured by CGM

End point description:

Continuous glucose monitoring is a minimally invasive device applied to the skin in the upper arm that provides a measure of interstitial glucose levels every 15 minutes. Continuous glucose monitoring measures glucose excursions during different meals and at different times of the day. End of dosing: Day 7 for MEDI0382 100 µg; Day 14 for MEDI0382 200 µg; and Day 28 for MEDI0382 300 µg. Euglycemic range is defined as glucose levels of >= 70 mg/dL (>= 3.9 mmol/L) and <= 180 mg/dL (<= 10.0 mmol/L). An ITT population was analysed which included all participants who received any dose of study drug (MEDI0382 or placebo) and analysed according to their randomized treatment group. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Day -1 (Baseline) through Day 7 for MEDI0382 100 µg, Day 14 for MEDI0382 200 µg, and Day 28 for MEDI0382 300 µg

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Percent of Euglycemic Range				
arithmetic mean (standard deviation)				
Day 7 (MEDI0382 100 µg) (n= 10, 12)	-5.61 (± 19.65)	7.12 (± 20.60)		
Day 14 (MEDI0382 200 µg) (n= 9, 13)	-2.79 (± 10.16)	5.31 (± 17.71)		
Day 28 (MEDI0382 300 µg) (n= 12, 18)	-4.17 (± 15.80)	6.54 (± 24.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Percentage of 24-hrs Glucose Readings That Falls Within the Hyperglycemic Range to the end of Each Dosing as Measured by CGM

End point title	Change From Baseline in the Percentage of 24-hrs Glucose

	Readings That Falls Within the Hyperglycemic Range to the end of Each Dosing as Measured by CGM

End point description:

Continuous glucose monitoring is a minimally invasive device applied to the skin in the upper arm that provides a measure of interstitial glucose levels every 15 minutes. Continuous glucose monitoring measures glucose excursions during different meals and at different times of the day. End of dosing: Day 7 for MEDI0382 100 µg; Day 14 for MEDI0382 200 µg; and Day 28 for MEDI0382 300 µg. Hyperglycemic (high glucose) range is defined as glucose levels of >180 mg/dL (> 10.0 mmol/L). An ITT population was analysed which included all participants who received any dose of study drug (MEDI0382 or placebo) and analysed according to their randomized treatment group. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Day -1 (Baseline) through Day 7 for MEDI0382 100 µg, Day 14 for MEDI0382 200 µg, and Day 28 for MEDI0382 300 µg

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Percent of hyperglycemic range				
arithmetic mean (standard deviation)				
Day 7 (MEDI0382 100 µg) (n= 10, 12)	3.62 (± 17.80)	-13.99 (± 14.95)		
Day 14 (MEDI0382 200 µg) (n= 9, 13)	0.36 (± 10.50)	-9.81 (± 13.68)		
Day 28 (MEDI0382 300 µg) (n= 12, 18)	6.08 (± 16.96)	-9.72 (± 20.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Percentage of 24-hrs Glucose Readings That Falls Within the Hypoglycemic Range to the end of Each Dosing as Measured by CGM

End point title	Change From Baseline in the Percentage of 24-hrs Glucose Readings That Falls Within the Hypoglycemic Range to the end of Each Dosing as Measured by CGM

End point description:

Continuous glucose monitoring is a minimally invasive device applied to the skin in the upper arm that provides a measure of interstitial glucose levels every 15 minutes. Continuous glucose monitoring measures glucose excursions during different meals and at different times of the day. End of dosing: Day 7 for MEDI0382 100 µg; Day 14 for MEDI0382 200 µg; and Day 28 for MEDI0382 300 µg. Hypoglycemic range is defined as glucose levels of < 70 mg/dL (< 3.9 mmol/L). An ITT population was analysed which included all participants who received any dose of study drug (MEDI0382 or placebo) and analysed according to their randomized treatment group. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Day -1 (Baseline) through Day 7 for MEDI0382 100 µg, Day 14 for MEDI0382 200 µg, and Day 28 for MEDI0382 300 µg

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Percent of hypoglycemic range				
arithmetic mean (standard deviation)				
Day 7 (MEDI0382 100 µg) (n= 10, 12)	1.17 (± 5.64)	6.08 (± 10.36)		
Day 14 (MEDI0382 200 µg) (n= 9, 13)	2.00 (± 3.79)	3.44 (± 12.72)		
Day 28 (MEDI0382 300 µg) (n= 12, 18)	-2.08 (± 4.14)	2.84 (± 12.20)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Percentage of 24-hrs Glucose Readings That Falls Within Clinically Significant Hypoglycemic Range to the end of Each Dosing as Measured by CGM

End point title	Change From Baseline in the Percentage of 24-hrs Glucose Readings That Falls Within Clinically Significant Hypoglycemic Range to the end of Each Dosing as Measured by CGM

End point description:

Continuous glucose monitoring is a minimally invasive device applied to the skin in the upper arm that provides a measure of interstitial glucose levels every 15 minutes. Continuous glucose monitoring measures glucose excursions during different meals and at different times of the day. End of dosing: Day 7 for MEDI0382 100 µg; Day 14 for MEDI0382 200 µg; and Day 28 for MEDI0382 300 µg. Clinically significant hypoglycemic range is defined as glucose levels of < 54 mg/dL (3.0 mmol/L). An ITT population was analysed which included all participants who received any dose of study drug (MEDI0382 or placebo) and analysed according to their randomized treatment group. Here, number analysed "n" signifies participants who were analysed for the specified day.

End point type	Secondary

End point timeframe:

Day -1 (Baseline) through Day 7 for MEDI0382 100 µg, Day 14 for MEDI0382 200 µg, and Day 28 for MEDI0382 300 µg

End point values	Placebo	MEDI0382		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Percent of hypoglycemic range				
arithmetic mean (standard deviation)				
Day 7 (MEDI0382 100 µg) (n= 10, 12)	0.76 (± 3.64)	1.61 (± 5.03)		
Day 14 (MEDI0382 200 µg) (n= 9, 13)	0.27 (± 1.19)	-0.06 (± 2.18)		
Day 28 (MEDI0382 300 µg) (n= 12, 18)	-0.26 (± 0.90)	0.93 (± 4.91)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day -2 through 28 days post last dose (approximately 07 months)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	MEDI0382
Reporting group description:	
Participants received subcutaneous dose of MEDI0382 daily (titrated up from 100 µg for 7 days to 200 µg for 7 days and to 300 µg for 14 days) for 28 days. Participants were on metformin and dapagliflozin background dual therapy during the treatment period.	
Reporting group title	Placebo
Reporting group description:	
Participants received subcutaneous dose of placebo matched to MEDI0382 daily for 28 days. Participants were on metformin and dapagliflozin background dual therapy during the treatment period.	

Serious adverse events	MEDI0382	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	MEDI0382	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 25 (52.00%)	14 / 24 (58.33%)	
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	2	
Procedural nausea			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			

Tachycardia			
subjects affected / exposed	1 / 25 (4.00%)	2 / 24 (8.33%)	
occurrences (all)	3	2	
Palpitations			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	
occurrences (all)	3	0	
Tachycardia paroxysmal			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 25 (20.00%)	1 / 24 (4.17%)	
occurrences (all)	5	1	
Dizziness			
subjects affected / exposed	2 / 25 (8.00%)	0 / 24 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Tinnitus			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	3 / 25 (12.00%)	0 / 24 (0.00%)	
occurrences (all)	5	0	
Constipation			
subjects affected / exposed	3 / 25 (12.00%)	0 / 24 (0.00%)	
occurrences (all)	3	0	
Diarrhoea			

subjects affected / exposed	1 / 25 (4.00%)	2 / 24 (8.33%)	
occurrences (all)	1	2	
Nausea			
subjects affected / exposed	5 / 25 (20.00%)	2 / 24 (8.33%)	
occurrences (all)	7	4	
Vomiting			
subjects affected / exposed	5 / 25 (20.00%)	0 / 24 (0.00%)	
occurrences (all)	6	0	
Abdominal distension			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	
occurrences (all)	2	0	
Dyspepsia			
subjects affected / exposed	1 / 25 (4.00%)	1 / 24 (4.17%)	
occurrences (all)	1	1	
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Dysmenorrhoea			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Pruritus genital			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 25 (0.00%)	2 / 24 (8.33%)	
occurrences (all)	0	2	
Rash pruritic			

subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 25 (4.00%)	1 / 24 (4.17%)	
occurrences (all)	1	1	
Pain in extremity			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 25 (12.00%)	3 / 24 (12.50%)	
occurrences (all)	3	3	
Bronchitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Genital infection fungal			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Oral herpes			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Otitis media			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 25 (4.00%)	1 / 24 (4.17%)	
occurrences (all)	1	1	
Food craving			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	2	
Hypoglycaemia			

subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 24 (4.17%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 December 2017	Amended rationale for conducting the study, schedule of treatment period procedures, treatment regimen, and schedule of treatment period procedures. Updated selection of participants with type 2 diabetes mellitus with a glycated haemoglobin (Range of 7.0% to 10.0%). Added Inclusion criteria allowing participants on stable doses of metformin (maximum tolerated dose [MTD] > 1 g) with canagliflozin (maximum dose of 300 mg/day) or metformin (MTD > 1 g) with empagliflozin (maximum dose of 25 mg/day) for at least 3 months prior to screening to enter the study, after switching to dapagliflozin 10 mg at least 2 weeks prior to Day -2. Updated exclusion criterion to clarify that investigational sodium-glucose cotransporter-2 (SGLT2)-containing preparations (excluding canagliflozin and empagliflozin) within the last 30 days or 5 half-lives of the drug (whichever is longest) at the time of screening are exclusionary. Corrected schedule of run-in period procedures. Added Day -2 for training of participant on glucose and ketone monitoring. Added triglycerides test (screening only) to the serum chemistry and "Plasma glucose" was amended to "FPG". The starting point for AE and SAE collection was changed from "the time of admission to the clinic (Day -2)" to "from the time of informed consent".

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported